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BUSINESS, CONSUMER SERVICES AND HOUSING AGENCY
DEPARTMENT OF CONSUMER AFFAIRS
GOVERNOR EDMUND G. BROWN JR.

ENFORCEMENT AND COMPOUNDING COMMITTEE
MEETING MATERIALS
SEPTEMBER 16, 2014

I. PUBLIC COMMENT FOR ITEMS NOT ON THE AGENDA/AGENDA ITEMS FOR FUTURE MEETINGS

Note: The committee may not discuss or take action on any matter raised during this public comment section that is not included on this agenda, except to recommend whether to place the matter on the agenda of a future meeting. [Government Code Sections 11125, 11125.7(a)]

II. ENFORCEMENT MATTERS

a. FOR DISCUSSION: Evaluation of 16 CCR section 1744 Regarding Required Warning Labels on Prescription Container Labels

Attachment 1

Background

Existing law requires a pharmacist to inform a patient orally or in writing of the harmful effects of a drug: (1.) if the drug poses a substantial risk to the person consuming the drug, when taken in combination with alcohol, or if the drug may impair a person's ability to drive a motor vehicle, whichever is applicable, and (2.) the drug is determined by the Board of Pharmacy to be a drug or drug type for which the warning shall be given.

Assembly Bill 1136 (Levine), signed by the Governor on September 9, 2013, amends existing law to require a pharmacist on or after July 1, 2014, to include a written label on a prescription drug container indicating that the drug may impair a person's ability to operate a vehicle or vessel, if in the pharmacist's professional judgment, the drug may impair a person's ability to operate a vehicle or vessel. The required label may be printed on an auxiliary label that is affixed to the prescription container. The revised version of Business and Professions Code section 4074, which AB 1136 amended, is provided in **Attachment 1.**

Section 1744 of the board's regulations provides the specific classes of drugs which trigger a pharmacist's verbal or written notice to patients where a patient's ability to operate a vehicle (and now a vessel) may be impaired. This section has not been revised in a number of years, so recently the schools of pharmacy were asked to provide comments to the list of medications listed in this regulation.

A number of California's schools of pharmacy, through their deans, offered to assist, but not all schools have yet provided comments.

The proposed changes received have been aggregated onto the draft below. The changes themselves are provided in **Attachment 1.**

Attachment 1 also includes Business and Professions Code section 4074.

The committee needs to review these aggregate comments and determine how it wishes to proceed, whether to include any or all of the comments.

1744. Drug Warnings.

Pursuant to Business and Professions Code Section 4074, a pharmacist shall inform the patient or his or her representative of the harmful effects of certain drugs dispensed by prescription.

(a) The following classes of drugs may impair a person's ability to drive a motor vehicle or operate machinery when taken alone or in combination with alcohol:

(1) Muscle relaxants.

~~(2) Analgesics with central nervous system depressant effects.~~

(3) Antipsychotic drugs with central nervous system depressant effects ~~including phenothiazines~~.(one commenter left the strike out in)

(4) Antidepressants with central nervous system depressant effects.

(5) Antihistamines, motion sickness agents, antipruritics, antinauseants, anticonvulsants and antihypertensive agents with central nervous system depressant effects.

(6) All Schedule II, III, IV and V central nervous system depressant ~~or narcotic controlled substances~~ opioids or sedative-hypnotic as set forth in Health and Safety Code at Section 11055 et seq. prescribed in doses which could have an adverse effect on a person's ability to operate a motor vehicle.

(7) Anticholinergic agents and other drugs which may impair vision.

(8)Ramelteon (Sedation)

(9) Minoxidil (Hypotension)

(10) Phosphodiesterase V inhibitors (hearing and visual impairment)

(11) Bromocriptine (dizziness and fatigue exacerbates alcohol)

(b) The following are examples of drugs which may have harmful effects when taken in combination with alcohol. These may or may not affect a person's ability to operate a motor vehicle.

(1) Disulfiram and other drugs (e.g. ~~chlorpropamide~~, sulfonylureas, cephalosporins, trimethoprim, isoniazid, isotretinoin, griseofulvin, ketoconazole, metronidazole) which may cause a disulfiram-like reaction.

(2) Mono amine oxidase inhibitors.

(3) Nitrates.

(4) Cycloserine

(5) Verapamil (enhanced alcohol intoxication)

(6) Insulin (hypoglycemia) antidiabetic agents including insulin and sulfonylureas (due to risk of hypoglycemia)

(7) Niacin (increased risk of flushing and pruritis)

(8) Erythromycin (may increase absorption of alcohol

Or/and

(b)(2) Monoamine oxidase inhibitors (due to the risk of hypertensive crisis if the alcohol contains significant amounts of tyramine (some beer, red wine)

(b)(3)Nitrates due to the risk of additive cardiovascular effects.

Or/And

(c) Cortiscosteroids (BEERS list to avoid in the elderly)

(d) Dipydridamole (BEERS list to avoid in the elderly)

One commenter stated;

I recommend since specific labeling is required on containers by AB 1136, pharmacy software programs need a list of specific drugs to link to the warnings so they can be indexed to the drug by the software.

However another stated the current list primarily contains drug classes rather than individual drugs. That approach should be maintained since listing individual drugs will quickly become outdated as new drugs are marketed, and again the pharmacist

can exercise judgment regarding which individual drugs within a class are of concern.

b. FOR DISCUSSION AND POSSIBLE ACTION: <u>Remaining Need for Health and Safety Code Section 11164.5(a), Approval to Receive Electronic Prescriptions for Controlled Substance Prescriptions</u>

Attachment 2

<u>Background</u>
Health and Safety Code section 11164.5(a) requires the approval of the Board of Pharmacy and the CA Department of Justice before a hospital or pharmacy may receive electronic data transmission prescriptions or computer entry prescriptions or orders. This provision was enacted before the Drug Enforcement Administration promulgated their e-prescribing requirements several years ago.

Kaiser Permanente recently requested the board's position on whether this provision is operative and how is the board compiling with it.

Board staff do not believe that there is any need to retain this provision since the DEA has promulgated the required regulations to permit e-prescribing, and the staff recommend amending subdivision (a) out of 11164.5. There will likely need to be additional conforming changes to 11164.5 if subdivision (a) is removed. This should be part of the committee's discussion.

Sections 11164.5(a) and section 11164 which is reference by 11164.5 is provided in **Attachment 2,** as is the inquiry from Kaiser Permanente.

c. FOR DISCUSSION AND POSSIBLE ACTION: <u>Proposed Regulation for Pharmacies Aimed at Reducing Losses of Controlled Substances</u>

Attachment 3

At the March 2014 Enforcement and Compounding Committee, Chairperson Gutierrez led a discussion of losses of controlled substances reported to the board as required by California Pharmacy law. A pharmacy or a wholesaler must report any loss of controlled substances to the board within 14 days.

The board's staff has compiled some statistics regarding drug losses reported to the board over the last few years. The following tables display the losses of controlled substances reported to the board.

California State Board of Pharmacy Data Captured from Controlled Substance Drug Loss Reports

Year	2009	2010	2011	2012	2013	2014 (6 mo.)
Number of Reports	614	749	536	639	1224	678
Loss Type		**Total Count Reported**				
Armed Robbery			70,786	35,773	106,787	80,464
Customer Theft			9,550	4,598	5,684	13,175
Employee Pilferage			252,225	452,877	372,926	125,305
Lost in Transit			13,239	412,168	*1,657,875	22,310
Night Break In			505,016	80,971	689,925	154,156
Other			121,635	532,441	518,432	94,267
Totals			972,450	1,518,828	3,351,628	489,677

* In transit losses

DEA 106 Reports by License Category

Category	2011	2012	2013	2014
Pharmacy	376	460	943	551
Hospital	115	104	230	97
Wholesaler	33	35	58	35
Out of State Distributor	1	6	8	4
Correctional Facility	10	5	2	5
Clinic	1	2	0	0
Non Resident Pharmacy	0	1	0	0
Drug Room	0	0	1	0
Other	0	0	2	1
Total	536	613	1244	693

2013 Losses

	No. of Reports	Dosage Units Lost
Chain Store:	652	564,061
Community:	291	533,045
Hospital:	230	28,073

2014 Losses (6 months only)

Chain Store	443	226,866
Community	108	289,751
Hospital	97	990

In 2013, 3.06 million dosage units of controlled substances were reported to the board as lost. This includes 1.7 million units that were from a major manufacturer who had a truck stolen.

At the last meeting, it was noted that these numbers are only estimates provided by the entity when they first realize there has been a loss. As such, the reported numbers are most likely significantly less than actual losses.

The committee expressed concern about the significant losses and the need for more stringent inventory controls in pharmacies to identify losses resulting from employee pilferage. Comments from the committee included developing steps for inventory controls, which could be done either by regulation, statute or policy and perhaps reconciling the top ten drugs for the pharmacy.

At the April 2014 Board Meeting when this topic was discussed, the board asked the committee to draft regulation language to require monthly counts of a pharmacy's fastest controlled substances as a form of inventory control.

Staff's Proposed Language: Add as section 1715.65 to 16 California Code of Regulations:

1715.65 Monthly Inventory Counts of Fastest Moving Controlled Substances

(a) Every June 30th, each pharmacy and clinic licensed by the board shall identify its top 10 controlled substances dispensed by the licensee as measured in dosage units in the prior 12 months (July 1 – June 30).

(b) Effective July 1 and each month thereafter until the next June 30 (for a total of 12 months), the pharmacy or clinic shall count and reconcile the inventory of the top 10 controlled substances identified pursuant to subdivision (a). This reconciliation shall include for each of the controlled substances:

(1) The inventory recorded on the first of the preceding month

(2) The additions to inventory made in the preceding month (e.g., purchases, transfers in, will-call items that were never handed out that were counted as dispositions the prior month)
(3) The dispositions (e.g., dispensing, saleable returns to a wholesaler, drugs provided to a reverse distributor for destruction) from inventory made in the preceding month
(4) The drugs in quarantine waiting for the reverse distributor,
(5) The final inventory count on the first of the month
(6) The pharmacy shall attempt to reconcile overages or shortages. Shortages must be reported to the board.
(7) The name of the individual conducting the inventory and date the inventory required by this subdivision was performed

(c) Losses of controlled substances identified from the monthly audit shall be reported to the board as required by section 1716.5 and Business and Professions Code section 4104.
(d) The pharmacist-in-charge or consultant pharmacist for the clinic shall sign each monthly inventory performed under this section indicating he or she has reviewed the inventory taken.
(e) The pharmacist-in-charge or consultant pharmacist shall perform a quality assurance review of the monthly and annual inventories to establish secure methods to prevent losses of all dangerous drugs.

Recent articles on drug diversion from pharmacies are provided in **Attachment 3.**

d. FOR DISCUSSION: <u>Use of Automated Technology in Hospitals and Skilled Nursing Facilities and the Tools for identification of Medication Diversion from These Units</u>

Chairperson Gutierrez is considering a future meeting agenda item where the committee can learn about drug storage security features to deter diversion that are built into automated dispensing and storage devices used in hospitals and skilled nursing facilities. Time will be devoted at this meeting for a discussion of this topic, but a more in-depth will be scheduled for a future meeting where the committee will be able to view some of the anti-diversion technology or features in use in California.

e. FOR DISCUSSION: <u>The Drug Enforcement Administration's Regulations for the Take Back of Prescription Medication</u>

Attachment 4

On Tuesday, September 9, the DEA released its regulations on the take back of drugs from the public – specifically the take back of controlled substances.

The Final Rule authorizes certain DEA registrants (manufacturers, distributors, reverse

distributors, narcotic treatment programs, retail pharmacies, and hospitals/clinics with an on-site pharmacy) to modify their registration with the DEA to become authorized collectors. All collectors may operate a collection receptacle at their registered location, and collectors with an on-site means of destruction may operate a mail-back program. Retail pharmacies and hospitals/clinics with an on-site pharmacy may operate collection receptacles at long-term care facilities.

Attachment 4 contains the DEA's requirements for drug take back (starting approximately on page 150) along with their comments to written comments received in response to the prior proposed regulation.

The committee will have the opportunity to discuss the DEA's requirements and options for future action, if any, by the board in this area. **Attachment 4** also contains a *NY Times* article about the regulations.

f. FOR DISCUSSION: <u>Rescheduling of Hydrocodone to Schedule II</u>

Attachment 5

<u>Background</u>

Hydrocodone combination products are pharmaceuticals containing specified doses of hydrocodone in combination with other drugs in specified amounts. These products are approved for the marketing for the treatment of pain and for cough suppression.

The Drug Enforcement Administration (DEA) has secured the "up scheduling" of hydrocodone combination products from Schedule III to Schedule II of the federal Controlled Substances Act. At the April 2014 board meeting, the board directed that the board submit a letter of support to the DEA, along with a request for a transition period to fully implement this change. .

Attachment 5 includes a copy of the board's letter of support and the article from the Federal Register / Vol. 79, No. 39 / Thursday, February 27, 2014 / Final Rule

Below is a copy of a subscriber alert we will release after our discussion at this meeting.

> The DEA has announced that it is rescheduling all hydrocodone combination products (HCPs) from federal Schedule III to federal Schedule II effective October 6.
>
> This change will impact how hydrocodone combination products are prescribed and dispensed in California. Federal requirements for prescribing and dispensing Schedule II controlled substances will apply to all hydrocodone combination products. This means, among other thing, a very limited ability to orally prescribe HCPs (see below) and ability to authorize refills.

This “up scheduling” is a major change for California. According to CURES, over 1 billion dosage units of HCPs were dispensed last fiscal year in California.

This guidance document provides information on some of the questions that will likely arise regarding the transition of hydrocodone combination products to federal Schedule II.

From the federal announcement:
On Friday, August 22, 2014, the DEA published in the Federal Register the final rule to transfer HCPs from federal Schedule III to federal Schedule II. HCPs have been controlled in schedule III since enactment of the Controlled Substances Act (CSA) in 1971. HCPs are the most frequently prescribed opioid in the United States: nearly 137 million prescriptions for HCPs were dispensed in 2013.

- Effective October 6, 2014, HCPs will be controlled as Schedule II substances under the Controlled Substances Act (CSA).
- DEA is also permitting legitimate HCP prescriptions issued before October 6, 2014 to be refilled until April 8, 2015, if the prescription authorizes refills.
- The Notice of Proposed Rulemaking (NPRM), Final Rule, and its supporting documents (i.e., medical and scientific evaluations, and economic impact analysis) may be viewed online at www.regulations.gov<http://www.regulations.gov>, Docket No. DEA-389.
- Alternatively, the documents can be obtained on the DEA website at www.deadiversion.usdoj.gov<http://www.deadiversion.usdoj.gov>.

Questions and Answers;

1. Starting October 6, 2014, all HCPs will be reclassified at the federal level as Schedule II controlled substances, does this mean California law has also reclassified all hydrocodone combination products as Schedule II controlled substances?

A: Technically, no; there has been no equivalent change to California law, or to the controlled substance schedules in California. But for many intents and purposes, the practical effect will be the same: that all prescribers and practitioners in California will be required to treat HCPs as Schedule II controlled substances.

2. Prescriptions written for HCPs **before** October 6, 2014 that are presented to the pharmacy for dispensing on October 6, 2014: are these dispensed as a Schedule II or Schedule III controlled substance?

A: On and after October 6, 2014, under federal law, all HCPs must be prescribed according to federal Schedule II requirements. This means no HCP prescription issued on or after this date may authorize any refills. Also, for example, as of October 6, 2014, oral, telephone or fax-transmitted prescriptions for HCPs are no longer possible. The DEA has stated, however, that it will allow refills on HCPs

written and initially filled before October 6 (under Schedule III requirements and limitations), to be dispensed up to six months from October 6, 2014 (until April 8, 2015). This extends the Schedule III treatment of prescriptions for HCPs written and initially dispensed prior to October 6, 2014 to the maximum allowable period for Schedule III refills.

3. Prescriptions written for hydrocodone combination products dispensed before October 6, 2014 as a Schedule III, but with refills remaining, can the remaining refills be dispensed?

A: According to guidance from the DEA, yes.

4. If a patient presents a prescription for a hydrocodone combination product on or after October 6, 2014 that is written on October 6, 2014 with refills, can the refills be honored?

A: No, the DEA stated the prescription needed to be presented before October 6 to use the refills.

5. When transmitting to CURES, should I change my computer software to report all HCPs dispensed as Schedule II controlled substances or keep HCPs as Schedule III controlled substances until California law (also) reschedules all HCPs to a Schedule II controlled substance?

A: Health and Safety Code section 11165, subdivision (d) references and incorporates the federal controlled substance schedules for the purpose of defining the reporting requirements under CURES. As a result, dispensers in California are responsible for reporting to CURES controlled substances dispensed according to the federal schedules. Thus, a software change will be required.

g. FOR DISCUSSION: Rescheduling of Tramadol to Schedule IV

Attachment 6

Background

Tramadol is a centrally acting opioid analgesic that has been on the market since the mid-1990s. Subsequently, the FDA approved for marketing generic, combination, and extended release tramadol products as dangerous drugs but not as controlled substances. However, over the years, the board and other entities have identified instances where tramadol was misused in part because as a dangerous drug, it was more readily available than a controlled substance would be.

In mid- August, the DEA secured the scheduling of tramadol into Schedule IV of the controlled substances schedule.

Attachment 6 includes a copy the board's subscriber alert and the article from the Federal Register / Vol. 79, No. 127 / Wednesday, July 2, 2014 / Final Rule

h. FOR INFORMATION: <u>Update on the Alternative Process for Pharmacists to Become Registered to Access CURES</u>

Last year, SB 809 (DeSaulnier) was enacted to enhance and rev up the CURES prescription drug monitoring program.

Part of the discussion associated with the bill's progression through the Legislature was the growing concern about the need for pharmacists and prescribers to access CURES before dispensing or prescribing controlled drugs. To access CURES to see the history of controlled drugs dispensed to a single patient over the last year, a prescriber or pharmacist must have preapproval by the CA Department of Justice. However, an abysmally low number of prescribers and dispensers have applied for and been granted access to CURES.

Provisions enacted in SB 809 require all prescribers and pharmacists to be registered with the DOJ to access CURES by January 1, 2016. However, the new computer system and funding for staffing for the DOJ to operate the system will not be available until perhaps July 2015. Meanwhile, the Department of Consumer Affairs' agencies are transferring to a new computer system of their own that will create new systems for license issuance and renewal. Only the first one-third of DCA's boards have converted to the new BreEZe system.

As such, it looks likely that few if any DCA boards will be able to comply with the January 1, 2016 CURES registration deadline for licensees.

The current process for CURES registration is frustrating and laborious. Individuals must start an email contact with the DOJ, then fill out an application they download, and then copy various documents (driver's license, professional license) and have the whole package notarized and then mailed to the DOJ. The DOJ is currently taking about one month to process this material.

Board staff has implemented a process whereby the board can authenticate the identity of a pharmacist and aid the DOJ in getting this individual registered. The board began accepting applications in July 2014 and has to date received approximately 150 applications.

Currently there are 9,268 pharmacists registered with CURES, about 25 percent of all pharmacists.

i. FOR DISCUSSION: Presentation by Rita Shane, PharmD, FASHP, FCSHP on Medication Reconciliation in Health Care Facilities

Attachment 7

Medication reconciliation is intended to ensure the accuracy of a medication list of drugs taken by a patient. It involves the review, update, and reconciliation of medications at each encounter.

Rita Shane, PharmD, has advised that given the errors in medication lists that occur when patients are admitted to the hospital, evidence supports that pharmacy staff need to ensure these lists are updated and corrected in order to prevent hospital medication errors, reduce readmissions and prevent medication errors when the patients go home.

A physician colleague of Dr. Shane recently completed a randomized controlled trial showing there were seven errors per medication list for patients admitted to the hospital. The same trial also showed the impact of pharmacy staff on reducing these errors.

At this meeting
A PowerPoint presentation will be provided by Dr. Shane regarding medication reconciliation in health care facilities.

A related article on this topic is provided in **Attachment 7.**

III. COMPOUNDING MATTERS

a. FOR DISCUSSION: FDA's Expectations for Human Drug Compounders

Attachment 8

The Food and Drug Administration (FDA) is proposing to amend its regulations to revise the list of drug products that may not be compounded under the exemptions provided by the Federal Food, Drug, and Cosmetic Act (FD&C Act) because the drug products have been withdrawn or removed from the market after the drug products or components of such drug products were found to be unsafe or not effective. Specifically, the proposed rule would add 25 drug products and modify the description of one drug product on this list to add an exception. These revisions are necessary because new information has come to the FDA's attention since March 8, 1999, when FDA published the original list as a final rule. FDA is also withdrawing the previous proposed rule regarding additions to this list (see the Federal Register of January 4, 2000).

Attachment 8 includes a copy of the FDA Press Release and the article from the Federal Register / Vol. 79, No. 127 / Wednesday, July 2, 2014 / Proposed Rule

This information is being provided to the committee for information.

b. FOR DISCUSSION: <u>Request by Kaiser Permanente for Clarification Regarding End-Product Testing as Required by 16 CCR section 1751.7</u>

Attachment 9

<u>Background</u>
Kaiser Permanente has requested an opportunity to discuss enforcement of Title 16 California Code of Regulations section 1751.7. This section specifies the requirements of a Quality Assurance Program for sterile compounding pharmacies. Specifically, the law provides that:

1751.7. Sterile Injectable Compounding Quality Assurance and Process Validation.

(a) Any pharmacy engaged in compounding sterile injectable drug products shall maintain, as part of its written policies and procedures, a written quality assurance plan including, in addition to the elements required by section 1735.8, a documented, ongoing quality assurance program that monitors personnel performance, equipment, and facilities. The end product shall be examined on a periodic sampling basis as determined by the pharmacist-in-charge to assure that it meets required specifications. The Quality Assurance Program shall include at least the following:
(1) Cleaning and sanitization of the parenteral medication preparation area.
(2) The storage of compounded sterile injectable products in the pharmacy and periodic documentation of refrigerator temperature.
(3) Actions to be taken in the event of a drug recall.
(4) Written justification of the chosen expiration dates for compounded sterile injectable products.

(b) Each individual involved in the preparation of sterile injectable products must first successfully complete a validation process on technique before being allowed to prepare sterile injectable products. The validation process shall be carried out in the same manner as normal production, except that an appropriate microbiological growth medium is used in place of the actual product used during sterile preparation. The validation process shall be representative of all types of manipulations, products and batch sizes the individual is expected to prepare. The same personnel, procedures, equipment, and materials must be involved. Completed medium samples must be incubated. If microbial growth is detected, then the sterile preparation process must be evaluated, corrective action taken, and the validation process repeated. Personnel competency must be revalidated at least every twelve months, whenever the quality assurance program yields an unacceptable result, when the compounding process changes, equipment used in the compounding of sterile injectable drug products is repaired or replaced, the facility is modified in a manner that affects airflow or traffic patterns, or whenever improper aseptic techniques are observed. Revalidation must be documented.

(c) Batch-produced sterile injectable drug products compounded from one or more non-sterile ingredients shall be subject to documented end product testing for sterility and pyrogens and shall be quarantined until the end product testing confirms sterility and acceptable levels of pyrogens.

(d) Batch-produced sterile to sterile transfers shall be subject to periodic testing through process validation for sterility as determined by the pharmacist-in-charge and described in the written policies and procedures.

Kaiser Permanente indicates that various inspectors are interpreting section 1751.7(a) differently. They have asked for the board to clarify. A copy of the request is provided in **Attachment 9.**

c. FOR INFORMATION: <u>Results of the Board's Implementation and Inspections of California Sterile Compounding Facilities</u>

Attachment 10

<u>At this meeting</u>
Supervising Inspector, Robert Ratcliff, PharmD, will provide an update regarding the board's implementation and inspections of sterile compounding pharmacies.

Attachment 10 includes the data found as a result of sterile compounding inspections in California.

d. FOR INFORMATION: <u>Data on Violations Found During Out of State Compounding Inspections</u>

<u>At this meeting</u>
Supervising Inspector, Robert Ratcliff, PharmD, will provide an update regarding the board's inspections of out of state sterile compounding pharmacies.

Attachment 10 also includes the data found as a result of sterile compounding inspections of out of state sterile compounding pharmacies.

e. FOR INFORMATION: <u>Recalls of Compounded Drugs Throughout the United States</u>

Attachment 11

Between November 8, 2013 and September 11, 2014, the board posted seven subscriber alerts related to compounding drug recalls.

Attachment 11 includes copies of the subscriber alerts.

IV. MEETING DATES FOR 2014

Only one future meeting date for the remainder of 2014 has been scheduled:

- December 17, 2014

V. FUTURE MEETING DATES

The committee will select meeting dates for 2015. Once established, these dates will be posted on the board's website under the Board and Committee Meetings tab (under About the Board from the board's website).

Attachment 1

B&PC 4074

BUSINESS AND PROFESSIONS CODE - BPC

DIVISION 2. HEALING ARTS [500 - 4999.129] *(Division 2 enacted by Stats. 1937, Ch. 399.)*

CHAPTER 9. Pharmacy [4000 - 4426] *(Chapter 9 repealed and added by Stats. 1996, Ch. 890, Sec. 3.)*

ARTICLE 4. Requirements for Prescriptions [4070 - 4078] *(Article 4 added by Stats. 1996, Ch. 890, Sec. 3.)*

4074. (a) A pharmacist shall inform a patient orally or in writing of the harmful effects of a drug dispensed by prescription if both of the following apply:

(1) The drug poses substantial risk to the person consuming the drug when taken in combination with alcohol or the drug may impair a person's ability to drive a motor vehicle, whichever is applicable.

(2) The drug is determined by the board pursuant to subdivision (c) to be a drug or drug type for which this warning shall be given.

(b) In addition to the requirement described in subdivision (a), on and after July 1, 2014, if a pharmacist exercising his or her professional judgment determines that a drug may impair a person's ability to operate a vehicle or vessel, the pharmacist shall include a written label on the drug container indicating that the drug may impair a person's ability to operate a vehicle or vessel. The label required by this subdivision may be printed on an auxiliary label that is affixed to the prescription container.

(c) The board may by regulation require additional information or labeling.

(d) This section shall not apply to a drug furnished to a patient in conjunction with treatment or emergency services provided in a health facility or, except as provided in subdivision (e), to a drug furnished to a patient pursuant to subdivision (a) of Section 4056.

(e) A health facility shall establish and implement a written policy to ensure that each patient shall receive information regarding each drug given at the time of discharge and each drug given pursuant to subdivision (a) of Section 4056. This information shall include the use and storage of each drug, the precautions and relevant warnings, and the importance of compliance with directions. This information shall be given by a pharmacist or registered nurse, unless already provided by a patient's prescriber, and the written policy shall be developed in collaboration with a physician, a pharmacist, and a registered nurse. The written policy shall be approved by the medical staff. Nothing in this subdivision or any other law shall be construed to require that only a pharmacist provide this consultation.

(Amended by Stats. 2013, Ch. 304, Sec. 1. Effective January 1, 2014.)

16 CCR 1744

1744. Drug Warnings.

Pursuant to Business and Professions Code Section 4074, a pharmacist shall inform the patient or his or her representative of the harmful effects of certain drugs dispensed by prescription.

(a) The following classes of drugs may impair a person's ability to drive a motor vehicle or operate machinery when taken alone or in combination with alcohol:

(1) Muscle relaxants.

(2) ~~Analgesics with central nervous system depressant effects.~~

(3) Antipsychotic drugs including phenothiazines.

(4) ~~Antidepressants.~~

(5) Antidepressants, a~~A~~ntihistamines, motion sickness agents, antipruritics, antinauseants, anticonvulsants and antihypertensive agents with central nervous system depressant effects.

(6) All Schedule II, III, IV and V central nervous system depressant or ~~narcotic~~ opioid ~~controlled substances~~ as set forth in Health and Safety Code at Section 11055 et seq. prescribed in doses which could have an adverse effect on a person's ability to operate a motor vehicle.

(7) Anticholinergic agents and other drugs which may impair vision.

(b) The following are examples of drugs which may have harmful effects when taken in combination with alcohol. These may or may not affect a person's ability to operate a motor vehicle.

(1) Disulfiram and other drugs (e.g. chlorpropamide, metronidazole) which may cause a disulfiram-like reaction.

(2) ~~Mono-amine oxidase inhibitors.~~

(3) Nitrates.

Comment [JJG1]: This is essentially referring to opioids which is covered under (6)

Comment [JJG2]: Most commonly used antidepressants like SSRI's have a low risk for sedation and do not warrant this warning. They should be under this category instead.

Comment [JJG3]: Opioid is the correct term. Narcotic is an outdate law enforcement jargon that carries negative connotations and is used nonspecifically.

Comment [JJG4]: Schedules II-V are controls so no need to restate

Comment [JJG5]: The tyramine content of alcoholic beverages has been overestimated. Many if not most can be safely consumed with MAOI's. Shulman KI, Walker SE, MacKenzie S et al. Dietary restriction, tyramine, and the use of monoamine oxidase inhibitors. J Clin Psychopharmacol 1989; 9:397-402.

COMMENTS

I am pleased to see that you are interested in ensuring the list of drugs is accurate – certainly what is listed below under **1744. Drug Warnings** does need to be updated and clarified.
As an example, phenothiazines are rarely used today in favor of newer atypical antipsychotic drugs, some of which should be included as drugs of concern with alcohol.
Or, just listing antidepressants is not accurate – some antidepressants are sedating and a concern with alcohol, but others are in fact activating and should not require an alcohol warning.
It would be much more accurate to say "antidepressants with central nervous system depressant effects" like is done with antihistamines.
I would ask how you prefer to receive specific input on this issue. I can expand on what I have indicated above, or participate on a phone call with others, ... Please let me know how I might help.

GENERAL COMMENTS

The current list allows some judgment by the pharmacist to determine which drugs within a drug class have sufficient potential for concern with driving or alcohol. That flexibility should be maintained.

The current list primarily contains drug classes rather than individual drugs. That approach should be maintained since listing individual drugs will quickly become outdated as new drugs are marketed, and again the pharmacist can exercise judgment regarding which individual drugs within a class are of concern. If desired, there could be a few examples cited of individual drugs within a class that are of particular concern as indicated below (e.g., olanzapine, quetiapine) (e.g., mirtazapine, paroxetine, fluvoxamine).

SPECIFIC COMMENTS

1744 (a) items 1,2,5,6,7 are valid as written

(3) Antipsychotic drugs including phenothiazines – phenothiazines are now rarely used today while there are several atypical antipsychotic drugs with prominent sedative side effects (e.g., olanzapine, quetiapine) that would be of concern. Recommend delete phenothiazines, and state as:
(3) Antipsychotic drugs with central nervous system depressant effects.

(4) Antidepressants – there are <u>some</u> antidepressants with sufficient sedative effect to be of concern with driving and/or alcohol (e.g., mirtazapine, paroxetine, fluvoxamine), but there are other antidepressants with prominent activating effects that are not of concern (e.g., fluoxetine, bupropion). Recommend modify statement to read:
(4) Antidepressants with central nervous system depressant effects.

(6) All Schedule II, III, IV and V depressant or narcotic controlled substances:
This statement as written includes all the sedative hypnotic drugs (benzodiazepines, zolpidem & other similar) though if we want to offer a more clear statement, and emphasize these drugs as probably being the greatest concern on the list, then maybe the term sedative-hypnotic should be added into this statement.

Section (b) is an odd assortment of drug concerns with alcohol, actually 3 different reasons. Since there is a brief explanation given for the disulfiram (disulfiram-like reaction), it would be better to also give a brief explanation for the other two items. Recommend:

(b) (2) Mono amine oxidase inhibitors due to the risk of hypertensive crisis if the alcohol contains significant amounts of tyramine (some beer, red wine).
(b) (3) Nitrates due to the risk of additive cardiovascular effects
The alternative position on this is that pharmacists should know the reason why these 3 drug classes are of concern, so they need no further explanation.

From a practical standpoint, since Assembly Bill 1136 now mandates a label in addition to the verbal counseling, I can see the need to provide specific lists of individual drugs for Section 1744 so pharmacy software programs can automatically generate these labels. If so, more time will be needed for generating such a specific list that can be agreed upon by your consulting group of pharmacists. This issue will likely be a key discussion point for your September 16 meeting.

Comment 2

After reviewing a few sources, a few additions that the Board may want to consider are:

1. Anti-diabetic agents, including, but not limited to sulfonylureas and insulin due to the risk of hypoglycemia
2. Cortiscosteroids, on the BEERS list of medications to avoid in the elderly
3. Dipyridamole, on the BEERS list of medications to avoid in the elderly.
4. Cephalosporins, ketoconazole, may cause a disulfram reaction
5. Erythromycin, may increase the absorption of alcohol.

Please let me know if you have additional questions or need any clarifications

Comment 3

Drug/ Drug class that can impair driving	Mechanism of how they cause impairment
Muscle relaxants	Sedation
Analgesic with central nervous system depressant effects	Sedation
Antipsychotic drugs including phenothiazines	Sedation
Antidepressants	Sedation
Antihistamines, motion sickness agents, antipruritics, antinauseants, anticonvulsants and antihypertensive agents with central nervous system depressant effects	Sedation
All schedule II, III, IV and V depressant or narcotic controlled substances	Sedation
Ramelteon	Sedation
Anticholinergic agents and other drugs which may impair vision	Sedation Affects visual acuity
Minoxidil	Hypotension
Phosphodiesterase V inhibitors	Potential for hearing and visual impairment
Bromocriptine	Dizziness and fatigue (exacerbated by ETOH)
Drug-interactions with Alcohol	
Disulfiram and drugs (e.g., sulfonylureas, metronidazole, trimethoprim, isoniazid, isotretinoin, griseofulvin, ketoconazole) which cause a disulfiram-like reaction	Disulfiram-like reactions
Mono amine oxidase inhibitors	Sedation
Nitrates	Sedation via hypotension, blurred vision, possible disulfiram-like reaction
Cycloserine	Increased risk of seizures
Verapamil	Enhanced ETOH intoxication
Insulin	Hypoglycemia
Niacin	Increased risk of flushing and pruritis

Attachment 2

HEALTH AND SAFETY CODE - HSC

DIVISION 10. UNIFORM CONTROLLED SUBSTANCES ACT [11000 - 11651] *(Division 10 repealed and added by Stats. 1972, Ch. 1407.)*

CHAPTER 4. Prescriptions [11150 - 11209] *(Chapter 4 added by Stats. 1972, Ch. 1407.)*

ARTICLE 1. Requirements of Prescriptions [11150 - 11180] *(Article 1 added by Stats. 1972, Ch. 1407.)*

11164. Except as provided in Section 11167, no person shall prescribe a controlled substance, nor shall any person fill, compound, or dispense a prescription for a controlled substance, unless it complies with the requirements of this section.

(a) Each prescription for a controlled substance classified in Schedule II, III, IV, or V, except as authorized by subdivision (b), shall be made on a controlled substance prescription form as specified in Section 11162.1 and shall meet the following requirements:

(1) The prescription shall be signed and dated by the prescriber in ink and shall contain the prescriber's address and telephone number; the name of the ultimate user or research subject, or contact information as determined by the Secretary of the United States Department of Health and Human Services; refill information, such as the number of refills ordered and whether the prescription is a first-time request or a refill; and the name, quantity, strength, and directions for use of the controlled substance prescribed.

(2) The prescription shall also contain the address of the person for whom the controlled substance is prescribed. If the prescriber does not specify this address on the prescription, the pharmacist filling the prescription or an employee acting under the direction of the pharmacist shall write or type the address on the prescription or maintain this information in a readily retrievable form in the pharmacy.

(b) (1) Notwithstanding paragraph (1) of subdivision (a) of Section 11162.1, any controlled substance classified in Schedule III, IV, or V may be dispensed upon an oral or electronically transmitted prescription, which shall be produced in hard copy form and signed and dated by the pharmacist filling the prescription or by any other person expressly authorized by provisions of the Business and Professions Code. Any person who transmits, maintains, or receives any electronically transmitted prescription shall ensure the security, integrity, authority, and confidentiality of the prescription.

(2) The date of issue of the prescription and all the information required for a written prescription by subdivision (a) shall be included in the written record of the prescription; the pharmacist need not include the address, telephone number, license classification, or federal registry number of the prescriber or the address of the patient on the hard copy, if that information is readily retrievable in the pharmacy.

(3) Pursuant to an authorization of the prescriber, any agent of the prescriber on behalf of the prescriber may orally or electronically transmit a prescription for a controlled substance classified in Schedule III, IV, or V, if in these cases the written record of the prescription required by this subdivision specifies the name of the agent of the prescriber transmitting the prescription.

(c) The use of commonly used abbreviations shall not invalidate an otherwise valid prescription.

(d) Notwithstanding any provision of subdivisions (a) and (b), prescriptions for a controlled substance classified in Schedule V may be for more than one person in the same family with the same medical need.

(e) This section shall become operative on January 1, 2005.

(Amended by Stats. 2006, Ch. 286, Sec. 2. Effective January 1, 2007.)

HEALTH AND SAFETY CODE - HSC

DIVISION 10. UNIFORM CONTROLLED SUBSTANCES ACT [11000 - 11651] *(Division 10 repealed and added by Stats. 1972, Ch. 1407.)*

CHAPTER 4. Prescriptions [11150 - 11209] *(Chapter 4 added by Stats. 1972, Ch. 1407.)*

ARTICLE 1. Requirements of Prescriptions [11150 - 11180] *(Article 1 added by Stats. 1972, Ch. 1407.)*

11164.5. (a) Notwithstanding Section 11164, with the approval of the California State Board of Pharmacy and the Department of Justice, a pharmacy or hospital may receive electronic data transmission prescriptions or computer entry prescriptions or orders as specified in Section 4071.1 of the Business and Professions Code, for controlled substances in Schedule II, III, IV, or V if authorized by federal law and in accordance with regulations promulgated by the Drug Enforcement Administration. The California State Board of Pharmacy shall maintain a list of all requests and approvals granted pursuant to this subdivision.

(b) Notwithstanding Section 11164, if approved pursuant to subdivision (a), a pharmacy or hospital receiving an electronic transmission prescription or a computer entry prescription or order for a controlled substance classified in Schedule II, III, IV, or V shall not be required to reduce that prescription or order to writing or to hard copy form, if for three years from the last day of dispensing that prescription, the pharmacy or hospital is able, upon request of the board or the Department of Justice, to immediately produce a hard copy report that includes for each date of dispensing of a controlled substance in Schedules II, III, IV, and V pursuant to the prescription all of the information described in subparagraphs (A) to (E), inclusive, of paragraph (1) of subdivision (a) of Section 4040 of the Business and Professions Code and the name or identifier of the pharmacist who dispensed the controlled substance.

(c) Notwithstanding Section 11164, if only recorded and stored electronically, on magnetic media, or in any other computerized form, the pharmacy's or hospital's computer system shall not permit the received information or the controlled substance dispensing information required by this section to be changed, obliterated, destroyed, or disposed of, for the record maintenance period required by law, once the information has been received by the pharmacy or the hospital and once the controlled substance has been dispensed, respectively. Once the controlled substance has been dispensed, if the previously created record is determined to be incorrect, a correcting addition may be made only by or with the approval of a pharmacist. After a pharmacist enters the change or enters his or her approval of the change into the computer, the resulting record shall include the correcting addition and the date it was made to the record, the identity of the person or pharmacist making the correction, and the identity of the pharmacist approving the correction.

(d) Nothing in this section shall be construed to exempt any pharmacy or hospital dispensing Schedule II controlled substances pursuant to electronic transmission prescriptions from existing reporting requirements.

(Added by Stats. 2000, Ch. 293, Sec. 4. Effective January 1, 2001.)

KAISER PERMANENTE®

Kaiser Permanente Pharmacy Administration
12254 Bellflower Blvd
Downey, CA 90242

*****SENT VIA E-MAIL*****
Virginia.Herold@dca.ca.gov

June 5th, 2014

California State Board of Pharmacy
Attn: Virginia Herold, Executive Officer

1625 N. Market Blvd., N-219
Sacramento, CA 95834

RE: Request to add agenda item for upcoming Licensing or Enforcement & Compounding Subcommittee Meeting

TOPIC: Health and Safety Code (H&S) 11164.5(a) requirement to receive approval from the Board of Pharmacy and Department of Justice before a hospital or pharmacy may receive electronic data transmission prescriptions

We are writing to request that the above topic be added as an agenda item for discussion at either the next Licensing or Enforcement & Compounding Subcommittee meeting scheduled.

As the law currently reads, H&S 11164.5 requires that pharmacies obtain approval from the California Board of Pharmacy and the Department of Justice prior to a pharmacy being able to receive electronic prescriptions for controlled substance prescriptions

H&S 11164.5(a) also states that the "California State Board of Pharmacy shall maintain a list of all requests and approvals granted pursuant to this subdivision." It seems that approval can be implied as the Board inspectors have already inspected pharmacies without commenting on not having received approval from the Board or the Department of Justice. We have inquired on how pharmacies may take steps to receive such approval and were informed that there is no such approved list, as the Board's policy is to accept any pharmacy's system that meets the DEA requirements.

In the alternative to placing this on the agenda of one of the committee meetings, if a process has already been adopted for approval or if approval is not necessary, please consider this a request for approval or exemption and respond affirmatively so that we have documentation for future reference. Our system will comply with the DEA's regulatory compliance certification mandate for controlled substances prescribing.

Sincerely,

Kaiser Permanente Pharmacy Administration

Attachment 3

SPECIAL FEATURE

The opioid abuse and misuse epidemic: Implications for pharmacists in hospitals and health systems

Daniel J. Cobaugh, Carl Gainor, Cynthia L. Gaston, Tai C. Kwong, Barbarajean Magnani, Mary Lynn McPherson, Jacob T. Painter, and Edward P. Krenzelok

Purpose. The current epidemic of prescription opioid abuse and misuse in the United States is discussed, with an emphasis on the pharmacist's role in ensuring safe and effective opioid use.

Summary. U.S. sales of prescription opioids increased fourfold from 1999 to 2010, with an alarming rise in deaths and emergency department visits associated with the use of fentanyl, hydrocodone, oxycodone, and other opioid medications. Signs and symptoms of opioid toxicity may include altered mental status, hypoventilation, decreased bowel motility, central nervous system and respiratory depression, peripheral vasodilation, pulmonary edema, hypotension, bradycardia, and seizures. In patients receiving long-term opioid therapy for chronic pain, urine drug testing is an important tool for monitoring and assessment of therapy; knowledge of opioid metabolic pathways and assay limitations is essential for appropriate use and interpretation of screening and confirmatory tests. In recent years, there has been an increase in federal enforcement actions against pharmacies and prescription drug wholesalers involved in improper opioid distribution, as well as increased reliance on state-level prescription drug monitoring programs to track patterns of opioid use and improper sales. Pharmacies are urged to implement or promote appropriate guidelines on opioid therapy, including the use of pain management agreement plans; policies to ensure adequate oversight of opioid prescribing, dispensing, and waste disposal; and educational initiatives targeting patients as well as hospital and pharmacy staff.

Conclusion. Pharmacists in hospitals and health systems can play a key role in recognizing the various forms of opioid toxicity and in preventing inappropriate prescribing and diversion of opioids.

Am J Health-Syst Pharm. 2014; 71:1539-54

Misuse and abuse of prescription opioids in the United States constitute a public health crisis that has grown to epidemic proportions over the last decade. The Centers for Disease Control and Prevention (CDC) has identified prescription drug abuse and overdose as one of the top five health threats for 2014.[1] It is imperative that pharmacists across the health system have a complete understanding of this epidemic. This article reviews the role of opioids in pain management, the epidemiology of opioid misuse and abuse, the clinical toxicology of these medications, and the role of laboratory analyses in monitoring opioid therapy, as well as legal issues surrounding opioid distribution and therapy, the use of prescription drug monitoring programs to combat opioid abuse and misuse, and implications for medication-use policy in hospitals and health systems.

Opioid use in pain management

The term *opium* refers to a mixture of alkaloids from the poppy seed, and the term *opiates* refers to naturally occurring alkaloids (e.g., morphine, codeine). The term *opioid* refers to all compounds that bind to opioid receptors.[2] Opioids have been used for thousands of years for the treatment of moderate-to-severe acute and chronic pain. In 1806,

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Sertürner isolated morphine from opium; beginning in the 1850s, injectable morphine was used to treat both acute and chronic pain.

Opioids provide their pharmacologic effects by binding to opioid receptors located both within and outside of the central nervous system.[2] Depending on which receptors they bind to and their level of intrinsic activity, opioids are classified as full or partial agonists, mixed agonist–antagonists, or opioid antagonists. The primary opioid receptor is the μ receptor. The μ receptor is responsible for supraspinal analgesia, respiratory depression, euphoria, sedation, decreased gastrointestinal motility, pruritus, anorexia, sedation, and physical dependence. The κ receptor, another opioid receptor, is responsible for spinal analgesia, dyspnea, opioid dependence, sedation, respiratory depression, and dysphoria. The σ receptor is responsible for dysphoria, psychotomimetic effects, and stress-induced depression. The role of the δ-opioid receptor has not been well studied.[2]

Opioids are used routinely to treat both acute and chronic cancer pain and noncancer pain. Numerous clinical guidelines have been published over the past 20 years to guide practitioners in the appropriate use of opioids to treat moderate-to-severe pain.[3-7] The management of acute and chronic pain is generally best accomplished through a multimodal approach that includes nonpharmacologic interventions, as well as nonopioid analgesics (e.g., acetaminophen, nonsteroidal antiinflammatory drugs [NSAIDs]), opioids, and coanalgesics (e.g., anticonvulsants, antidepressants, skeletal muscle relaxants, topical or oral anesthetics).[6] Appendix A lists the American Pain Society recommendations for considerations when selecting analgesics to treat acute or chronic pain.

Opioid therapy for acute pain

One potential strategy to reduce postoperative pain is the use of preemptive analgesics. However, there is limited evidence that demonstrates major clinical benefits (e.g., consistent immediate postoperative pain relief, reduced need for supplemental analgesia) after the use of preemptive analgesics.[8-12] Despite these findings, it is clear that optimal postoperative pain management begins preoperatively, continues through the perioperative period, and is sustained through the postoperative period as indicated clinically. One useful strategy is the use of a multimodal approach.[13,14]

Opioids are used to treat acute pain when the pain cannot be managed with nonopioid therapy alone. For example, the acute pain after a dental procedure may be primarily controlled with the use of nonopioids such as an NSAID, possibly supplemented with an oral opioid as needed. Alternatively, a patient who has had major surgery will likely require parenteral opioid therapy for several days, potentially supplemented with nonopioid analgesics or coanalgesics. While morphine, hydromorphone, and fentanyl are the most frequently used parenteral opioids for acute pain, the selection of a specific opioid for a given patient must be individualized. It is imperative that the clinician obtain a pain medication history that captures previous opioid therapy and adverse reactions. For example, a patient may report that morphine causes significant itching whereas hydromorphone does not. Genetic polymorphisms may explain the interpatient variability often seen with opioid dosing. In 2013 the Food and Drug Administration (FDA) added a boxed warning to the drug label of codeine-containing products regarding overdose deaths experienced by children after tonsillectomy or adenoidectomy.[15,16] Children from certain ethnic groups are ultrarapid metabolizers of codeine, which can lead to higher-than-expected serum concentrations of morphine and a risk of death.

When opioids are part of the acute pain management regimen, they may be administered by the oral, parenteral, and neuraxial routes. Research dating back almost 50 years demonstrated that small i.v. doses of morphine administered on an as-needed basis for acute pain are superior to scheduled dosing.[17,18] The use of patient-controlled analgesia is a standard intervention used in contemporary pain management for the treatment of acute pain. Increasingly, neuraxial opioid administration is part of an effective multimodal acute pain management plan.[19]

When determining the dose of an opioid for acute pain, it is critically important for clinicians to take into account whether the patient is opioid naive or opioid tolerant. Opioid-tolerant patients are those who have been taking regularly scheduled prescribed opioids or have a history of substance abuse related to illicit use of prescription opioids, illicit drug use, or participation in an opioid maintenance program. To avoid underdosing the patient with acute pain and possibly precipitating opioid withdrawal, this opioid tolerance must be taken into consideration. One possible strategy is to continue a previously used opioid while treating the acute pain separately; another involves calculating a larger opioid dose to treat the acute pain that incorporates an equianalgesic dose of the previous opioid.[20,21]

Another important skill for practitioners is the ability to safely and accurately calculate equianalgesic opioid doses when converting a patient from one opioid to another or from one route of administration or dosage formulation to another.[22] A commonly seen error occurs when postoperative patients are switched from an effective dosage of parenteral hydromorphone (e.g., 1 mg i.v. every four hours) to a nonequivalent and ineffective oral opioid (e.g., oral oxycodone 5 mg every four hours). This could result in pain relief failure

as well as a loss of trust in the health care team by the patient and assumptions by providers that the patient is exhibiting drug-seeking behavior when the patient is actually demonstrating appropriate pain relief–seeking behavior.

Opioids to treat chronic pain

Chronic pain management strategies are often viewed differently by practitioners depending on whether it is chronic cancer pain or noncancer pain, although the same analgesics are used to treat both. Both nonpharmacologic and pharmacologic strategies are used to treat chronic cancer pain and noncancer pain in a multimodal strategy. The prevalence of pain in cancer patients and persistent pain in cancer survivors is high, and opioids are frequently part of the treatment strategy. Researchers who conducted a recent systematic review of observational studies on the effectiveness of opioid therapy for cancer pain assigned a strong recommendation to the use of these agents to treat cancer-related pain.[23]

The use of opioids in the management of acute pain and chronic cancer pain is more widely accepted than their use in treating chronic noncancer pain. There are many reasons to explain this finding. The available evidence that opioids conclusively reduce pain severity and increase function (e.g., activities of daily living) in patients with chronic noncancer pain is not convincing. A review by Trescot and colleagues[24] concluded that there was weak evidence of the long-term (i.e., six months or longer) effectiveness of morphine and transdermal fentanyl in reducing pain and improving function. This review found no evidence of effectiveness of other opioids. Long-term opioid therapy may be associated with tolerance, opioid-induced hyperalgesia, physical and psychological dependence, persistent adverse effects, a lower quality of life, higher rates of depression, and increased healthcare utilization.[25]

Role of the urine drug test

Published practice guidelines for opioid therapy for noncancer pain from governmental agencies and professional organizations (Appendix B) recommend using urine drug testing as part of the initial patient evaluation, the treatment plan agreement, and monitoring and assessment of therapy.[26,27] The urine drug test supplements tools such as patient self-reporting and behavioral monitoring, identifies noncompliance with the prescribed medications, and detects the use of alcohol, undisclosed medications, and illicit drugs.

The advantage of urine drug tests is that there are well-established analytical methods and extensive experience in result interpretation[28]; the disadvantages include specimen collection and the potential for tampering and adulteration. Oral fluid testing, or saliva testing, is gaining in popularity and has an advantage over urinalysis in that it entails a simple and noninvasive specimen collection process. Oral fluid testing, however, faces technical challenges with regard to both screening and confirmation methodologies.[29]

The urine drug test menu, whether performed inhouse or by a reference laboratory, should test for commonly prescribed opioids and the typical illicit drug groups (Table 1). The urine drug test is performed in most clinical settings by immunoassays, which, if positive, may lead to confirmation testing.

Proper utilization of immunoassay-based urine drug testing and correct interpretation of results must take into consideration the limitations of immunoassays.

Most immunoassays, such as those for the amphetamines, benzodiazepines, and opioids, are class assays; they detect not one target drug but a family of related compounds.[28,30] For example, the opiates immunoassays detect morphine (the target analyte) and codeine and also the related opioids with a phenanthrene ring, such as hydromorphone, hydrocodone, dihydrocodeine, and oxycodone, with varying sensitivities; these opioids, when present singly or in combination, can also produce a positive immunoassay result. Thus, an immunoassay cannot be used to monitor a patient using a prescribed opioid for possible abuse of another (i.e., nonprescribed) opioid.

Immunoreactivity assays for a drug determine the assay sensitivity for that drug.[28] For example, the opiates assay is less reactive to hydromorphone than to morphine and thus requires that a comparatively higher hydromorphone concentration be present for a positive result. Therefore, a patient may test negative for the prescribed opioid due to lower assay sensitivity, especially if the drug is taken in low doses, which can result in urine drug concentrations that fall below the assay cutoff; this is a "clinical" false-negative result and does not necessarily indicate nonadherence.[30,31] In this case, an alternative (and more sensitive and specific) assay should be able to detect the specific opioid. For example, oxycodone is poorly detected by the opiates assay, and the nonopiate opioids buprenorphine, fentanyl, and methadone are not detected by the opiates assay at all. Detection of these drugs requires analyte-specific (i.e., drug-specific) immunoassays.

Most clinical laboratories perform confirmation testing using mass spectrometry (MS) assays such as liquid chromatography–mass spectrometry (LC/MS). The MS assays offer specific identification of drugs and metabolites and quantitative measurement at low concentrations, thus allowing interpretation of cases involving the presence of minor opioid metabolites or pharmaceutical impurities.[30] MS, however, is costly and technologically challenging, and its deployment is limited to large laboratories.

Correct interpretation of urine drug test results requires knowledge of the limitations of the assay meth-

odology. Moreover, there should not be unrealistic expectations of what information can be obtained from the urine drug test. For example, the urine drug concentration cannot be extrapolated reliably to gauge the serum drug concentration, nor can it be used to infer patient adherence with the prescribed dosage regimen.

When interpreting an unexpected negative urine drug test, nonadherence may not be the only explanation. Besides the reasons mentioned previously, other possible explanations include dilution or substitution of the urine sample; genetic polymorphism in enzymes and transporters involved in opioid metabolism and transport (e.g., cytochrome P-450 enzymes, uridyl glucuronide transferase, P-glycoprotein), which can result in lower drug concentrations; and altered pharmacokinetics due to disorders involving reduced gastrointestinal absorption (e.g., diarrhea, short-gut syndrome), concurrent medications, or diet.[32]

An unexpected positive result suggests the patient may have taken undisclosed medications or illicit drugs. Other explanations, however, must also be considered. For example, the unexpected opioid may be present as a minor metabolite of the prescribed opioid and not as a result of abuse of the unexpected (nonprescribed) opioid. For example, hydromorphone is a prescription opioid but also a minor

Table 1.
Recommended Urine Drug Test Menu for Patients Receiving Opioids for Noncancer Pain[a]

	Immunoassays		
Drug/Class[b]	**Target Analyte(s)[b]**	**Cutoff Values (ng/mL)[b]**	**Typical Confirmation Assay Targets[b]**
Amphetamines	*d*-Methamphetamine	500, 1000	Amphetamines Methamphetamine Methylenedioxymethamphetamine (MDMA) Methylenedioxyamphetamine (MDA)
Barbiturates	Secobarbital	200, 300	Amobarbital Butalbital Pentobarbital Phenobarbital Secobarbital
Benzodiazepines	Nordiazepam	200, 300	Diazepam Nordiazepam Oxazepam Temazepam Clonazepam, 7-aminoclonazepam Alprazolam, α-hydroxyalprazolam Flunitrazepam, 7-aminoflunitrazepam Lorazepam
Buprenorphine	Buprenorphine	5	Buprenorphine, norbuprenorphine
	Norbuprenorphine	10	Buprenorphine, norbuprenorphine
Cocaine	Benzoylecgonine	150, 300	Benzoylecgonine, cocaine, cocaethylene
Fentanyl	Fentanyl	2	Fentanyl, norfentanyl
Marijuana	Δ9-Tetrahydrocannabinolcarboxylic acid	20, 50	Δ9-Tetrahydrocannabinolcarboxylic acid
Methadone	Methadone	300	Methadone, methadone metabolite[c]
	Methadone metabolite[c]	300	Methadone, methadone metabolite[c]
Opiates	Morphine	300, 2000	Morphine Codeine Oxycodone Oxymorphone Hydrocodone Hydromorphone
Oxycodone	Oxycodone	100	Oxycodone, noroxycodone, oxymorphone

[a]Reproduced, with permission, from reference 31.
[b]Consult laboratory for specifics of assays in use.
[c]2-Ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP).

metabolite of morphine[33] (Figure 1). Knowing the metabolic pathway and the relative concentrations of both morphine and hydromorphone may help to distinguish between the two scenarios.[33]

An alternative explanation for an unexpected positive urine test result is that high-sensitivity MS assays can detect opioids at very low concentrations, and some opioids are impurities created during pharmaceutical manufacturing processes; specifically, hydrocodone and codeine are impurities in pharmaceutical preparations of oxycodone and morphine, respectively.[34,35] A very low ratio (<1%) of the unexpected opioid (e.g., hydrocodone) to the prescribed opiate (e.g., oxycodone) suggests that the unexpected opioid is present as a manufacturing impurity.[34]

The urine drug test is a useful laboratory test for the management of patients on chronic opioid therapy. Consultation with a clinical laboratory professional can help to maximize the clinical efficacy of the urine drug test.

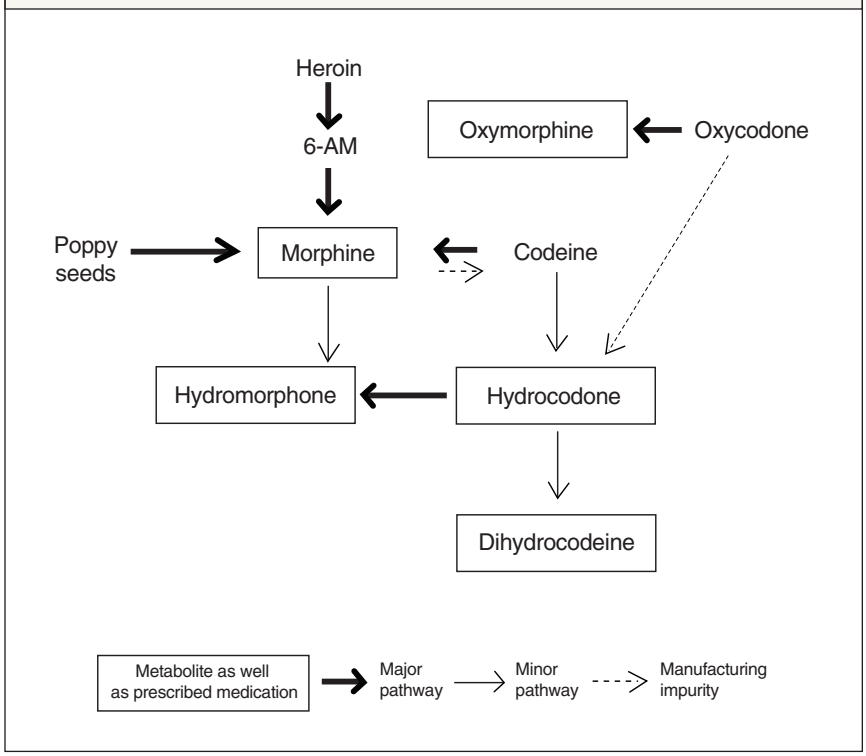
Epidemiology of opioid misuse and abuse

Reports from CDC, the Drug Abuse Warning Network (DAWN), and the National Poison Data System have demonstrated an alarming increase in opioid misuse and abuse over the last two decades.[1,36-41] Poisoning deaths in the United States nearly doubled from 1999 to 2006, from 20,000 to 37,000. This was due largely to deaths from prescription opioid analgesics, with methadone, oxycodone, and hydrocodone most frequently implicated. This increase in deaths coincided with a nearly fourfold increase in the use of prescription opioids nationally.[36] A review of data on individuals with adverse drug events who were treated in emergency departments from January 1, 2004, through December 31, 2005, found that central nervous system agents constituted the most frequently implicated therapeutic category (21.4% of cases); within that category, opioid-containing analgesics were the most frequently implicated medication class, accounting for an estimated 1,167 (24.8%) of the evaluated cases.[37] Sales of prescription opioids in 2010 were four times those in 1999. Overdose deaths involving opioid medications now exceed deaths involving heroin and cocaine combined. In 2010 alone, 16,500 people died from analgesic-related overdoses, the majority of which involved opioids.[38] Deaths from opioid analgesics have been reported across the United States, in all age groups, and specific opioids such as hydrocodone, methadone, morphine, and oxycodone have been implicated. In 2008, overdose death rates ranged from 5.5 per 100,000 population in Nebraska to 27.0 per 100,000 in New Mexico.[39] The prevalence of nonmedical use of opioids in 2008–09 ranged from 3.6% in Nebraska to 8.1% in Oklahoma. Rates of prescription opioid sales in 2008 ranged from 3.7 kg per 10,000 population in Illinois to 12.6 kg per 10,000 in Florida, with the highest sales rates reported in the Southeast and the Northwest.

In a review of 295 unintentional pharmaceutical overdose deaths in West Virginia, opioids were implicated in 93% of cases.[40] However, 44% of the decedents had not been prescribed an opioid. Ninety percent of the decedents were men ranging in age from 18 to 70 years, with a mean age of 39 years. Sixty-three percent of the deaths were associated with pharmaceutical diversion, and 21% involved evidence of doctor shopping. The 35- to 44-years age range was associated with a notably higher rate of doctor shopping. Substance abuse indicators were identified in 95% of the decedents, and having prescriptions for five or more controlled substances was more common in women (30.9%) than in men (16.7%).[40]

DAWN also collects important data that provide insights into recent national trends in drug-related mor-

Figure 1. Pathways of opiate metabolism. 6-AM = 6-acetylmorphine. Modified from reference 30.



bidity and mortality. A 2010 report from DAWN on emergency department visits for the misuse and abuse of all drugs estimated an increase from 1.6 million cases in 2004 to 2 million cases in 2008.[41] The number of visits related to opioid analgesics increased by 111% (from 144,600 to 305,900 visits) in the same time period. Visit rates increased across the five years for fentanyl, hydrocodone, hydromorphone, methadone, morphine, and oxycodone; for oxycodone, estimated annual emergency department visits increased from 41,700 to 105,200.[38]

In Florida, from 2003 through 2009, the death rate due to prescription drugs increased by 84.2%, from 7.3 to 13.4 per 100,000 people.[41] The greatest increases in rates were observed with oxycodone (264.6%), alprazolam (233.8%), and methadone (79.2%). Figure 2 compares Florida overdose trends for opioids as a group and for hydrocodone, methadone, morphine, and oxycodone specifically.

Clinical toxicology

While all opioids have some degree of affinity for the μ-, δ-, and κ-opioid receptors, the μ-opioid receptor is responsible for the majority of the adverse effects associated with opioid misuse, abuse, and overdose.[43] The classical elements of the opioid toxidrome include altered mental status, hypoventilation, decreased bowel motility, and miosis. Contrary to conventional wisdom, miosis is not a universal finding in opioid-toxic patients and neither its presence nor absence is pathognomonic of opioid toxicity or the lack thereof. For example, hypoxic patients and those who coingest anticholinergic agents may exhibit mydriasis. Other findings may include peripheral vasodilation, pulmonary edema, hypotension, bradycardia, chest wall rigidity, and myoclonus (with fentanyl) and seizures (with meperidine).[42-44] Opioids induce a delay in gastric emptying and may increase the risk of vomiting and pulmonary aspiration that can complicate respiratory depression.[45] Respiratory depression, modulated by the effects of opioids on medullary chemoreceptors' ability to detect hypercapnia, and the consequential reduced respiratory rate are diagnostic of opioid toxicity; a respiratory rate of less than 12 breaths per minute is characteristic.[46] Each opioid has unique pharmacokinetic and pharmacodynamic properties that determine the extent and duration of toxicity and affect treatment decisions, and these differences must be considered when evaluating the patient with opioid toxicity. While not yet applicable clinically, human genomics is linked to the magnitude of toxicity for some drugs, and, as mentioned previously, at least one opioid receptor polymorphism has been identified and may have diagnostic and treatment implications in the future.[47]

Characteristics of selected opioids

Buprenorphine. Buprenorphine is a potent semisynthetic opioid with partial agonist activity at the μ receptor. Its primary indication is treatment of opioid addiction since it has an extraordinarily high affinity for the μ receptor and the ability to prevent binding of other opioids. Buprenorphine formulations for opioid maintenance therapy are sublingual tablets and a sublingual film that are coformulated with naloxone, which serves as a deterrent to the i.v. abuse of buprenorphine. Unlike methadone, whose use requires the individual to obtain a daily dose at a methadone clinic, buprenorphine is dispensed through licensed office-based practices, and multiple doses can be dispensed.[48,49] Consequently, unintentional exposures to buprenorphine are now commonplace in the pediatric population and may be associated with significant morbidity.[48-51] Due to the long half-life of buprenorphine, children who may have been exposed to a single dose should be hospitalized for 24 hours and even longer if the use of naloxone was necessary to reverse the associated central nervous system and respiratory depression.[50] The high affinity of buprenorphine for the μ receptor may necessitate doses of naloxone that exceed customary doses in both children and adults or the use of a naloxone infusion.[52] Buprenorphine has minimal bioavailability, and since most pediatric exposures involve the sublingual route, the use of activated charcoal is unnecessary unless there are coingestants that dictate its use.

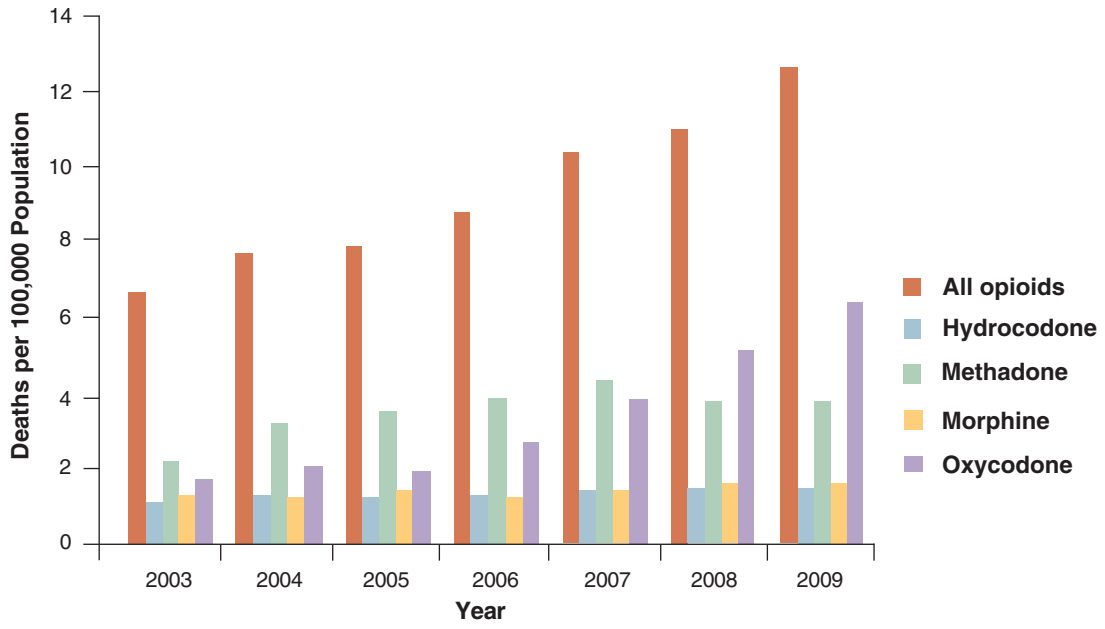
Fentanyl. Fentanyl is a pure synthetic opioid agonist of high potency (80–100 times that of morphine) with a short duration of action.[53] It is a μ-opioid receptor agonist indicated for the treatment of chronic pain, with delivery achieved via transdermal patches, nasal spray, and transmucosal products. Intravenous fentanyl is used in the perioperative setting, postoperatively for pain management, and as a sedative in the emergency department and critical care settings, and it is associated with notable morbidity and mortality when abused or when prescribed inappropriately to opioid-naive individuals. Fentanyl patch ingestion for abuse purposes is common; unused or spent patches contain fentanyl in a matrix or reservoir that becomes bioavailable when ingested.[54-58] Additionally, the inappropriate use of fentanyl patches on compromised skin (e.g., sunburned skin) or with external heat sources such as heating pads and blankets, saunas, and hot tubs increases transdermal absorption and may result in fentanyl toxicity.[59] Fentanyl toxicity is characterized by the classical opioid toxidrome along with sustained central nervous system and respiratory depression. Unlike the parenteral therapeutic use of fentanyl, the ingestion of patches is associated with an extremely long duration of action that may necessitate the prolonged use of naloxone.

Hydrocodone. The fixed combination of hydrocodone and acet-

aminophen is the most commonly prescribed generic medication in the United States.[60] Given the prominent presence of hydrocodone-containing products in U.S. homes, children are at a pronounced risk of being exposed to hydrocodone. Hydrocodone has considerable abuse potential and is associated with substantial morbidity and mortality.[61] As with other opioids, hydrocodone has considerable affinity for μ receptors and its toxic effects are consistent with the classical opioid toxidrome. Hydrocodone has been approved for manufacture in a single-entity extended-release form as a Schedule II product, but currently it is always combined with acetaminophen as an oral analgesic product.[62] Therefore, overdoses of hydrocodone-containing analgesics are also complicated by the presence of acetaminophen and are one of the leading causes of acetaminophen-related fatalities due to hepatic necrosis.[63,64] Consequently, when an exposure to a hydrocodone-containing product is suspected, serum acetaminophen and salicylate concentrations should be obtained. Hydrocodone is also available with ibuprofen as a combination product. The treatment of an overdose may include the use of activated charcoal to prevent drug absorption, naloxone to reverse the effects of hydrocodone, and acetylcysteine to treat acetaminophen toxicity. If the patient develops salicylate toxicity from a combination hydrocodone–aspirin product, appropriate supportive care (e.g., airway protection and ventilatory support, sodium bicarbonate to reverse acidemia, sedatives, anticonvulsants) and interventions (e.g., hemodialysis) must be initiated to prevent possibly life-threatening salicylate toxicity.

Methadone. The use of methadone, a synthetic μ agonist, has evolved beyond its traditional role in helping to prevent opioid withdrawal in patients enrolled in methadone maintenance programs. Methadone is now also used in the management of severe pain in patients with cancer or non-cancer-related chronic pain. Methadone's long half-life of approximately 24 hours (range, 8–59 hours) makes it suitable for once-daily dosing and ideal for the prevention of opioid withdrawal[65]; that characteristic is also one of its major toxicological drawbacks, since methadone toxicity, especially a decreased level of consciousness and respiratory depression, may be prolonged considerably. Therefore, a naloxone infusion is often necessary to prevent the recurrence of respiratory depression.[66] Opioid-addicted individuals who rely on or abuse methadone often use multiple pharmaceuticals that produce synergistic toxicity and increased morbidity and mortality.[67-69] This is especially true when methadone users take benzodiazepines concurrently.[68-70] Methadone, like all opioids, may cause airway musculature relaxation and resultant airway obstruction and sleep apnea. Benzodiazepines contribute to death by exacerbating the adverse effects of methadone. Researchers who evaluated 1193 opioid overdoses that occurred in one Australian state over a 10-year period reported that nearly

Figure 2. Opioid overdose deaths in Florida in 2003–09, with death rates shown for opioids as a class and for specific opioid medications.[41]



63.7% of methadone-related fatalities ($n = 193$) were complicated by the concurrent presence (and likely the abuse) of benzodiazepines.[68] Another often overlooked adverse event that is associated with both methadone maintenance use and overdose is Q-T interval prolongation, which increases the risk of developing ventricular dysrhythmias, including torsades de pointes.[70-73]

Oxycodone. Oxycodone is a potent semisynthetic opioid and, like other potent opioids, has a high affinity for the μ receptors. It has been used commonly in combination with both aspirin and acetaminophen. However, when oxycodone was introduced in 1995 as a single-entity sustained-release preparation, its use became widespread and its abuse became epidemic.[74] Abusers ingested, injected, and nasally insufflated the product, since crushing and snorting the drug resulted in its rapid release and high blood concentrations. The sustained-release product has been reformulated to reduce the abuse potential.[75] Similar to methadone, oxycodone is often abused concurrently with benzodiazepines such as alprazolam and other psychoactive drugs that enhance toxicity.[76,77] Especially in overdose, oxycodone is associated with an increased risk of Q-T interval prolongation.[78,79]

Diagnosis and treatment

Respiratory depression is the result of opioid toxicity, and supportive care to restore ventilation and oxygenation is the cornerstone of patient management. The conventional management of respiratory depression in most poisoned patients is to perform endotracheal intubation and provide ventilatory support. In contrast, respiratory depression in the patient with opioid toxicity can be treated with the competitive μ-opioid receptor antagonist naloxone.[42] Unless the patient has a traumatic brain injury, has prolonged hypoxia, or has used an additional substance or substances that produce central nervous system or respiratory depression, naloxone will reverse the adverse effects of opioids. Therefore, intubation is unnecessary in most patients experiencing opioid intoxication. Naloxone is generally administered intravenously. Opioid-dependent individuals who abuse substances intravenously may have inadequate vascular access; naloxone is effective via any parenteral route (intramuscular, subcutaneous, or sublingual), through an endotracheal tube, intranasally, or by nebulization.[42,80-84]

While naloxone can rapidly reverse the symptoms of opioid toxicity, its administration can precipitate acute opioid withdrawal. Opioid withdrawal is unlikely to be life-threatening. However, it is extremely uncomfortable for the patient, who may become agitated and combative. In the emergency department setting, naloxone should be administered intravenously at the smallest effective dose and then adjusted accordingly to reverse respiratory depression. The initial adult i.v. dose is 0.04 mg and can be followed (if necessary) by progressively larger doses every 2–3 minutes until opioid toxicity is reversed[42,85]; some clinicians advocate adjusting the dose by 0.04-mg increments to prevent withdrawal.[85] The half-life of naloxone is approximately 30 minutes, whereas the half-life of most opioids exceeds that notably, necessitating the continued administration of naloxone to prevent recurrent respiratory depression; this is often accomplished through the use of a naloxone infusion. Patients who receive naloxone must not be discharged until several hours have passed since the last naloxone dose in order to ensure that opioid toxicity is no longer a risk. In the prehospital setting, it may be difficult for emergency medical providers and companions of opioid users to administer naloxone parenterally. The administration of intranasal naloxone has been determined to be as effective as parenteral administration, and this intervention has been implemented in many cities worldwide.[81-84] Additionally, in early 2014 FDA approved a naloxone delivery system that enables subcutaneous or intramuscular naloxone administration by individuals who are not health professionals.[86] The apparatus is technically similar to the automatic defibrillators that are located in public venues. When activated, it provides the person who is administering the naloxone with verbal instructions on the use of the drug. The device delivers 0.4 mg of naloxone per dose.

Opioids may be taken by any route (e.g., orally, intravenously, via nasal insufflation); therefore, gastrointestinal decontamination may not be indicated or effective. If the opioid was ingested, the only gastrointestinal decontamination that may be effective is the administration of an aqueous slurry of activated charcoal within two hours of the ingestion[87]; gastric lavage, emesis, and cathartics have no role in these cases. The clinician must recognize that coingestants (e.g., acetaminophen) or illicit drugs (e.g., cocaine) may have been used and that the patient may require additional treatment to prevent or reverse the effects of these agents.

With some overdoses, such as those involving acetaminophen, laboratory testing is diagnostic and determines the appropriate therapeutic interventions (e.g., acetylcysteine administration). However, laboratory testing has limited value in the treatment of the patient with opioid toxicity.[88] Most initial laboratory toxicology screens focus on analyzing a urine specimen, which provides only qualitative evidence of exposure to opioids with a phenanthrene ring (e.g., morphine). The semisynthetic (e.g., hydrocodone) and synthetic (e.g., fentanyl) opioids may be detected only at higher concentrations (as with hydrocodone) or not at all (as with fentanyl) with the conventional assays that are utilized by most hospitals.[88] In a patient with

respiratory depression, waiting for the results of a laboratory test delays the use of appropriate therapy. The patient history and the clinical presentation are the best indicators that the patient is experiencing opioid toxicity and requires treatment.

Legal implications

As a result of the increases in opioid-related deaths, over the last two years the Drug Enforcement Administration (DEA) has become much more aggressive in its enforcement of the Controlled Substances Act (CSA) with respect to prescription drug wholesalers, physicians, pharmacists, and pharmacies that distribute, prescribe, and dispense controlled substances. Historically, DEA focused its enforcement actions on independent community pharmacies more than retail chain or hospital pharmacies, but in 2012 that focus expanded to include legal actions against large chain pharmacies, long-term care pharmacies, and prescription drug wholesalers.

A brief review of some of the prosecutions undertaken by DEA and a state government in 2012 and 2013, as well as the resulting court actions (summarized in news releases available from the U.S. Department of Justice website [www.justice.gov/dea/pr/news.shtml]), is illustrative of the current practice environment:

1. DEA issued an immediate suspension order on a wholesaler's distribution facility. DEA alleged that the wholesaler endangered the public health by selling excessive quantities of oxycodone to certain pharmacies in Florida. This was one of the first times DEA argued that a drug wholesaler had a responsibility for the actions of its customers. This action was settled with the wholesaler agreeing to not sell any controlled substances from its Florida facility until May 2014, establish a customer monitoring program, and report suspicious orders to DEA.
2. DEA suspended the controlled substance registrations of two retail chain pharmacies in central Florida, alleging that the pharmacies had improperly sold massive quantities of oxycodone. Although the parent corporation argued that the pharmacies had adopted new policies to verify the legitimacy of prescriptions for such drugs, DEA revoked the registrations in October 2012.
3. A national long-term care pharmacy agreed to pay $50 million to resolve claims that its facilities dispensed controlled substances improperly. Two of the allegations against the long-term care pharmacy were that some prescriptions did not contain all the items required by CSA regulations (21 C.F.R. 1306.14 and 1306.24) and that the pharmacy had not properly documented partially filled prescriptions. The DEA administrator was quoted as saying, "This case highlights the responsibilities of pharmacists, doctors and others when prescribing and dispensing controlled substances."
4. The attorney general of West Virginia filed legal actions against over a dozen drug wholesalers, alleging that the distributors failed to properly assure that orders for controlled substances were for legitimate quantities, thereby contributing to the drug abuse problems in West Virginia.
5. DEA took separate actions against at least six Florida chain pharmacies and issued an immediate suspension of registration against the chain's wholesale distribution center. The agency alleged that the pharmacies did not keep adequate records and filled prescriptions that were not issued for a legitimate medical use. These cases and others pending in additional states were resolved when the pharmacy chain agreed to pay $80 million—the largest settlement in DEA history—and to the suspension of dispensing privileges in some stores until 2015.

Health-system pharmacists are subject to the same level of DEA scrutiny as retail pharmacists and have similar responsibilities in relation to controlled substances. Numerous health systems operate outpatient and retail pharmacies, and hospitals have risks associated with employee theft, loss or destruction of controlled substances, record-keeping issues, and documentation of a legitimate medical need for the use of opioids.

The diversion of opioids and other controlled substances from hospital pharmacies may result from improper actions by employees.[89] Hospitals, like many other employers, are subject to the risk that some employees will steal merchandise. In addition, hospital pharmacies are at risk for diversion related to the use of prefilled syringes or single-use vials of controlled substances when the prescriber orders a dose that is less than the total contents of the syringe or vial. If the syringe or vial contains 100 mg of an opioid but the prescribed dose is 75 mg, the disposal of the remaining 25 mg can become a diversion risk. As an example, a nurse could carry an empty sterile vial in a pocket and, instead of destroying the excess drug, inject it into the vial; this pattern could be repeated several times throughout the shift, and by the time the nurse left the hospital at the end of the day, he could have diverted a substantial quantity of a controlled substance that was extremely difficult to trace. In this case, the hospital could not identify or demonstrate a shortage from the patient records. A director of pharmacy must be vigilant to these risks and establish and consistently apply policies and procedures that will minimize the risk of employee theft or diversion of controlled substances.

The final area for legal consideration is the actual use of controlled substances in the health-system environment for inpatients and outpatients. Health-system pharmacists must be familiar with DEA regulations controlling the use of opioids in the inpatient setting. Hospitals have the same legal duty as retail pharmacies to ensure that controlled substances are ordered for

a legitimate medical purpose. The definition of legitimacy is subject to change, however, as evidenced by the September 2013 change in the FDA labeling standards for long-acting and extended-release opioid analgesics.[90] The new labeling indicates that these drugs should only be used for pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative options are inadequate.

This issue of appropriate opioid therapy may appear to be less of a problem in the hospital environment than in the retail sector, but health-system pharmacists must remain vigilant for questionable orders or prescriptions. As individuals who abuse drugs find it more difficult to obtain opioids from retail pharmacies, they may turn to emergency departments and outpatient pharmacies to obtain these medications. Further, health-system pharmacists must also remember that all orders, prescriptions, and prescription labels must be complete and accurate, as mandated by DEA regulations. Policies should be in place to ensure that these record-keeping requirements are met.

In addition to ensuring that opioids are being ordered for a legitimate medical purpose and that proper record-keeping and labeling procedures are followed, health-system pharmacists must understand the restrictions on using opioids for maintenance or detoxification of patients who are drug addicted. The basic rule is that only an opioid treatment program registered with DEA is permitted to use an opioid drug to maintain or detoxify an opioid-addicted individual; the one exception is if a buprenorphine product is ordered by a specially certified prescriber. However, there is a critical exception in the DEA regulations pertaining to hospitalized patients: Provisions of 21 C.F.R., section 1306.07(c), stipulate that the hospital staff is permitted to provide opioid maintenance or detoxification therapy to a patient as an incidental adjunct to medical or surgical treatment of conditions other than addiction, thereby allowing a hospitalized addicted person to avoid the risk of withdrawal while being treated for some other condition. It is even possible to withdraw the patient from the opioid addiction if the withdrawal is accomplished during legitimate treatment for some other medical or surgical condition. The other important exception found in section 1306.07(c) is that hospital staff may administer or dispense opioids to an addicted patient with intractable pain for whom no relief or cure is possible or none has been found after reasonable efforts. As an example, this provision protects health-system pharmacists treating a patient with cancer (as either an inpatient or an outpatient) who has become addicted to opioids.

Prescription drug monitoring programs

Prescription drug monitoring programs (PDMPs) are electronic databases created and overseen at the state level to collect data on opioids and other controlled substances as well as noncontrolled drugs with potential for abuse. PDMPs are currently active in 47 states.[91] New Hampshire and Maryland are in the process of implementing systems, and the District of Columbia has pending legislation. Missouri is the only state without a PDMP and no pending legislation. The goals of individual PDMPs vary from state to state, but in general these programs are designed to (1) monitor prescribing and dispensing to individual patients, thereby providing treatment history information to the health professionals responsible for a patient's care, (2) provide information to parties, including law enforcement, for the identification and deterrence of prescription drug abuse and diversion, (3) provide information to practitioners and third parties for the identification of individuals at risk for addiction to a controlled substance, and (4) provide information to researchers and public health officials for identification of drug-use trends and public health needs.[92]

Because PDMP laws flow from state legislatures and the rules and regulations are determined by the executive body identified in each state's statutes, each state has determined its own laws, regulations, rules for implementation, and program structure. There is state-to-state variation in terms of which agency houses the program (e.g., department of public health, office of attorney general, board of pharmacy), which controlled substances are monitored (e.g., Schedule II only, Schedules II–V, other drugs), how often pharmacy reporting is required (e.g., weekly, biweekly, monthly), and who can query the database (e.g., prescribers, pharmacists, law enforcement).[93] Another key factor differing among states is whether the system is proactive or reactive. In proactive systems, information is delivered to prescribers or dispensers when certain prescribing or dispensing thresholds are met by a patient under their care. Reactive systems query available information, but the system is utilized only at the discretion of the prescriber or dispenser.[93] Finally, states differ in requirements for prescribers or pharmacists to utilize the PDMP. Currently, 16 states require mandatory PDMP use when various conditions are met before certain controlled substances can be prescribed.[93]

The effectiveness of PDMPs in accomplishing the goals listed above has not been investigated thoroughly. Research that has been conducted in this field has generally examined either the effect programs have on opioid-related outcomes (e.g., hospital admissions, mortality) or the ability of the program to influence behaviors associated with abuse and misuse of opioids.

There are conflicting findings regarding the ability of PDMPs to

reduce mortality related to opioid abuse. A 2011 study of opioid overdose deaths in 19 states found that PDMP status was not associated with decreased drug overdose or opioid-related mortality.[94] However, new data from the RADARS (Researched Abuse, Diversion and Addiction-Related Surveillance) System's Poison Center Program and Opioid Treatment Program surveillance databases show an association between the presence of a PDMP and a decrease in the number of poison center interventions as well as a decrease in admissions for opioid overdose.[95] One weakness in this area of research thus far has been the treatment of PDMP presence as a dichotomous variable. Because of the varying structures of these programs, their effectiveness is likely to vary from state to state; this is especially true when comparing reactive and proactive programs.

While the effectiveness of PDMPs at reducing poor outcomes associated with opioids has not been shown definitively, the ability of these programs to influence the behavior of prescribers, pharmacists, and patients is well established. Studies using survey methods have shown that providers who utilize PDMP reports are likely to change their prescribing practices in response to the new information. These studies have taken place in a variety of settings (e.g., primary care,[96] emergency department,[97] substance abuse treatment programs[98]) and in several distinct geographic locations.[99-101] While studies of pharmacists are more limited, pharmacists' attitudes toward PDMPs have been positive, with their primary use of the programs being to help reduce doctor shopping.[102] One of the most straightforward uses of PDMPs is altering this aberrant patient behavior by providing a coordinated and convenient source of controlled substance use information to prescribers, pharmacists, and law enforcement. One study showed that PDMP implementation reduced the time necessary to conduct investigations into possible doctor shopping from 156 to 16 days.[101]

CDC and the Office of National Drug Control Policy have identified PDMPs as important strategies in the response to the opioid abuse and misuse epidemic.[103] The continued expansion of PDMPs to cover all 50 states and the District of Columbia is a good first step in implementing this strategy; however, looking beyond this, the National Alliance for Model State Drug Laws and the National Safety Council have recommended PDMP best practices for states to consider.[104] Interstate data sharing, the expansion of authorized users (including allowing delegate access), and the determination of compulsory-use requirements by professional licensing boards are key components of these recommendations.[104] As the expansion of PDMPs across the nation continues, utilization of the growing body of evidence relating to these programs to identify and implement program improvements will be important. Implementing evidence-based policy changes to increase PDMP effectiveness at achieving the various program goals described above will ensure greater utility for all stakeholders in the future.

Implications for medication-use policy in health systems

Opioids are included on the Institute for Safe Medication Practices list of high-alert medications (i.e., agents associated with a high risk of patient harm when used inappropriately) and require heightened oversight in hospitals and health systems.[105] Institutional policies, beyond federal and state legal requirements, further direct appropriate use and monitoring of opioids and promote standardized practices to prevent and identify diversion. Clinical policies can address appropriate treatment of severe pain with opioid medications, which requires ongoing assessment and reassessment of analgesia, activities of daily living, adverse effects, and aberrant behavior along with appropriate documentation. Operational policies outline procedures to ensure proper control and accountability and prevent diversion.

Consistent practice for appropriate screening, assessment, and prescribing for pain can be directed through computerized prescriber order entry (CPOE), clinical decision support (CDS), pharmacy and therapeutics committee–approved guidelines, and formulary restrictions. Printed or computerized order sets should include best practices and standardize prescribing of appropriate doses, patient-controlled analgesia, epidural opioid infusions, procedure-specific dosing protocols, and monitoring. Discharge and ambulatory care order sets or protocols can be utilized to ensure consistent discharge analgesia regimens and minimize the amount of opioid dispensed after routine outpatient procedures or minor surgeries. If the prescriber concludes that opioids are required, a standard minimal number of doses for each procedure can be designated (e.g., 5–10 doses) instead of an ample supply to cover any and all pain. By minimizing the amounts of opioids that are prescribed routinely but are not used by patients, the amounts of opioids available in the community for misuse and abuse can be reduced.

Prescribers can receive additional direction through best-practice alerts or red flags built into CPOE and CDS systems regarding dose limits and the risks of respiratory depression or misuse. Safe prescribing through formulary restrictions and guidelines further minimizes risk and liability from high-harm opioids such as meperidine and codeine. Due to the risk of neurotoxicity, meperidine is not recommended for pain treatment and should be removed from the formulary or restricted to treatment of rigors.[106,107] Codeine use should also be limited due to the drug's unpredictable analgesia arising from a genetic polymorphism and a recent FDA boxed warning on its use

in children after tonsillectomy or adenoidectomy.[108,109]

Some emergency departments restrict the prescribing of opioids by limiting quantities to a small amount for the short-term treatment of acute pain and restricting treatment of patients with chronic pain.[110,111] In some emergency departments, patients with chronic pain are treated with nonopioid analgesics and then referred for follow-up care. In conjunction with these policies, emergency physicians do not replace lost or stolen opioids, and signage in the emergency department delineates the policy clearly. These policies and practices are most effective if coordinated within a geographic area.

Management of opioid-dependent chronic pain can be challenging due to common comorbidities of depression, anxiety, and addiction.[112,113] Development of institutional guidelines or protocols can provide a consistent and safe method of initiating and monitoring therapy for these patients.[114,115] Along with a thorough history and physical examination, chronic pain management plans should include universal screening for illicit drug use and addictive disorders prior to initiation of treatment. One exception is the patient with limited life expectancy. Screening may include the urine drug screen, review of public records for prior convictions, and evaluation of state PDMPs. Similarly, as discussed in Appendix B, a pain management agreement plan (PMAP), or "opioid contract," should be constructed for most patients. The intent of the PMAP is to provide full disclosure of the risks and benefits of opioid therapy and institutional policies with regard to ongoing regular pain assessment, random urine drug screening, and the use of a single opioid prescriber group and pharmacy. In addition, the PMAP addresses consequences of missed appointments, aberrancies in urine drug tests, and illegal actions related to substance abuse. Violation of a PMAP may require the placement of limits on a patient's opioid supply, more frequent clinic appointments and urine drug screening, selection of therapy with a lower street value, or referral to a substance abuse specialist. In addition to these measures, some facilities require more frequent monitoring and documentation of therapeutic benefit for patients receiving opioid doses over a target threshold (e.g., greater than 120 mg of oral morphine equivalents per day) to identify potentially inappropriate use and minimize harmful consequences associated with high opioid doses.[116]

The pharmacist's role in opioid therapy and developing guidelines, policies, and patient education to promote safe practices is paramount in both the inpatient and ambulatory care settings.[117] In addition to their important legal responsibilities to ensure appropriate prescribing and dispensing, ambulatory care pharmacists should further define organizational practices for consistent dispensing of opioids. For example, pharmacies could require a check of the state PDMP prior to the dispensing of opioids to new or unfamiliar patients, especially those residing a long distance from the pharmacy, along with a government-issued identification for picking up opioid prescriptions. Other standards might include criteria for contacting prescribers and law enforcement officials regarding potentially forged or altered prescriptions, frequent requests for early prescription refills, and unusual patient behavior. A standard documentation process for the steps required for prescription validation should be implemented as well. Despite their best efforts to identify inappropriate prescriptions, pharmacists may face the challenge of opioid prescriptions written by valid prescribers for large quantities of opioids with questionable indications (sometimes referred to as "pill-mill" operations) but with insufficient information to validate a patient–prescriber relationship. One pharmacy chain limited the dispensing of inappropriate prescriptions by identifying prescribers writing for larger quantities of high-risk medications more frequently than others within the same specialty and geographic area.[118] Pharmacists from these facilities stopped filling prescriptions if the prescribers were unable or unwilling to justify their practice of prescribing high volumes of high-risk medications. As discussed above, the absence of these types of measures can place health-system pharmacies and pharmacists in legal jeopardy.

Education of healthcare staff, as well as patients, on appropriate treatment of pain, including nondrug and nonopioid therapy, and the risk of opioid diversion is recommended to minimize opioid abuse.[116,117] Pharmacists can be instrumental in developing educational content for their institution, patients, and the public. Medication counseling during dispensing provides the perfect opportunity to counsel patients to lock up opioids, never share medications with others, and appropriately dispose of unused medications.

Prevention of opioid diversion within the healthcare system occurs through implementation of comprehensive policies accounting for opioids from the point of ordering to administration to the patient.[119]

The numbers of personnel responsible for ordering, receiving, and taking inventory of controlled substances should be limited, and those responsibilities should be rotated. Preemployment criminal background checks and urine drug screening should be considered for employees with these direct responsibilities. Technology and automated dispensing devices further facilitate tracking and documentation of opioids and generate utilization reports. One vulnerable step in the process is opioid waste disposal.[120] A "second-witness" policy (i.e., a requirement that not just one but two coworkers be present during the disposal of drug waste), with appropriate documentation,

should be required for all instances of waste disposal at the point of patient care as well as in the pharmacy. Also, pharmacy policy must reinforce actual witnessing, as opposed to "virtual witnessing," which occurs when a coworker attests to but does not actually visualize the disposal of waste. Reconciliation of the number of opioid medication doses administered in the operating room with the amount disposed as waste is one method of oversight to prevent the diversion of anesthesia agents. Routine surveillance along with timely and thorough investigation of diversion reports is also required. Random audits by independent personnel not responsible for opioid tracking or documenting opioid use should be conducted to help ensure appropriate ordering, stocking, dispensing, disposal, and returns of controlled substances. All staff can conduct informal surveillance if educated on the risk of diversion and provided a means of anonymous reporting.[120] Any report on questionable behavior or discrepancies must be investigated fully. Some institutions utilize a formal controlled substance diversion team consisting of experts from multiple disciplines to further investigate aberrancies.[120]

Despite the web of policy for prescribing, dispensing, and tracking opioids throughout a facility, addicts and those diverting opioids for financial profit are innovative and willing to take risks. Policies, procedures, and guidelines require ongoing review and updating. Healthcare practitioners must be vigilant and collaborate to ensure appropriate treatment of pain while minimizing misuse and abuse.

Opioid misuse and abuse have reached epidemic proportions in the United States, and there has been an increase in associated morbidity and mortality. Pharmacists in hospitals and health systems must play a key leadership role in preventing diversion and inappropriate prescribing and dispensing of opioids. In order to most effectively develop health system–based medication-use policies that aim at reducing the misuse and abuse of opioids, it is imperative that health-system pharmacists understand the appropriate role of opioids in the treatment of pain, the epidemiology of the opioid abuse epidemic and the clinical toxicology of these agents, legal implications for individual pharmacists and departments of pharmacy, and state-level monitoring programs that can be incorporated into prescribing, dispensing, and monitoring processes.

Conclusion

Pharmacists in hospitals and health systems can play a key role in recognizing the various forms of opioid toxicity and in preventing inappropriate prescribing and diversion of opioids.

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Appendix A—Key considerations in analgesic selection[6]

- Cause of the patient's pain
- Patient's age and general health, and the presence of comorbidities
- Potential for adverse outcomes associated with medication-related adverse effects
- Potential drug interactions
- Comorbidities that may be relieved by the nonanalgesic effects of the medications (e.g., sleep disturbances, depression, anxiety)
- Comorbidities that may be exacerbated by the nonanalgesic effects of the medications (e.g., hypertension, gastrointestinal ulceration, renal impairment, sleep apnea, cognitive impairment)
- Costs of therapy
- Potential risks for medication abuse
- Risks of intentional or unintentional overdose

Appendix B—Summary of American Pain Society–American Academy of Pain Medicine recommendations on use of chronic opioid therapy in chronic noncancer pain[7]

Patient selection and risk stratification. Before beginning opioid therapy, clinicians should conduct a history and a physical examination and collect other information as appropriate, including a risk assessment for opioid use. Chronic opioid therapy should be started only when the perceived benefit outweighs any real or potential risk.

Informed consent and opioid management plans. When starting opioid therapy, the risks and benefits of therapy should be explicitly discussed with the patient. The patient needs to have a clear understanding of the goals of therapy, probable outcomes, and alternatives to chronic opioid therapy. For many if not most chronic noncancer pain conditions, nonpharmacologic therapies (e.g., physical, cognitive behavioral) and nonopioid therapies (e.g., adjuvant analgesics) are critically important to the overall success of the therapeutic plan, and patients must be willing to attempt a trial of these interventions in addition to opioid therapy.

Initiation and titration of chronic opioid therapy. The initiation of opioid therapy should be considered a short-term therapeutic trial, with frequent assessment of whether or not the goal is achieved. It is critically important that practitioners set realistic therapeutic goals in treating chronic noncancer pain, which include not only a reduction in pain severity but demonstrated improvement in functioning. Selection of a specific opioid to treat chronic noncancer pain is also a patient-specific decision based on patient- and drug-related variables. Patient-related variables include considerations such as renal and hepatic functions, body habitus (for transdermal opioids), ability to swallow tablets or capsules, history of responsiveness to opioids in the past (positive and negative), and history of opioid allergy or intolerance, among others. The six opioids recommended for the management of chronic severe pain in the elderly by an international expert panel are buprenorphine, fentanyl, hydromorphone, methadone, morphine, and oxycodone.

Methadone. Methadone is an opioid with complicated and variable pharmacokinetic and pharmacodynamic parameters. Clinicians who choose to use methadone for chronic opioid therapy must become expert in the use of this agent. This includes a keen understanding of whether or not a patient is an appropriate candidate for methadone after performing a careful risk assessment, including a cardiac assessment; dosing strategies for both opioid-naive and opioid-tolerant patients; and how to monitor a patient receiving methadone. Methadone has a very long and variable half-life; therefore, starting doses should be conservative, patients should be monitored closely, and doses should not be adjusted before four to seven days.

Monitoring. Patients receiving chronic opioid therapy must be regularly monitored to ensure progress is being made toward achieving therapeutic goals, adherence to the prescribed therapy, and avoidance of adverse effects. Efforts (e.g., urine drug screening) to ensure the prescribed opioid is not being abused or diverted may be part of the monitoring plan.

High-risk patients. Patients with a concurrent history of drug abuse, psychiatric issues, or aberrant drug-related behaviors should only receive chronic opioid therapy if the clinician is able to implement more stringent and frequent monitoring. In difficult cases, patients may benefit from referral to an appropriate healthcare provider.

Dose escalations, high-dose opioid therapy, opioid rotation, and indications for discontinuation of therapy. When repeated dosage escalations have occurred or the patient experiences adverse effects from opioid therapy, the clinician should reevaluate the benefits and burdens of therapy. Patients may require tapering and discontinuation of opioid therapy or conversion to a different opioid.

Opioid-related adverse effects. Practitioners should be knowledgeable of opioid-related adverse effects and prevent, identify, and manage such adverse effects as they occur.

Use of psychotherapeutic cointerventions. Psychotherapeutic interventions, functional restoration, interdisciplinary therapy, and nonopioid therapies should routinely be integrated into the patient's plan of care.

Driving and work safety. Patients should be counseled about the risks of driving and work safety while taking opioids and counseled about avoiding unsafe behaviors.

Identifying a medical home and when to obtain consultation. If the patient's primary care provider is not prescribing the chronic opioid therapy, there should be close communication between this provider and other prescribers. Patients with chronic pain often benefit from interdisciplinary pain management.

Breakthrough pain. Patients with persistent pain that requires around-the-clock opioid therapy should be evaluated for a trial of "as-needed" opioid therapy after considering the risks and benefits of such an intervention.

Opioids in pregnancy. Women of childbearing age should be counseled about the risks and benefits of chronic opioid therapy during pregnancy and after delivery. The use of opioids during pregnancy is not encouraged, and risks to the patient and newborn must be considered and dealt with.

Opioid policies. Practitioners need to be aware of state and federal laws and guidelines as they pertain to chronic opioid therapy. Opioids are an effective tool in the management of acute and chronic pain, but as with all pharmacotherapeutic interventions, risks and benefits must be assessed before and during therapy to ensure safe and effective outcomes for patients.

Four Case Studies on Diversion Prevention

Jerry Siegel, PharmD, FASHP, Ryan A Forrey, PharmD, MS

Effectively addressing drug diversion is a challenging pursuit for hospitals throughout the United States, but failure to do so can easily jeopardize patient safety. Although it is common to believe that one's own hospital is an exception—since diversion could never happen here—this is certainly a misconception. The exact prevalence of drug diversion is unknown, because the deceptive and secretive nature of the problem, as well as health care institutions' reluctance to acknowledge lapses in medication security, makes quantifying its pervasiveness difficult. However, recognizing that drug diversion is occurring at your hospital is the first step toward preventing it.

To develop an effective diversion-prevention program, one must gain an understanding of who diverts, what drugs are the most common targets, which areas of the hospital are most likely to be targeted, and when and why diverters misdirect drugs. A program that addresses all of these points is most likely to be successful. At the Ohio State University (OSU) Wexner Medical Center, our diversion-prevention program—named Code N (for narcotics)—emphasizes the urgency of combating diversion. The key functions of the Code N program are enabled via a team of practitioners that quickly convene if evidence indicates a diversion scenario is in progress. The team comprises the director of pharmacy, the director of nursing, and representatives from risk management (the department responsible for calling the code), human resources, hospital security, hospital administration, as well as the manager of the discipline or patient care area under review. This team will meet within 24-48 hours of the discovery of potential diversion to review evidence and determine if a course of intervention is necessary. The success of this program is highly dependent on the multidisciplinary nature of our team and the rapid rate of response.

Who May Become a Diverter?

Anyone with access to desirable drugs—controlled substances, high-cost medications, and other drugs deemed valuable—may become a diverter. In any case of diversion, patients, their families, physicians, pharmacists, nurses, technical staff, and others are put at risk. In health care settings that comply with secure medication storage requirements, diversion detection and prevention efforts focus primarily on staff with access to that storage.

CASE REPORT: The Unexplained Empty Vial

While cleaning under the bed of a discharged patient in the medical/surgical unit, housekeeping found an empty sufentanil vial. The director of pharmacy was perplexed as to why this medication was found in this location, as it is never stocked or dispensed outside of the pharmacy and was not administered to the discharged patient. Suspecting diversion, she began an internal investigation and found no anomalies, despite careful review of administration records for the patient's medical/surgical unit nurses, the anesthesiologist, and the operating room and post-anesthesia care unit nurses.

Three weeks later, hospital security requested a review and identification of medications found in the belongings of Jane Doe, an employee being terminated for performance issues. The director of pharmacy identified several tablets and nearly empty vials of controlled substances in her possession. Jane Doe also tested positive for several controlled substances in a urine toxicology screen.

Five years prior, Jane Doe was hired as a third-shift pharmacy technician. After exemplary performance in that role, she obtained a nursing position in the medical/surgical department. However, after changing positions, her pharmacy access was not revoked, an oversight that Jane Doe eventually discovered. She began entering the satellite pharmacies after hours to remove used controlled substance vials from hazardous waste receptacles and obtained sufficient medication to inject herself by pooling multiple vials. Jane Doe was working in the unit the night before the empty sufentanil vial was discovered. Had Jane Doe's diversion been discovered prior to (or in absence of) her termination proceedings pursuant to her performance, she would have been offered treatment through the hospital. In this case, her diversion was reported to the police as well as the state board of nursing. Jane Doe was subjected to criminal charges and her license was suspended pending successful completion of a rehab treatment program.

Access to Medications

A comprehensive diversion-prevention program should focus on nurses, pharmacists, anesthesiologists, and pharmacy technicians—practitioners who regularly access medications as a function of their job duties. Many hospitals design their diversion-prevention programs to address the nursing staff first because of the sheer size of this workforce. Nurses who administer drugs daily, and may perceive drug availability due to poor or nonexistent workplace controls, have twice the normal rates of drug misuse.[1] Knowledge of drugs has not been shown to prevent addiction among nurses, but rather to promote self-medication. Nurses who are abusing drugs often cite the nature of their work as a component driving their addiction. Contributing factors include[2]:

- Stress
- Access to controlled substances
- Belief that medications are safe, efficacious, and helpful
- Caregiver burnout
- Belief that their training and knowledge of controlled substances can protect them from addiction

Some hospitals and risk managers are wary of sharing cases of confirmed diversion, as they can create a negative perception of the hospital. Regardless, it is essential that drug abuse education be emphasized in the training of all health care practitioners and that all employees be made fully aware that a stringent diversion program is in place at the institution and that it will be strictly enforced. Knowledge about addiction does not prevent the pharmacologic action of the agents. Thus, from a management standpoint, we have to temper staff from working excessive overtime and beware of proffering rewards and accolades for doing so. Working long hours may be a root cause of diversion as long hours ensure continuous access to drugs.

Controlling Access

When medication access is no longer appropriate for a given employee, for whatever reason, procedures must be in place to remove that person's access to the electronic medical record, ADCs, and any form of electronic security (such as badge readers) that grant physical access to a restricted space. To enable this, establish a process whereby departments notify the information technology (IT) data security group (or its equivalent) of upcoming employment transfers or terminations daily or whenever they occur; immediate or urgent terminations should be communicated rapidly as well. Moreover, the IT department must notify the department requesting an access change after the user's access has been revoked. Implementing enhanced technology to coordinate and synchronize these notifications with minimal human intervention is key. Integrating ADC systems into the institution's

user database can increase control and decrease the risk of invalid users retaining access to controlled substances. However, even advanced systems cannot prevent all instances of unauthorized access, so continuous vigilance is required.

When an employee transfers from one position to another within the hospital, medication access must be re-evaluated prior to the move. Because the human resources department often manages transfers, rather than IT data security staff, coordination and early warning can be challenging. Our hospital requires a background check for all employees before initial hire and at the time of each transfer. Coupling an access review with a background check is an effective method to formalize a systematic procedure for medication security.

The pharmacy department also must conduct a regular audit of all pharmacy users' access to secured medication storage areas. Ensure that support and ancillary employees (such as office assistants or clerks) whose job descriptions do not include medication handling do not have access to medication storage areas.

What Drugs are Targeted for Diversion?

Opioids are the most commonly diverted medications in the health care setting by far, but narcotics are not the only drugs at risk of diversion. The choice to divert one drug over another is contingent on the goal of the diverter, as well as whether the drug is stolen for personal use or to sell to others.

Diversion for Personal Use

Diverters who redirect products for personal use tend to begin with less potent oral agents, such as acetaminophen with codeine or acetaminophen with hydrocodone, as access and inventory of these DEA Schedule III drugs is often less restricted compared with Schedule II drugs. As the diverter's tolerance to the narcotic grows, the diversion pattern is likely to intensify. Schedule II and injectable opioids may become the next target.

In an anonymous study of drug misuse among nurses, 20% of those surveyed admitted to misusing one or more prescription substances. Easy access was highly correlated with drug misuse. Among these practitioners[1]:

- 60% used an opioid
- 45% used a tranquilizer
- 11% used sedatives
- 3.5% used amphetamines
- 1.9% used inhalants

Diversion for Sale

An individual who is diverting opioids for sale typically focuses on oral, brand name medications with the highest street value, such as OxyContin and Percocet, or their generic equivalents. Controlled non-opioid medications that may be diverted for sale include the sedatives ketamine and midazolam (see **SIDEBAR**).

CASE REPORT: No Perceived Problem

An inpatient charge nurse called the pharmacy ADC manager to report that furosemide 20 mg tablets were out of stock twice in one week. ADC records indicated that an inventory of 15 tablets should have been in the machine, but the pocket was empty. The ADC manager refilled the pocket and

reviewed the usage reports, finding that the furosemide pocket had been refilled six times in the last three months. One particular nurse had been working every day that the furosemide stock had been refilled. Upon questioning, the nurse admitted that she had an eating disorder and had been taking the furosemide to assist with weight loss. She did not think that taking the diuretic would be a problem because, in her words, it was just furosemide, not a narcotic. In this institution, all diversion was treated equally, regardless of the substance being diverted. The hospital reported the nurse to the police for theft, as well as the state board of nursing. She had to appear before the board and ultimately had action against her license, which remained a permanent part of her professional record.

Where Does Diversion Occur?

Diversion can occur in numerous areas of the hospital; consequently, more than one approach is required for prevention. Quite often, diversion occurs at the patient's bedside.

- **Substitution:** A common method of drug substitution is to replace a patient's prescribed opioid with another agent, such as saline or sterile water. An injection of sterile water will provide a sting (a feeling similar to an injection of the medication), but no therapeutic effects, so the diverter may sedate the patient with diphenhydramine or lorazepam to mask the lack of analgesia. Sometimes the diverter will not remove all of the opioid but dilute it so the patient receives partial pain relief. In one instance, the antipsychotic medication haloperidol was substituted for a diverted opioid.
- **Improper Charting:** Diverters will often put forth considerable effort to identify patients who can be used to cover for their diversion. Non-verbal patients, or those whose reports are considered unreliable, may have difficulty reporting inadequately controlled pain. For patients who are able to respond to a simple pain scale, improper charting may be used to obfuscate the reason for a dosage increase. The diverter will then administer the original dose to the patient, while keeping the remainder for personal use (see **TABLE 1**).

Indicators of Medication Diversion by Staff

TABLES 1 AND 2 were developed at OSU to help guide the Code N team in making decisions about interventions. When reviewing the evidence from software reports, dispensing, and charting, these additional tables help determine the behavioral practices of the suspected diverter. The more Yes answers that are prevalent, the more likely the suspect is diverting medications and an intervention will be planned.

TABLE 1

Patient Care Indicators

Inconsistent or incorrect charting	❑ Yes ❑ No ❑ Unknown
Displays inconsistent work quality with times of high and low efficiency	❑ Yes ❑ No ❑ Unknown
Offers to medicate other nurses' patients on a regular basis	❑ Yes ❑ No ❑ Unknown
Obtains larger dose of narcotics when the ordered dose is unavailable, then documents the remaining amount wasted	❑ Yes ❑ No ❑ Unknown
Requests to care for specific patients	❑ Yes ❑ No ❑ Unknown
Illustrates specific narcotic use with patients under his/her care	❑ Yes ❑ No ❑ Unknown
His/her patients reveal consistent pain scale patterns or complain that narcotics are not having the desired effect (especially when administered PRN) only on that shift	❑ Yes ❑ No ❑ Unknown

TABLE 2

Behavioral Indicators

Isolates self from others, eats meals alone, avoids staff social events	❑ Yes ❑ No ❑ Unknown
Frequent, unexplained disappearances during shift	❑ Yes ❑ No ❑ Unknown
Often shows up on off days to finish work or retrieve forgotten items	❑ Yes ❑ No ❑ Unknown
Frequently volunteers to work extra shifts	❑ Yes ❑ No ❑ Unknown
Frequently spills or wastes narcotics	❑ Yes ❑ No ❑ Unknown
Chaotic home/personal life	❑ Yes ❑ No ❑ Unknown
Refuses to comply with narcotic diversion investigational procedures	❑ Yes ❑ No ❑ Unknown

Click here to view a larger version of these Tables

CASE REPORT: Too Much Information

The pharmacy department set up a phone hotline to enable anonymous reporting of suspicious behavior. The call is recorded and will trigger a page to the narcotics manager. The manager can then alert the pharmacy manager on-call for review and potential action. The intent of the hotline is for immediate reporting of a caregiver impaired while on duty or in the act of diversion.

The hotline received a tip that a nursing unit manager had improperly removed a controlled medication from an ADC that was intended for a patient who had been discharged that day. The ADC had been set to automatically remove patients from the profile eight hours after discharge. When questioned, the manager stated that the patient was coming back to the hospital to pick up the medication. An inventory of the ADC revealed that the manager removed numerous 4 mg syringes of hydromorphone, which is not a medication that would be given to a discharged patient. A search of her office and locker found no evidence of the diverted medication. Further investigation revealed that she had been injecting diverted opioids into grapes and eating them in plain sight of her staff.

The manager had received diversion prevention training, and therefore knew how to run reports and determine if certain activities would be detected. As a manager, she had access to four ADC units. She deduced that if she removed opioids from more than one unit, the standard deviation (SD) report would not compile all of her activity, but instead compare activity on each unit separately. By keeping her activity on each unit less than 2 standard deviations (SD), she could stay below the 4+ SD that would have triggered an investigation. This incident drove home the fact that no one is above suspicion and that caution must be applied in how we train and how much we train. The facility

should be cognizant of not providing the means by which to divert.

Be aware that while training personnel in how to identify diversion, you could be inadvertently providing information that teaches methods for successful diversion. Interestingly, in this instance, the pharmacy department's training program provided the nurse manager with the information that allowed her to divert, while the hospital's anonymous diversion hotline assisted in uncovering her diversion. Nevertheless, educating staff to be observant and vigilant will improve diversion detection and prevention.

Why Do Medical Professionals Divert?

It can be difficult to understand why medical professionals would risk their years of training, professional reputations, and personal livelihoods to engage in drug diversion. However, addiction knows no bounds, and anyone can develop a substance use disorder. Among all drug users, most are functioning in the community and nearly 66% are employed.[3] Furthermore, an estimated 10% to 20% of nurses have substance abuse problems,[4,5] and they tend to abuse prescription drugs instead of street drugs.[6]

CASE REPORT: The Supernurse

Monthly reports from the controlled substances vault showed that a registered nurse on one of our patient care units had a 3+ SD use of controlled substances compared with fellow nurses in the same time frame. Further investigation revealed that this nurse was the only one who gave several patients acetaminophen with oxycodone after charting their pain scales. Review of the charts showed that the highest doses were always removed, and no doses were wasted. The unit's head nurse vouched for the nurse in question, saying he was one of the most well-respected and reputable nurses in the department. She insisted that this nurse was beyond reproach—never taking vacation, always volunteering to work overtime, and available whenever someone called in sick.

Because never wanting to be away from work—where there is access to narcotics—is a potential red flag for diversion (see **TABLE 2**), the decision was made to interview this nurse and ask for an explanation for why his utilization patterns were notably different than his peers. For confidentiality, we interviewed him in a conference room outside his own unit. The nurse denied any wrongdoing and was insulted that we were questioning him. (That reaction was not surprising, as denial is common in substance use interventions.) After he regained his composure, we again asked him to explain the high volume of use and the unusual usage pattern. He emphasized how concerned he was for his patients and that he did not want to see them suffer, unlike some of his colleagues who encouraged patients not to use narcotic pain medication.

When the head nurse questioned his judgment in always offering patients the highest dose, the nurse said that he always removed the highest dose, and if all tablets were not used he would save them for later. We then inquired why he did not follow policy and waste the medication per protocol, and the nurse replied that he did not want to waste other nurses' time and throw away viable medication. The next question was whether or not he sometimes forgot he had the drugs and accidentally took them home after his shift, which he strongly denied. As he became increasingly upset, he was asked how long had he been taking medications from the unit and why he was taking them. At this time, the nurse finally confessed to diverting the drugs. He said he had received prescription pain medications several years ago for a work-related back injury, but that his doctor had refused to prescribe additional narcotics when he would not take time off from work for physical therapy. One day a patient only

wanted one of the two tablets offered, so he took the other tablet. Because no one seemed to notice, this became his method for diversion. He apologized profusely, but explained that using the pain medication was the only way he could get through a shift. As his addiction increased, he volunteered to work more often. He rationalized that his ability to keep working was in the best interest of the hospital. This nurse was placed in a rehabilitation program.

Technology to Monitor for Diversion

In our experience, automated surveillance programs detect about one-half of diversions that are discovered; the other 50% are revealed through direct observation and tips reported to the pharmacy. Although not a substitute for human instinct and evaluation, technology is a vital component of any diversion-prevention program.

Automated Dispensing Cabinets (ADCs): To prevent diversion in the operating suite, accountability requires accurate record keeping for dispensing and waste. The use of ADCs may assist with dispensing accountability, but reconciliation of the inventory is essential.

Spectrophotometry: Some institutions use spectrophotometers to perform a qualitative assay of returned narcotics, as these devices can detect a wrong drug, diluted drug, or missing drug. It is important to be aware of the limitations of these devices, as they cannot detect all types of drugs. When staff is aware that a spectrophotometer is being used, this may deter diversion, but spectrophotometry is only one tool in a comprehensive diversion-prevention program. Keep in mind that a diverter may research which narcotics the spectrophotometer cannot detect. To increase the odds of detection, run random, unpredictable sample assays, and also assay all suspicious returns, whether late, left behind, or returned with missing information.

High-performance liquid chromatography (HPLC) is required to do a quantitative analysis of returned narcotics, but HPLC is beyond the scope of many pharmacies. Waste samples for HPLC must be sent to a toxicology laboratory for evaluation, a process that can be time-consuming and costly.

Diversion Monitoring Software: Diversion-monitoring systems can be useful to screen for variations in utilization. However, for this software to be effective, the pharmacist or technician must be trained to accurately interpret the results. For example, screens set to detect all users at 1+ SD of variance from the mean will return hundreds of false-positive reports, making follow-up impossible. We have found the monthly reports of all users with a threshold of 3+ SD narrows the reports to a more manageable sample group. Each user with 3+ SDs then must be investigated to determine if a reasonable explanation exists for the higher utilization. Although this report works for unit-based users, float nurses may avoid accurate screening unless they themselves are compared as a user group.

Conclusion

Potential diversion opportunities in a health care setting are too numerous for any one individual or technology to monitor effectively. Successful prevention and detection must rely on multiple strategies, and the following have demonstrated effectiveness:

- Incorporate dispensing by users within the pharmacy department in routine diversion-monitoring programs
- Connect time-keeping (clocking-in) devices with ADCs so that access to dispensing systems outside of an employee's work hours can be prevented or more easily detected
- Link pain scale charting to dispensing devices to better correlate higher doses of medication with the patient condition and nursing documentation

- Use bedside bar coding and bar code dispensing to facilitate tracking and detection of discrepancies
- Retrieve data from the EHR on uncharted doses dispensed and review these unreconciled medication reports for trends
- Work with IT data security to program financial/billing systems to identify cases of dispensed but uncharted controlled substances or other medications targeted for diversion

Utilizing multiple diversion-prevention strategies will best ensure diversion is effectively detected, addressed, and prevented at your hospital. While a percentage of hospital staff will always seek to divert drugs, developing and implementing a comprehensive, robust diversion-prevention program is the most effective tool to combat this ongoing challenge.

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Tips for Nurse Training in Diversion Prevention

Fostering a sense of responsibility for controlled substances and other medication products that are commonly diverted should be essential to any nurse training program. Emphasizing accountability and clearly demonstrating the hospital's commitment to diversion prevention and policy enforcement will serve as a powerful measure in creating a safe and responsible work environment. The following are just a sample of actions aimed at this goal:

- Only remove medications for your assigned patients
- Only remove current dose of medication for your patient
- Properly document medication administration and pain scores
- All wastes of medications must have a documented witness
- Do not be a virtual witness to medication wasting
- Do not loan your ID badge or pass-codes to anyone
- Return unused medications according to procedure
- Report medication discrepancies promptly to pharmacy (on-line reporting available)
- Report attempted, inappropriate access to medications to pharmacy
- Report witnessed or suspected medication diversion to pharmacy (hotline number)

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SIDEBAR

Diversion for Sale

Diversion of controlled substances for sale occurs in hospital settings, but is less common than diversion for personal use. Dealing in narcotics often requires large quantities of controlled substances to meet customers' demands. In a patient care area, high-volume diversion should trigger even a basic surveillance system early on.

Larger-scale diversion is more likely to occur in a hospital when the same person orders and receives the inventory. Other diversion-for-sale schemes involve robbery rather than passive diversion. Robberies have increased at outpatient and retail pharmacies as access to prescriptions for controlled substances has become more restricted. Therefore, outpatient pharmacies should be aware of this potential threat.

A proactive diversion program should not focus exclusively on controlled substances, because non-controlled medications of high value also may be diverted. Diversion may occur during shortages (eg, ciprofloxacin tablets during the anthrax scare of 2001) or where health care workers' access make certain agents tempting (eg, fluconazole tablets or diuretics).

Attachment 4

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U.S. NEWS

U.S. to Allow Pharmacies to Take Back Unused Prescription Drugs

New Regulation Will Allow People to Mail Back Unused Pills

By DEVLIN BARRETT

Updated Sept. 8, 2014 7:42 p.m. ET

The government will now allow pharmacies and clinics to accept unused prescription medicine as a way to stop them from ending up on the street. WSJ's Devlin Barrett discusses on the News Hub with Sara Murray. Photo: AP

Federal authorities will soon allow pharmacies and clinics to take back customers' unused prescription drugs such as opioid painkillers in an effort to get addictive medications off the street.

The change, to be issued in new Drug Enforcement Administration regulations effective next month, will address a long-standing complaint from people fighting opioid addiction that government rules make it difficult to safely dispose of unused pills.

Under current rules for controlled substances, even a pharmacy that fills a painkiller prescription can't take back unused pills. Instead, consumers can flush unused drugs or throw them out in the trash, though both those options are discouraged because of environmental worries. They can also hand in unused pills to law-enforcement agencies that participate in special drug-take-back programs.

While pharmacies haven't generally wanted the hassle of being responsible for old pills, some are expected to heed the government's call, in part to show they are making a good-faith effort to keep drugs out of the wrong hands.

WSJ Radio

Devlin Barrett and WSJ This Morning's Gordon Deal discuss this pill return program

00:00 | 06:15

Attorney General Eric Holder announced the new rule in a video posted on the Justice Department's website, noting that close to four in 10 teens who misused prescription drugs obtained them from family medicine cabinets. "These shocking statistics illustrate that prescription drug addiction and abuse represent nothing less than a public health crisis," he said in the video message. "Every day, this crisis touches—and devastates—the lives of Americans from every state, in every region, and from every background and walk of life."

The new rule, which covers all prescription drugs, will also allow people to mail unused pills for collection. It wasn't immediately clear how many businesses would offer the service to its customers. Any pills collected will be destroyed.

Hydrocodone pills, also known as Vicodin, are arranged for a photo at a pharmacy in Montpelier, Vt. on Tuesday, Feb. 19, 2013. *ASSOCIATED PRESS*

The DEA runs its own pill-take-back events. A nationwide effort in April brought in 390 tons of prescription drugs at more than 6,000 sites, according to the Justice Department.

CVS Health Corp. is considering the new regulations, a spokeswoman said, noting the company already participates in drug take-back programs involving local police departments and the DEA. The chain also offers customers postage-paid envelopes to mail back unused pills.

A Walgreen Co. spokesman said the company's pharmacies offer a product that renders pills unusable and safe to toss in the trash, as well as envelopes to mail them to a disposal facility. "We are studying the DEA's new regulatory requirements and considering the options they present to us," he said.

In 2011, more than half of the 41,300 unintentional overdose deaths in the U.S. involved prescription drugs, and opioids—a group of painkillers that include oxycodone and hydrocodone—were involved in nearly 17,000 of those, according to the Justice Department.

Laurey Collins Burris of Shelburne, Vt., who lost her 25-year-old son to an overdose, called the government move "an amazing step forward in getting these drugs off the streets."

Painkiller addiction has led some addicts to seek cheaper highs from heroin, and that is what killed Ms. Burris' son Zachary last October. Getting pills out of homes will make it harder for teenagers and adults to start down that road, she said.

Avi Israel, a Buffalo, N.Y., man whose son killed himself after a battle with prescription drug addiction, said he was skeptical of the rule change, and feared it will invite new forms of abuse.

"Taking the pills back to pharmacies, I think that will open a Pandora's box. It's going to create problems where there's temptation there, there's money to be made," said Mr. Israel, who has advocated instead for every police station to have a drop-off box for prescription drugs.

Write to Devlin Barrett at devlin.barrett@wsj.com

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DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR PARTS 1300, 1301, 1304, 1305, 1307, and 1317

[Docket No. DEA-316]

RIN 1117-AB18

Disposal of Controlled Substances

AGENCY: Drug Enforcement Administration (DEA), Department of Justice.

ACTION: Final rule.

SUMMARY: This rule governs the secure disposal of controlled substances by registrants and ultimate users. These regulations will implement the Secure and Responsible Drug Disposal Act of 2010 by expanding the options available to collect controlled substances from ultimate users for the purpose of disposal, including: take-back events, mail-back programs, and collection receptacle locations. These regulations contain specific language allowing law enforcement to voluntarily continue to conduct take-back events, administer mail-back programs, and maintain collection receptacles. These regulations will allow authorized manufacturers, distributors, reverse distributors, narcotic treatment programs (NTPs), hospitals/clinics with an on-site pharmacy, and retail pharmacies to voluntarily administer mail-back programs and maintain collection receptacles. In addition, this rule expands the authority of authorized hospitals/clinics and retail pharmacies to voluntarily maintain collection receptacles at long-term care facilities. This rule also reorganizes and consolidates previously existing regulations on disposal, including the role of reverse distributors.

DATES: *Effective date*: This rule is effective [INSERT DATE 30 DAYS AFTER PUBLICATION IN THE FEDERAL REGISTER].

Compliance date: All Memoranda of Agreement (MOAs) and Memoranda of Understanding (MOUs) issued pursuant to current 21 CFR 1307.21 will not be effective after [INSERT DATE 30 DAYS AFTER PUBLICATION IN THE FEDERAL REGISTER]. Registrants may consult § 1317.05(a)(5) for information on requesting new MOAs and MOUs for disposal of controlled substances.

FOR FURTHER INFORMATION, CONTACT: Imelda L. Paredes, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION:

Outline

I. Executive Summary

A. Purpose of the Regulatory Action

B. Summary of the Major Provisions of the Regulatory Action

C. Summary of Changes in the Final Rule

II. Background and Legal Authority

III. Discussion of Comments

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C. Types of Entities That May Operate a Collection Program (9 issues)

D. Locations Where Authorized Collectors May Maintain Collection Receptacles or

Host Take-Back Events (1 issue)

E. Registration Requirements for Authorized Collectors (5 issues)

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K. Long-Term Care Facilities (LTCFs) (21 issues)

L. Disposing on Behalf of Ultimate Users (Other than Residents of LTCFs) (3 issues)

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S. Miscellaneous Comments (2 issues)

IV. Regulatory Analyses

I. Executive Summary

A. *Purpose of the Regulatory Action*

On October 12, 2010, the Secure and Responsible Drug Disposal Act of 2010 (Disposal Act) was enacted (Pub. L. 111-273, 124 Stat. 2858). Before the Disposal Act, ultimate users

who wanted to dispose of unused, unwanted, or expired pharmaceutical controlled substances had limited disposal options. The Controlled Substances Act (CSA) only permitted ultimate users to destroy those substances themselves (e.g., by flushing or discarding), surrender them to law enforcement, or seek assistance from the United States Drug Enforcement Administration (DEA). These restrictions resulted in the accumulation of pharmaceutical controlled substances in household medicine cabinets that were available for abuse, misuse, diversion, and accidental ingestion.

The Disposal Act amended the CSA to authorize ultimate users to deliver their pharmaceutical controlled substances to another person for the purpose of disposal in accordance with regulations promulgated by the Attorney General. 21 U.S.C. 822(g), 828(b)(3). This final rule implements regulations that expand the entities to which ultimate users may transfer unused, unwanted, or expired pharmaceutical controlled substances for the purpose of disposal, as well as the methods by which such pharmaceutical controlled substances may be collected. Specified entities may voluntarily administer any of the authorized collection methods in accordance with these regulations.

B. *Summary of the Major Provisions of the Regulatory Action*

The DEA is implementing new regulations for the disposal of pharmaceutical controlled substances by ultimate users in accordance with the Disposal Act. In drafting the implementing regulations, the DEA considered the public health and safety, ease and cost of program implementation, and participation by various communities. To this end, the DEA found that in order to properly address the disposal of controlled substances by ultimate users, it was necessary to conduct a comprehensive review of DEA policies and regulations related to each element of the disposal process, including the transfer, delivery, collection, destruction, return,

and recall of controlled substances, by both registrants and non-registrants (i.e., ultimate users). The reverse distributor registration category, which is pertinent to the process of registrant disposal, was included in this comprehensive review. These regulations are incorporated into a new part 1317 on disposal. Definitions relating to the disposal of controlled substances are added to § 1300.05(b), including definitions for "employee," "law enforcement officer," "non-retrievable," and "on-site" and definitions relating to controlled substances generally are revised or added to § 1300.01.

The goal of this new part on disposal, consistent with Congress's goal in the Disposal Act, is to set parameters for controlled substance diversion prevention that will encourage public and private entities to develop a variety of methods for collecting and destroying pharmaceutical controlled substances in a secure, convenient, and responsible manner. Also, consistent with the Disposal Act's goal to decrease the amount of pharmaceutical controlled substances introduced into the environment, particularly into the water, these regulations provide individuals with various additional options to dispose of their unwanted or unused pharmaceutical controlled substances beyond discarding or flushing the substances. As a result of these regulations, the DEA hopes that the supply of unused pharmaceutical controlled substances in the home will decrease, thereby reducing the risk of diversion or harm.

Ultimate User Disposal

An ultimate user is defined by the CSA as a "person who has lawfully obtained, and who possesses, a controlled substance for his own use or for the use of a member of his household or for an animal owned by him or by a member of his household." 21 U.S.C. 802(27). This rule provides three voluntary options for ultimate user disposal: (1) take-back events, (2) mail-back programs, and (3) collection receptacles. Individuals lawfully entitled to dispose of an ultimate

user decedent's property are authorized to dispose of the ultimate user's pharmaceutical controlled substances by utilizing any of the three disposal options. All of the collection methods are voluntary and no person is required to establish or operate a disposal program. The rule also does not require ultimate users to utilize any of these three methods for disposal of controlled substances. Although the three methods of disposal allowed by this rule seek to help protect the environment and prevent controlled substances from being diverted to illicit uses, this rule does not prohibit ultimate users from using existing lawful methods.

The DEA regulations provide specific language that will continue to allow Federal, State, tribal, and local law enforcement to maintain collection receptacles at the law enforcement's physical location; and either independently or in partnership with private entities or community groups, to voluntarily hold take-back events and administer mail-back programs. 21 CFR 1317.35. Thus, ultimate users will continue to be able to surrender their unwanted pharmaceutical controlled substances to law enforcement.

The DEA is also authorizing certain registrants (manufacturers, distributors, reverse distributors, narcotic treatment programs (NTPs), hospitals/clinics with an on-site pharmacy, and retail pharmacies) to be "collectors," with authorization to conduct mail-back programs. 21 CFR 1317.40 and 1317.70. All registrants that choose to establish mail-back programs must provide specific mail-back packages to the public, either at no cost or for a fee, 21 CFR 1317.70. Collectors that conduct mail-back programs must have and utilize an on-site method of destruction to destroy returned packages, 21 CFR 1317.05.

These DEA regulations authorize collectors to maintain collection receptacles at their registered location. 21 CFR 1317.40. Thus, ultimate users will be able to carry their unwanted pharmaceutical controlled substances to an authorized retail pharmacy or other authorized

collector location and deposit those controlled substances in a secure container for disposal. Hospitals/clinics and retail pharmacies that are authorized to be collectors may also maintain collection receptacles at long-term care facilities (LTCFs). 21 CFR 1317.40. LTCFs may dispose of pharmaceutical controlled substances on behalf of an ultimate user who resides, or has resided, at that LTCF, 21 CFR 1317.80, through a collection receptacle that is maintained by an authorized hospital/clinic or retail pharmacy at that LTCF. 21 CFR 1317.40 and 1317.80.

With this rule, the DEA allows all pharmaceutical controlled substances collected through take-back events, mail-back programs, and collection receptacles to be comingled with non-controlled substances, although such comingling is not required. 21CFR 1317.65, 1317.70, and 1317.75. Pharmaceutical controlled substances collected by collectors may not be individually counted or inventoried. 21 CFR 1317.75. This rule also imposes various registration, security, and recordkeeping requirements.

The DEA appreciates there is a cost to entities that choose voluntarily to provide these methods of collection and destruction. The DEA acknowledges that some State and local pharmaceutical disposal programs receive funding and other support from numerous sources, including conservation groups, local governments, State grants, and public and private donations. These expanded methods of disposal are expected to benefit the public by decreasing the supply of pharmaceutical controlled substances available for misuse, abuse, diversion, and accidental ingestion, and protect the environment from potentially harmful contaminants by providing alternate means of disposal for ultimate users. However, other advantages may accrue directly to those entities that opt to maintain a disposal program. For example, those authorized registrants that choose to maintain collection receptacles may be enhanced by the increased consumer presence at their registered locations and the goodwill that develops from providing a valuable

community service. In addition, mail-back program collectors may partner with third parties to make mail-back packages available to the public. Those authorized registrants that choose to administer mail-back programs may gain from the opportunity to distribute to consumers promotional, educational, or other informational materials with the mail-back packages.

DEA Registrant Disposal

The DEA has deleted the existing rule related to registrant disposal, 21 CFR 1307.21, and incorporated similar requirements on proper disposal procedure and security in a new part 1317 on disposal. These changes provide consistent disposal procedures for each registrant category, regardless of geographic location. In addition, the DEA has modified DEA Form 41 and is explicitly requiring that form to be used to record the destruction of controlled substances that remain in the closed system of distribution and also to account for registrant destruction of pharmaceutical controlled substances collected from ultimate users and other non-registrants pursuant to the Disposal Act. As stated in the NPRM, a controlled substance dispensed for immediate administration pursuant to an order for medication in an institutional setting remains under the custody and control of that registered institution even if the substance is not fully exhausted (*e.g.*, some of the substance remains in a vial, tube, transdermal patch, or syringe after administration but cannot or may not be further utilized, commonly referred to as "drug wastage" and "pharmaceutical wastage"). Such remaining substance must be properly recorded, stored, and destroyed in accordance with DEA regulations (*e.g.*, § 1304.22(c)), and all applicable Federal, State, tribal, and local laws and regulations, although the destruction need not be recorded on a DEA Form 41.

Reverse Distributors

The DEA is providing regulations for entities that reverse distribute that are clear and

consistent. Entities that reverse distribute are often the last registrant to possess controlled substances prior to destruction; however, the recordkeeping safeguards that exist when controlled substances are distributed between registrants are not present when these registrants destroy controlled substances. Because reverse distributors routinely acquire controlled substances for destruction from other registrants and may also be authorized as collectors, reverse distributors accumulate greater amounts of controlled substances that are destined for destruction in comparison to other registrants. The DEA is defining "reverse distribute;" revising the definition of "reverse distributor;" (21 CFR part 1300) outlining security (21 CFR part 1301), inventory, recordkeeping requirements, and other procedures that reverse distributors must follow to acquire controlled substances from registrants and to destroy such acquired substances. 21 CFR part 1304. The DEA also is clarifying that these security, inventory, and recordkeeping requirements apply to certain specified entities that reverse distribute but are not registered as reverse distributors. *See, e.g.*, 21 CFR 1304.11(e)(3) ("each person registered or authorized to reverse distribute"). The DEA believes that these regulations will help all registrants that reverse distribute comply with the CSA in a manner that decreases the risk of the diversion of controlled substances during the disposal process.

Return and Recall

This rule removes the existing regulation on return and recall, 21 CFR 1307.12, and incorporates separate return and recall requirements for registrants and non-registrants into new §§ 1317.10 and 1317.85. This rule also imposes various recordkeeping requirements pertaining to controlled substances acquired for the purpose of return or recall in §§ 1304.22 and 1305.03. The DEA has simplified the requirements of § 1317.10(a) to more clearly describe the records that registrants must keep.

Methods of Destruction

Existing DEA regulations do not specify a standard to which controlled substances must be destroyed. With this final rule, the DEA is implementing a standard of destruction—non-retrievable—for registrants that destroy controlled substances, and procedures for the destruction of controlled substances. 21 CFR 1300.05 ("non-retrievable"), 1317.90, and 1317.95. The DEA is not requiring a particular method of destruction, so long as the desired result is achieved. This standard is intended to allow public and private entities to develop a variety of destruction methods that are secure, convenient, and responsible, consistent with preventing the diversion of such substances. Destruction of controlled substances must also meet all other applicable Federal, State, tribal, and local laws and regulations. Once a controlled substance is rendered "non-retrievable," it is no longer subject to the requirements of the DEA regulations.

As explained above under "Compliance Date," this final rule supersedes all existing MOAs and MOUs that registrants may have pursuant to § 1307.21, including MOAs and MOUs pertinent to storage of controlled substances. The DEA retains in the new part 1317 the ability for practitioners to request assistance from the local Special Agent in Charge (SAC) regarding the disposal of controlled substances. 21 CFR 1317.05. Practitioners may request a new MOA or MOU pursuant to the new § 1317.05(a)(5).

C. *Summary of the Changes in the Final Rule*

The DEA carefully considered the 192 individually-submitted comments received in response to the Notice of Proposed Rulemaking (NPRM) on the Disposal of Controlled Substances.[1] 77 FR 75784, Dec. 21, 2012. The comment period closed on February 19, 2013.

[1] All of the comments submitted, except two comments, are available for public inspection online at www.regulations.gov. Two comments are not posted (at the commenters' request) in order to protect confidential business information.

The DEA is making a number of significant changes after thorough consideration of the issues raised by the comments and the potential diversion risks associated with these changes.

In response to concerns regarding ultimate users' ability to have convenient disposal options, the DEA is vastly expanding those entities that may be authorized as collectors, expanding the authority of those collectors to maintain collection receptacles at LCTFs, and relaxing some of the proposed security requirements related to storage and destruction of controlled substances.

Authorized Collectors

In addition to manufacturers, distributors, reverse distributors, and retail pharmacies, the final rule also authorizes registered NTPs, as well as hospitals/clinics with an on-site pharmacy, to operate disposal programs. 21 CFR 1317.40. By permitting these additional registrant categories to be collectors, the DEA anticipates that ultimate users will now have even more locations where they can securely, safely, responsibly, and conveniently dispose of their unwanted pharmaceutical controlled substances.

In this final rule, the DEA is permitting those entities registered as NTPs to become authorized collectors to manage collection receptacles at their registered locations. As stated in the Disposal Act, "the nonmedical use of prescription drugs is a growing problem in the United States." Multiple commenters, including a national organization that represents NTPs, recommended that the DEA include NTPs as authorized collectors. The DEA recognizes the valuable role that NTPs have in helping those seeking substance abuse treatment. After considering the importance of providing secure, convenient, and responsible disposal options for those ultimate users currently receiving treatment for narcotic substance abuse or entering a narcotic treatment program, and the benefits of allowing NTPs to provide the opportunity to

patients to dispose of unused controlled substances, the DEA is permitting NTPs to be collectors with certain enhanced security controls. 21 CFR 1317.75.

Due to the nature of the healthcare provided, NTPs face unique security challenges and heightened diversion risks and, as such, the final rule requires NTPs to securely place and maintain collection receptacles in a room that does not contain any other controlled substances and is securely locked with controlled access. 21 CFR 1317.75. The DEA understands that this security measure will require employees of the NTP to accompany the patient to the collection receptacle to facilitate the patient's disposal. *See* 21 CFR 1317.75. Additionally, as the Disposal Act and these regulations are intended to address the *prescription* drug abuse problem, NTPs and other collectors are not authorized to collect schedule I controlled substances. *E.g.*, 21 CFR 1317.75. Collectors must be vigilant in ensuring that such illicit substances are not collected intentionally or inadvertently. *E.g.*, 21 CFR 1317.70 and 1317.75.

After extensive review and careful deliberation, in this final rule, the DEA is also permitting registered hospitals/clinics with an on-site pharmacy to become authorized collectors to maintain collection receptacles inside their registered locations or at LTCFs, and to conduct mail-back programs. 21 CFR 1317.30, 1317.40, 1317.70, and 1317.80. In response to the NPRM, many commenters stated that collection receptacles located inside of hospitals would provide ultimate users with an opportunity to dispose of medication that may no longer be needed or may be expired. In determining whether to allow hospitals/clinics to become authorized collectors, the DEA carefully weighed the diversion risks with the convenience of authorizing such entities to be collectors. The DEA determined that the diversion risks require the DEA to limit those registered hospitals/clinics that may become collectors to those with on-site pharmacies, and also impose separate security conditions on the monitoring and location of

collection receptacles inside hospitals/clinics that become authorized collectors. 21 CFR 1317.75.

The DEA is requiring these additional security measures in order to help protect against the diversion of collected controlled substances because hospitals/clinics are generally much larger and are open to a much larger general population than the other registrants authorized to be collectors; and, as discussed in the NPRM, hospitals/clinics do not operate under the same business model or with similar theft and loss prevention procedures as the other registrants authorized to become collectors. For example, the general public typically enters retail pharmacies for short durations in order to conduct retail business and retail pharmacies generally have open, clearly observable common areas with little opportunity to conceal an unlawful purpose. It would be unusual and suspicious for a person to spend an extended amount of time in a retail pharmacy without a known, specific purpose, triggering routine theft and loss prevention measures.

In contrast, hospitals are generally open 24-hours per day and allow for unsupervised public access for extended periods of time; they are much larger than retail pharmacies and many interactions occur behind closed doors without routine theft and loss prevention measures; and foot traffic generally is not routinely monitored for unlawful purposes. The DEA believes that limiting authorized collection activities to hospitals/clinics with an on-site pharmacy is necessary to help protect against diversion because these hospitals/clinics routinely handle a large volume of controlled substances that are dispensed to in-patients as well as to the public, and these entities are more experienced with security, theft and loss prevention procedures, and inventory, recordkeeping and reporting requirements than those hospitals/clinics without an on-site pharmacy.

For reasons discussed in the NPRM, this final rule generally requires that, when authorized collectors choose to install collection receptacles, those collection receptacles must be placed inside their registered locations in the immediate proximity of a designated area where controlled substances are stored and at which an employee is present. 21 CFR 1317.75; *see also* 1317.05. The DEA recognizes that hospitals/clinics with an on-site pharmacy can be unique in their design and it may be more effective to install collection receptacles at various locations within the hospital/clinic, depending on factors such as security, convenience, and accessibility. As such, it would be challenging for authorized hospitals/clinics to adhere to the general rule to place collection receptacles in the immediate proximity of where controlled substances are stored and at which an employee is present. Accordingly, the DEA is requiring hospitals/clinics that are collectors to place collection receptacles in locations that are regularly monitored by employees. 21 CFR 1317.75. In addition, the DEA is prohibiting such collectors from placing collection receptacles in the proximity of any area where emergency or urgent care is provided. In the DEA's experience, the risk of diversion is particularly high in areas where emergency or urgent care is provided because of the often chaotic environment and the extended amounts of time persons spend in such areas.

This rule also makes clear that DEA registrants cannot use the collection receptacles to dispose of unused controlled substances in their inventory or stock. 21 CFR 1317.05 and 1317.75. Pharmaceutical controlled substances remain under the custody and control of the DEA registrant if they are dispensed by a practitioner for immediate administration at the practitioner's registered location (such as a hospital) pursuant to an order for medication. If that substance is not fully exhausted (*e.g.*, some of the substance remains in a vial, tube, or syringe after administration but cannot or may not be further utilized), then the DEA registrant is

obligated to destroy the remaining, unusable controlled substances, and record the destruction in accordance with § 1304.22(c). The DEA registrant shall not place such remaining, unusable controlled substance in a collection receptacle as a means of disposal. Hospital/clinic staff must also not dispose of any controlled substances in inventory or stock in a collection receptacle.

The security requirements described above are the minimum required in order to detect and prevent diversion in the unique circumstances of NTPs and hospitals/clinics. These registrants should be vigilant in the execution of their responsibilities as registrants to ensure that collected controlled substances are not diverted to illicit use, and that they do not collect illicit substances. Finally, all registrants are reminded of the responsibility to report theft and significant loss of controlled substances within one business day of discovery.

Long-Term Care Facilities (LTCFs)

Significant changes are made in this final rule to help ensure that LTCFs have adequate disposal options. In addition to allowing retail pharmacies to manage and maintain collection receptacles at LTCFs, the DEA is also allowing hospitals/clinics with an on-site pharmacy to manage and maintain collection receptacles at LTCFs. The DEA hopes that expanding those authorized to collect at LTCFs will maximize disposal opportunities for LTCF residents.

In addition, the DEA is alleviating two security requirements proposed to apply to collection receptacles located at LTCFs. First, the DEA is permitting authorized hospitals/clinics and retail pharmacies to store inner liners that have been sealed upon removal from a collection receptacle at LTCFs in a securely locked, substantially constructed cabinet or a securely locked room with controlled access for up to three business days until the liners can be transferred for destruction. The DEA encourages collectors to schedule inner liner removals and installations to coincide with existing LTCF visits when possible, for example, arranging a routine system in

which medication deliveries coincide with the removal and transfer of sealed inner liners for appropriate destruction, thereby making storage of sealed inner liners unnecessary. Collectors may not transfer sealed inner liners from LTCFs to their primary registered location (i.e., the hospital/clinic or retail pharmacy location). As echoed in the comments, the DEA remains concerned about the security risks of hospital/clinic and retail pharmacy employees transporting large quantities of collected substances, making them potential targets for drug seekers. Instead, collectors should deliver sealed inner liners to a reverse distributor or distributor's registered location by common or contract carrier pick-up or by reverse distributor or distributor pick-up at the LTCF, pursuant to § 1317.05(c)(2)(iv).

Second, the DEA relaxed the two-employee integrity requirement for inner liner installation, removal, storage, and transfer at LTCFs. Collectors will retain the option to authorize two of their own employees to install, remove, store, and transfer inner liners; however, the DEA is permitting collectors the option to designate a supervisor-level employee of the LTCF (*e.g.*, a charge nurse, supervisor, or similar employee) to install, remove, store, or transfer inner liners with only one employee of the collector.

The DEA modified the above security requirements (storage and two-person integrity) to provide flexibility sufficient to encourage authorized hospitals/clinics and retail pharmacies to collect at LTCFs, while ensuring the minimum protections required to prevent diversion at LTCFs. The DEA hopes that the inclusion of certain hospitals/clinics as authorized to maintain collection receptacles at LTCFs, and the modifications described above will result in expanded safe and secure disposal options for LTCF residents. The DEA emphasizes that if LTCFs dispose of LTCF residents' controlled substances in collection receptacles, such activity must be in accordance with this regulation and all other applicable Federal, State, tribal and local laws

and regulations, including environmental laws and regulations.

The DEA acknowledges that there may be some LTCFs that will not have a collection receptacle, and there will be instances where LTCF residents are incapable of disposing of their own unused or unwanted medication. As ultimate users, LTCF residents may use any of the disposal options afforded other ultimate users in this final rule (e.g., mail-back programs), in addition to the disposal options currently available to ultimate users (e.g., flushing or otherwise discarding) that will remain options even after this final rule is implemented. For example, an LTCF resident may request that LTCF personnel place the resident's unwanted medication in a mail-back package, seal the mail-back package, and deposit that package into the facility's outgoing mail system. 21 CFR 1317.70. LTCFs should be mindful however that the touchstone for this disposal method is the individual nature of the disposal activity; institutional facilities such as LTCFs should ensure that the individual patient is the disposer, and should be wary of establishing any protocols whereby the facility itself is engaging in collection activities. Simply providing the method of disposal (e.g., mail-back packages) does not implicate that concern.

Destruction

After careful and thorough consideration of comments received regarding the burdens associated with the proposed 14-day destruction requirement, the DEA is extending the time those registrants that reverse distribute have to destroy controlled substances to 30 days. 21 CFR 1317.15(d). The DEA anticipates that this extension will allow reverse distributors and distributors adequate time to collect and destroy controlled substances in a safe, convenient, and secure manner, while also preventing diversion and diversion opportunities.

Practitioner Physical Security

In this final rule, the DEA is not amending § 1301.75(b) pertaining to practitioner

physical security and is instead adding a new paragraph (c) to clarify that practitioners shall only store sealed mail-back packages and inner liners containing collected substances at their registered location in a securely locked, substantially constructed cabinet or a securely locked room with controlled access. The DEA has made corresponding changes to §§ 1317.05(c)(1)(ii) and (c)(2)(ii). Part of this requirement was included in the proposed rule; however, after careful consideration of a number of comments, the DEA believes that the proposed requirement did not provide sufficient controls to protect against diversion and was impracticable. Pharmacies and institutional practitioners cannot store sealed inner liners or returned mail-back packages by dispersing them throughout the stock of noncontrolled substances. 21 CFR 1301.75(b) and (c).

Other Changes to the final rule

In addition to the changes described above, the DEA determined that the rule, as proposed, required other modifications, as generally described below. The DEA is also implementing additional technical modifications that will not have a substantive effect on this rule (e.g., relocating some sections in proposed part 1317 to other sections within title 21 of the CFR, re-phrasing some sections from the proposed rule to be simpler, clearer and easier to understand, and eliminating redundancy).

In the general definitions section of the DEA regulations, the DEA is amending § 1300.01(b) to be clear that the definitions that generally apply to most other parts of chapter II of title 21 of the CFR also apply to part 1317. In response to a number of comments, in § 1300.01(b) the DEA is amending the definition of "reverse distributor" to clarify that a reverse distributor is a person registered with the DEA as a reverse distributor.

Definitions were moved from § 1317.02 to § 1300.05 to provide consistency within the CFR pertaining to definitions. The DEA adds § 1300.05 "Definitions relating to the disposal of

controlled substances," moves the terms "authorized employee," "law enforcement officer," and "non-retrievable" from part 1317 to § 1300.05(b), adds a definition of "on-site" to § 1300.05(b), and deletes the definitions of "for cause" and "inner liner" that were in proposed part 1317. The DEA also moves the definition of "collection" to § 1300.01(b). These changes are in response to comments or related to the movement of several other requirements from part 1317 to other parts, as discussed below.

In addition to moving them to § 1300.05(b), the DEA amends the definitions of "authorized employee" and "law enforcement officer." The DEA is omitting the word "authorized" from the definition of "authorized employee," and codifying the definition of "employee" in harmony with the general common law of agency. The DEA is modifying the definition of "law enforcement officer" in part 1317 to specifically include officers from law enforcement components of Federal agencies, and authorized police officers of the Veterans Health Administration and the Department of Defense. In addition, this rule clarifies who may qualify as a "law enforcement officer" for the purpose of disposal. The DEA is changing references to "law enforcement agencies" to "law enforcement" in order to include law enforcement components of Federal agencies.

Although the DEA defined "inner liner" in the NPRM, the final rule does not amend the CFR to add a definition for inner liner. As described below, inner liners used in the collection of controlled substances must meet the specifications outlined in § 1317.60. The DEA also is not amending the CFR to add a definition of "for cause," and instead is providing an explanation of "for cause" as it relates to the sections to which it applies.

The DEA added a definition of "on-site" to § 1300.05(b) to clarify that "on-site" means "located on or at the physical premises of the registrant's registered location" for purposes of

destruction and registration as a collector. Specifically, a controlled substance is destroyed "on-site" when destruction occurs on the physical premises of the destroying registrant's registered location, and a hospital/clinic has an "on-site" pharmacy when it has a pharmacy located on the physical premises of the registrant's registered location.

Text was added to the registration table in § 1301.13 to reflect that distributors, as a coincident activity to distribution, may acquire controlled substances from collectors for the purpose of destruction. The registration table was updated so that it would be consistent with the regulations in the final rule, which authorize distributors to destroy controlled substances acquired from collectors.

The DEA received a number of comments indicating confusion regarding the procedures a registrant must follow to modify their DEA registration to become a collector. In order to clarify such requirements, the DEA is further revising § 1301.51. The additional revisions clarify the requirements by listing them independently of other types of registration modifications (e.g., change of name or address) and clearly indicating that any modifications may be made in writing by mail or online. 21 CFR part 1301. Also, the submission method has been modified from "letter" to "written request" to accurately encompass the various ways the modification request may be submitted (e.g., online), and the phrase "to be paid" was deleted from § 1301.51(c) for stylistic reasons. Similarly, the DEA is further revising § 1301.52 to clarify that any registrant who has been authorized as a collector and who desires to discontinue their collection of pharmaceutical controlled substances from ultimate users must notify the DEA.

The DEA is also streamlining certain registration and security procedures by moving certain requirements from part 1317, as proposed in the NPRM, to part 1301. Reverse distributor

employee security requirements in proposed § 1317.20 were moved to § 1301.74(m) for ease of reference and consistency. Collector security requirements in proposed § 1317.45 were moved to § 1301.71(f) for clarity and consistency.

The DEA determined that inclusion of recordkeeping and reporting requirements in part 1317 may lead to confusion among registrants. As such, the DEA is moving all recordkeeping and reporting requirements from part 1317, as proposed in the NPRM, to part 1304—Records and Reports of DEA Registrants—in order to maintain consistency and consolidate all recordkeeping and reporting requirements into one part. In § 1304.03, "each" was changed to "every," and "who" was changed to "that" for stylistic reasons. In § 1304.11(e)(2), the first sentence, pertaining to an exception for reverse distributors, was removed and incorporated into § 1304.11(e)(3) of the final rule to accurately reflect the type of registrants to which the section applies.

The DEA is expanding the locations where a collector may maintain records in § 1304.04(a)(3). The text in § 1304.21(a) was updated to specifically include inner liners and mail-back packages, which were inadvertently overlooked in the NPRM. 21 CFR § 1304.21(c) was updated to include the general recordkeeping requirements for collection activities as outlined in the final rule. The recordkeeping requirements for disposal of controlled substances in 21 CFR § 1307.21 were moved to § 1304.21(e) and amended to include recordkeeping procedures for destruction. The title and introductory text in § 1304.22 were updated to accurately reflect their contents. Additionally, § 1304.22 was modified to include recordkeeping requirements for collected controlled substances. The second sentence in both § 1304.25(a)(9) and § 1304.25(b)(9), which required compliance with part 1317 when destroying narcotic controlled substances, were removed as superfluous. All disposal and destruction activities are

clearly delineated in part 1317. Also, various Automation of Reports and Consolidated Ordering System (ARCOS) requirements are removed from part 1317, as proposed in the NPRM, and are consolidated and moved to § 1304.33. In addition, the title of § 1304.33 has been changed to add clarity, and the acronym "ARCOS" is clearly spelled out. The formatting for § 1304.33(f) was modified for ease of understanding, and "who" was changed to "that" in two locations for consistency.

The DEA is also amending § 1305.03 to add a new paragraph (f) to clarify that collectors are exempt from order form requirements for pharmaceutical controlled substances collected through mail-back programs and collection receptacles for the purpose of disposal. The title of § 1307.11 no longer references reverse distributors and has been changed to "Distribution by dispenser to another practitioner" because reverse distributor activities were moved to part 1317.

As discussed in the preamble to the NPRM and as mentioned in proposed § 1317.100, the DEA clarifies in § 1304.21 of this final rule that, in addition to any other recordkeeping requirements, all registrants that destroy or cause the destruction of a controlled substance must maintain a record of that destruction on a DEA Form 41. This requirement had been discussed in the preamble to the proposed rule, and in proposed § 1317.100 the DEA stated "any registered person that destroys or causes the destruction of a controlled substance shall maintain a record of destruction on a form issued by DEA…." The DEA has determined that this requirement to keep such records on DEA Form 41 should be explicitly stated in the regulatory text, and not just the preamble, for registrants to clearly understand the requirements to which they are bound. As stated above, this requirement to record destruction activities on the DEA Form 41 does not apply to drug wastage or pharmaceutical wastage which must be properly recorded, stored, and destroyed in accordance with DEA regulations, and all applicable Federal, State, tribal, and local

laws and regulations. 21 CFR part 1304.

The DEA is modifying proposed § 1317.70 to address the procedures that a collector must follow when ceasing operation of a mail-back program. This modification requires such collector to make reasonable efforts to notify the public of their intent to cease mail-back collection activities. 21 CFR 1317.70. Such collector must also establish an agreement with another collector authorized to conduct a mail-back program to receive all remaining packages and arrange for the forwarding of such packages to the second collector's registered location. These procedures will ensure that another authorized entity will be responsible for receiving and destroying any mail-back packages that were disseminated but not received back by the collector prior to the time that they ceased operation of their mail-back program.

Finally, the DEA is modifying proposed § 1317.75 for two purposes. The first modification clarifies that collected controlled and non-controlled substances can be comingled, but are not required to be comingled. 21 CFR 1317.75. As previously discussed, the second modification to this section allows certain LTCF employees, as designated by the collector authorized to maintain a collection receptacle at that LTCF, to install, seal, remove, store, and transfer for destruction the inner liners of the collection receptacle along with an employee of the collector. 21 CFR 1317.80. This modification allows greater flexibility for collectors authorized to maintain collection receptacles at LTCFs.

II. Background and Legal Authority

The DEA implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. Titles II and III are referred to as the "Controlled Substances Act" and the "Controlled Substances Import and Export Act," respectively, but are collectively referred to as the "Controlled Substances Act" or the "CSA" for

the purpose of this action. 21 U.S.C. 801–971. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), parts 1300 to 1321. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while providing for a sufficient supply of controlled substances and listed chemicals for legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety. To this end, controlled substances are classified into one of five schedules based upon: the potential for abuse, currently accepted medical use, and the degree of dependence if abused. 21 U.S.C. 812. Listed chemicals are separately classified as list I or list II chemicals based on their use and importance to the manufacture of controlled substances. 21 U.S.C. 802(33)–(35).

The CSA establishes a closed system of distribution that requires the DEA to monitor and control the manufacture, distribution, dispensing, import, and export of controlled substances and listed chemicals until they reach their final lawful destination. The secure destruction of unused, recalled, tainted, expired, or otherwise unwanted pharmaceutical controlled substances is essential to preventing the diversion of these substances into the illicit market.

In order to maintain this closed system of distribution, persons who handle (manufacture, distribute, dispense, import, export, engage in research, or conduct instructional activities), or propose to handle, controlled substances and listed chemicals are required to register with the DEA at each principal place of business or professional practice. Persons registered with the DEA are permitted to possess controlled substances and listed chemicals as authorized by their registration and must comply with the applicable requirements associated with their registration. 21 U.S.C. 822.

Not all persons who possess controlled substances are required to register with the DEA. For example, a patient who receives a pharmaceutical controlled substance pursuant to a lawful prescription, i.e., an ultimate user, is not required to register with the DEA in order to receive and possess that substance. 21 U.S.C. 822(c)(3); *see also* 21 U.S.C. 957(b)(1)(C).[2] The CSA defines an "ultimate user" as "a person who has lawfully obtained, and who possesses, a controlled substance for his own use or for the use of a member of his household or for an animal owned by him or by a member of his household." 21 U.S.C. 802(27).

While Congress envisioned a closed system of distribution that would control a substance from its manufacture or import through the traditional chain of distribution moving from registrant to registrant until it reached its final lawful use (e.g., dispensed to the ultimate user, etc.), it did not account for circumstances in which pharmaceutical controlled substances were lawfully dispensed to, and possessed by, an ultimate user but not fully used. Although ultimate users are exempt from CSA registration requirements for the possession of pharmaceutical controlled substances, if they distribute (e.g., deliver or transfer) such substances without the appropriate registration, they are in violation of the CSA.[3] Such unlawful distribution includes the transfer of pharmaceutical controlled substances for the purpose of disposal.[4]

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[2] 21 U.S.C. 822(c)(3) and 957(b)(1)(C) except "ultimate users" who possess substances for purposes referenced in 21 U.S.C. 802(25); however, "ultimate user" is defined in 21 U.S.C. 802(27).

[3] It is unlawful to knowingly or intentionally manufacture, distribute, dispense, or possess with the intent to manufacture, distribute, or dispense, a controlled substance without the appropriate registration. 21 U.S.C. 841(a).

[4] The terms "disposal," "dispose," or "disposition" appear several times in the CSA and its implementing regulations, but are not defined. For example, in the CSA, see 21 U.S.C. 822(g); 824(f)–(g); 826(c), (e)–(f); 827(a)(3), (d)(1); 842(a)(7); 853(n); 880(a)(2); 881(e)(1); 958(d)(6); and in the CFR, see 21 CFR 1307.21(b) and 1304.22(a)(2)(ix). The term "net disposal," however, is defined at 21 CFR 1300.01(b). As used, the terms refer to a variety of activities that ultimately result in eliminating the availability of controlled substances for use. For example, within the meaning of the CSA, a controlled substance can be "disposed of" by destruction, return, recall, sale, or through the manufacturing process. The Disposal Act allows an ultimate user to deliver a lawfully obtained controlled substance to another person "for the purpose of disposal." The DEA believes that the ultimate user disposal authorized by the Disposal Act includes the transfer or delivery of controlled substances for purposes of destruction, return, and recall. Such ultimate user activities are consistent with the intent to remove unused, unwanted, tainted, and expired substances from households and out of the reach of children and teenagers thereby

The Disposal Act, enacted on October 12, 2010, amended the CSA to allow an ultimate user to "deliver" a pharmaceutical controlled substance "to another person for the purpose of disposal" if the person receiving the substance is authorized to receive it and the disposal takes place in accordance with regulations issued by the Attorney General to prevent the diversion of controlled substances. 21 U.S.C. 822(g)(1). The Attorney General delegated responsibility for promulgating the Disposal Act implementing regulations to the DEA.[5]

In addition to authorizing ultimate users to deliver their pharmaceutical controlled substances to another person for the purpose of disposal, the Disposal Act also authorizes any person lawfully entitled to dispose of an ultimate user decedent's property to deliver the ultimate user's pharmaceutical controlled substances to another person for the purpose of disposal if the ultimate user dies while in lawful possession of the substances. The Disposal Act also gives the DEA the ability, by regulation, to authorize LTCFs to dispose of pharmaceutical controlled substances on behalf of ultimate users who reside, or have resided, at the LTCF. Congress directed the DEA, in promulgating the Disposal Act implementing regulations, to consider the public health and safety, ease and cost of program implementation, and participation by various communities. The implementing regulations may not *require* any person to establish or operate a delivery or disposal program.

III. Discussion of Comments

The DEA had received 192 comments on the NPRM when the comment period closed on February 19, 2013. These comments are summarized below, along with the DEA's responses.

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reducing the risk of diversion and protecting the public health and safety. As used in this Final Rule, the DEA uses the terms "disposal" and "dispose" to generally refer to the wide range of activities that result in controlled substances being unavailable for further use. When necessary to specify a particular activity within the disposal process, the particular activity is identified (e.g., transfer, deliver, collect/collection, return, recall, and destroy/destruction).

[5] The Attorney General's delegation of authority to the DEA may be found at 28 CFR 0.100.

A. *Support for the Proposed Rule (1 issue)*

[1] **Issue:** The DEA received 192 comments for this rulemaking during the 60-day comment period. The vast majority of the comments were overwhelmingly positive with the commenters agreeing that there should be more options for secure, convenient, and responsible disposal of controlled substances. Nineteen commenters supported the rule as written in the NPRM. Almost every other commenter supported the rule to some degree, although many commenters had concerns with the implementation of the specific disposal procedures described in the NPRM.

Response: The DEA appreciates the support for this rulemaking and is privileged to implement regulations to allow for the collection and disposal of controlled substances in a secure, convenient, and responsible manner. The DEA considered all of the comments and ramifications of implementing proposed changes to the rule. In finalizing this rule, the DEA considered public health and safety, ease and cost of program implementation, and participation by various communities.

B. *Definitions and Terms*[6] *(12 issues)*

[1] **Issue:** Five commenters asked the DEA to define "ultimate user."

Response: An ultimate user is defined by the CSA as "a person who has lawfully obtained, and who possesses, a controlled substance for his own use or for the use of a member of his household or for an animal owned by him or by a member of his household." This definition, codified at 21 U.S.C. 802(27), was not amended or otherwise modified by the Disposal Act.

[2] **Issue:** Ten commenters asked the DEA to clarify the term "retail pharmacy" and to specify whether "closed-door pharmacies," such as those that service LTCFs, "Federal pharmacies," and

[6] Definitions and terms specific to particular comment categories, such as "Law Enforcement" and "Long-Term Care Facilities (LTCFs)," are located in those specific sections.

other pharmacies that only provide services to a distinct population are considered retail pharmacies.

Response: The intended meaning of "retail pharmacy" with regard to collectors was discussed in the NPRM but was not defined in the proposed rule itself. The DEA intends "retail pharmacy" to include any entity registered with the DEA as a retail pharmacy as opposed to those entities registered as a hospital/clinic. Depending on a variety of factors, including State authority and authorized business practices, some entities that dispense controlled substances may be registered with the DEA as either a retail pharmacy or a hospital/clinic. 21 CFR part 1301. In other words, pharmacies are not registered with the DEA as "Federal pharmacies," "LTCF pharmacies," or even "closed-door pharmacies." All of these pharmacies may be registered as retail pharmacies provided they meet the requirements of 21 U.S.C. 822 and 823, and they may be authorized as collectors upon proper application. As previously discussed, the DEA is also allowing entities registered as hospitals/clinics with an on-site pharmacy to be collectors. 21 CFR 1317.40. Therefore, patients of pharmacies that dispense controlled substances pursuant to a hospital/clinic registration may benefit if the hospital/clinic opts to modify its registration to become a collector.

[3] **Issue:** Approximately 10 commenters asked the DEA to expand the definition of "authorized employee." These commenters expressed concern that the definition of "authorized employee" in the NPRM was too limited in scope, and would result in a burden on smaller-staffed pharmacies, as well as pharmacies that employ contract pharmacists and part-time employees. One commenter asked whether or not physician-owners will be considered authorized employees.

Response: The DEA carefully considered the commenters' concerns and is modifying the proposed definition of "authorized employee." 21 CFR § 1300.05(b). In this rule, the DEA is omitting the word "authorized" from the definition of "authorized employee" because the rule already specifies what conditions qualify employees to conduct certain disposal activities (i.e., authorized collectors may not employ, as an agent or employee who has access to or influence over collected substances, any person who has been convicted of a felony offense related to controlled substances or who has, at any time, had an application for registration with DEA denied, had a DEA registration revoked or suspended, or surrendered a DEA registration for cause). Also, the DEA is modifying the definition of "employee" by adopting the general common law of agency's definition of the term and moving the definition from proposed part 1317 to part 1300. As a result of these changes, part-time personnel and physician-owners may be considered "employees" for the purpose of disposal if they meet the relevant criteria.

Where Congress does not define "employee," the DEA utilizes the common law to determine who is an "employee." Under U.S. Supreme Court precedent, the factors relevant to determining whether a person is an "employee" under the common law include, but are not limited to: the hiring party's right to control the manner and means by which the product is accomplished; the skill required; the source of the instrumentalities and tools; the location of the work; the duration of the relationship between the parties; whether the hiring party has the right to assign additional projects to the hired party; the extent of the hired party's discretion over when and how long to work; the method of payment; the hired party's role in hiring and paying assistants; whether the work is part of the regular business of the hiring party; whether the hiring party is in business; the provision of employee benefits; and the tax treatment of the hired party.

See Nationwide Mut. Ins. Co. v. Darden, 503 U.S. 318, 323–24 (1992). Other applicable factors may be considered and no one factor is dispositive. *See id.* at 324.

After evaluating the relevant factors in the context of controlled substance security and diversion prevention, in the context of disposal, the following criteria will determine whether a person is an "employee" regardless of the number of hours per week the person works: persons who are directly paid by the registrant; who are subject to direct oversight by the registrant; who are required, as a condition of employment, to follow the registrant's procedures and guidelines pertaining to the handling of controlled substances; who receive a performance rating or performance evaluation on a regular/routine basis from the registrant; who are subject to disciplinary action by the registrant; and who render services at the registrant's registered location. This definition is incorporated in the new § 1300.05, titled "Definitions Relating to the Disposal of Controlled Substances." These criteria focus on the degree of management and control that a registrant has over the person, and thus, adherence to these criteria will directly impact the security of controlled substances within the registrant's custody and control. The DEA believes that these criteria are the minimum required to ensure controlled substances are accounted for and not diverted to illicit purposes. Under the definition, contract personnel who do not meet these criteria are not "employees" for the purposes of disposal.

[4] **Issue:** One commenter stated that the proposed definition of "authorized employee" was too expansive, and that controlled substances should be handled only by individuals who hold a professional license.

Response: The DEA carefully considered the diversion risks associated with allowing various types of persons to handle collected substances. The definition of "employee," as stated in this final rule, will help reduce diversion risks while ensuring that authorized collectors have

sufficient ability to safely and securely manage the collection of controlled substances. 21 CFR part 1300. Individuals who do not hold a professional license are considered "employees" if they meet the criteria as explained above.

[5] **Issue:** Five commenters asked the DEA to define the term "common or contract carrier."

Response: The DEA declines to define this term for the purpose of this rule. The DEA's primary concern regarding common or contract carriers is not about how these terms are defined, but whether there is adequate security to prevent diversion when controlled substances are being transported. As explained in § 1301.74(e), when shipping controlled substances, non-practitioner registrants are responsible for selecting common or contract carriers that provide adequate security to guard against in-transit losses. In addition, non-practitioner registrants are responsible for employing precautions (e.g., assuring that shipping containers do not indicate that contents are controlled substances) to guard against in-transit losses. Although these specific requirements apply to non-practitioners, all registrants (practitioners and non-practitioners) shall provide effective controls and procedures to guard against theft and diversion of controlled substances. 21 CFR part 1301.

[6] **Issue:** One commenter suggested that the DEA modify the definition of "non-retrievable" to read: "means to ~~permanently~~ alter any controlled substance's physical and/or chemical state through *essentially* irreversible means in order to render that controlled substance unavailable and unusable for all practical purposes. This definition is not intended to require destruction beyond the state at which a controlled substance becomes unavailable, unusable, and, subsequently, no longer available for diversion."

Response: The DEA declines to modify the definition as suggested. Such a change would significantly weaken the non-retrievable standard to a state where controlled substances could

easily be diverted. The permanent and irreversible alteration of controlled substances is the cornerstone of the non-retrievable standard.

[7] **Issue:** Some commenters asked the DEA to clarify the meaning of the terms "regularly" and "practitioner" used in the proposed § 1317.05(a)(4).

Response: "Practitioner" is defined in the CSA at 21 U.S.C. 802(21) as "a physician, dentist, veterinarian, scientific investigator, pharmacy, hospital, or other person licensed, registered, or otherwise permitted, by the United States or the jurisdiction in which he practices or does research, to distribute, dispense, conduct research with respect to, administer, or use in teaching or chemical analysis, a controlled substance in the course of professional practice or research." The term "regularly" has its ordinary meaning, with no specific or technical implications. The DEA understands the ordinary meaning of "regularly" to generally be considered as being on a routine basis or at routine intervals.

[8] **Issue:** One commenter suggested that the DEA distinguish reverse distributors who only collect controlled substances for the purpose of disposal from reverse distributors who also handle non-controlled substances and other waste products. This commenter suggested that the DEA lessen the requirements for those reverse distributors that only collect controlled substances for disposal.

Response: The DEA does not distinguish between different "types" of reverse distributors. All reverse distributors receive controlled substances for the purpose of disposal—either through return to the manufacturer who accepts returns, or through destruction. 21 CFR part 1300. The regulations impose the minimum requirements for reverse distributors when handling controlled substances regardless of whether they also handle other substances. Therefore, there is no basis

to relax the requirements for reverse distributors whose activities are limited solely to the collection of pharmaceutical controlled substances for the purpose of disposal.

[9] **Issue:** One commenter asked the DEA to clarify the difference between "transfer" and "transport" as used in proposed § 1317.95.

Response: These terms have their ordinary meaning. Generally, the DEA uses the term "transport" to refer to the physical movement of an item from one location to another while "transfer" is used to refer to conveying possession or control (actual or constructive) from one entity to another.

[10] **Issue:** One commenter asked the DEA to clarify the phrase "causes the destruction" as it could be interpreted to mean any person involved in the process.

Response: As previously discussed, proposed § 1317.100 is relocated in this final rule to § 1304.21(e). The DEA included the term "causes the destruction" to encompass such circumstances where a registrant does not itself destroy the controlled substance but is still responsible for the destruction; for example, when a registrant or a registrant's employee initiates the destruction process by engaging a third-party destruction facility that will perform the actual destruction pursuant to § 1317.95(c). This final rule clarifies this distinction in §§ 1317.95(c) and 1304.21(e).

[11] **Issue:** One commenter stated that the rule should be clarified in use of the word "may" with regard to individual counting and inventorying of collected substances. The commenter indicated that the word seems open for interpretation.

Response: The commenter is specifically referring to the NPRM statement "[c]ontrolled substances collected by collectors may not be individually counted or inventoried." The DEA understands that this phrase may be misinterpreted to mean that authorized collectors are not

required to count or inventory collected substances. To clarify, the DEA is modifying §§ 1317.60 and 1317.70 to clearly indicate that sealed inner liners and returned mail-back packages "shall not be opened, x-rayed, analyzed, or otherwise penetrated." The DEA also modifies § 1317.75(c) to specify that this prohibition includes counting or inventorying collected substances prior to sealing and removing an inner liner that contains collected substances, as well as after the inner liner is sealed. The DEA discusses below the different requirements applying to law enforcement.

[12] **Issue:** One commenter noted that the DEA used inconsistent time requirements throughout the proposed rule, such as "timely," "prompt," and "as soon as practicable, but no later than 14 days." Additionally, several commenters requested clarification regarding the definition of the word "prompt" in the proposed rule, and commenters asked for clarification regarding how the DEA would determine whether an action is "prompt." Commenters asked for guidance as to what time range the DEA would find reasonably acceptable.

Response: The DEA's use of different time standards throughout the proposed rule was intentional as the different circumstances of each requirement warrant different standards. The various timing requirements are intended to be flexible enough to account for individual circumstances while also ensuring sufficient and adequate controls to prevent diversion and opportunities for diversion. The DEA considered imposing specific timelines (*e.g.*, three days, five days); however, the wide variety of business models and activities made it impossible in most circumstances to set a specific deadline that would prevent diversion and diversion opportunities. Additionally, violations of specific timelines would be *per se* violations of the regulations, whereas violations of the flexible "prompt" and "as soon as practicable" standards would be considered under each registrant's individual circumstances. The DEA's determination

will be guided by whether the registrant has fulfilled its responsibility to provide effective controls and procedures to guard against theft and diversion. All controlled substances destined for destruction must be rendered non-retrievable in order to be destroyed in a manner consistent with this rule. As such, a controlled substance will have been promptly destroyed if it is promptly rendered non-retrievable. 21 CFR 1317.95. "Timely" refers to actions that have a specific time period for compliance, *e.g.*, 30 days. Therefore, in each instance in which the rule uses the word "timely" to refer to destruction requirements for reverse distributors, it refers to the specific time period (14 days in the proposed rule, 30 days in the final rule) in which reverse distributors are required to destroy controlled substances. 21 CFR 1317.15.

C. *Types of Entities That May Operate a Collection Program (9 issues)*

[1] **Issue:** Several commenters asked the DEA to retain the provision in the proposed rule to permit retail pharmacies to maintain collection receptacles. These commenters stated that retail pharmacies will provide a convenient option for ultimate users who desire to safely and securely dispose of their unused or unneeded controlled substances. Commenters also asked the DEA to retain the provision to permit retail pharmacies to manage collection receptacles at LTCFs.

Response: The DEA appreciates the support for the provisions in the rule that permit retail pharmacies to manage collection receptacles at not only the primary registered location of the retail pharmacy, but also LTCFs. 21 CFR 1317.40 and 1317.80. The DEA believes that these two provisions will provide ultimate users and others with convenient options to safely and securely dispose of unused controlled substances. The DEA retained these provisions in the final rule.

[2] **Issue:** Eighteen commenters asked the DEA to permit hospitals to become authorized collectors so that they may maintain collection receptacles. An additional two commenters asked

the DEA to allow specialized hospitals and clinics to maintain collection receptacles. These commenters stated that collection receptacles located inside of hospitals would provide ultimate users with an opportunity to dispose of medication that may no longer be needed or may be expired.

Response: The DEA selected methods for disposal that provide opportunities for ultimate users to securely, conveniently, and responsibly dispose of their unused, unwanted, and expired pharmaceutical controlled substances while also preventing diversion. As previously discussed, after extensive review and careful deliberation, the DEA is permitting certain registered hospitals/clinics to become authorized collectors. 21 CFR 1317.40. In order to counterbalance the diversion risks of allowing collection receptacles to be located inside hospitals/clinics, the DEA is only allowing those hospitals/clinics with on-site pharmacies to become collectors. The DEA is requiring these collectors to place collection receptacles in locations that are regularly monitored by employees, and is prohibiting these collectors from placing collection receptacles in the proximity of any area where emergency or urgent care is provided. 21 CFR 1317.75.

[3] **Issue:** One commenter suggested that hospitals of a certain size be required to become authorized collectors.

Response: The DEA is not requiring, nor is the DEA authorized to require, any entity to implement a collection program or maintain a collection receptacle. The Disposal Act explicitly states that the "regulations may not require any entity to establish or operate a delivery or disposal program." 21 U.S.C. 822(g)(2).

[4] **Issue:** It was requested that the DEA allow military treatment facility pharmacies (registered with the DEA as a hospital/clinic), and the Indian Health Service (IHS), including IHS pharmacies (IHS, Tribal, and Urban programs) to become authorized collectors. One commenter

also suggested that the DEA permit collection receptacles in select areas of military installations, such as ambulatory care clinics and service member barracks.

Response: As previously discussed, any registered hospital/clinic with an on-site pharmacy and any retail pharmacy may be authorized to be a collector. 21 CFR 1317.40. Ambulatory care clinics and service member barracks are generally not registrants. As discussed in the NPRM, the Disposal Act did not give the DEA authority to create new classes of registration solely for the purpose of conducting ultimate user disposal activities. The DEA is allowing hospitals/clinics with an on-site pharmacy and retail pharmacies to be responsible for and manage collection receptacles in non-registrant LTCFs because the Disposal Act acknowledged that LTCFs "face a distinct set of obstacles to the safe disposal of controlled substances due to the increased volume of controlled substances they handle." 21 CFR 1317.80. LTCF residents generally have limited mobility; accordingly, this final rule authorizes LTCFs to dispose of controlled substances *on behalf of ultimate users who reside or have resided at the LTCF*. 21 CFR 1317.30. Furthermore, un-registered ambulatory care clinics and service member barracks generally lack adequate safeguards to ensure the security of collected pharmaceutical controlled substances; thus, allowing collection receptacles at such locations poses an unacceptable risk of diversion and threatens the public health and safety.

[5] **Issue:** Eight commenters asked the DEA to permit non-registrants to collect non-controlled substances for the purpose of disposal.

Response: The DEA's authority regarding drug disposal is specific to pharmaceutical controlled substances. Non-registrants may collect non-controlled substances pursuant to all applicable Federal, State, tribal, and local laws and regulations; however, all regulations and laws relevant to controlled substances will apply if controlled substances are collected, even inadvertently.

[6] **Issue:** One commenter asked the DEA to permit LTCFs to become authorized collectors.

Response: The DEA is without authority to permit LTCFs to become authorized collectors. As discussed in the NPRM, authorized collectors must first be registrants in order for the DEA to impose and enforce these regulations upon them. A majority of LTCFs do not have State authority with respect to controlled substances—a fundamental prerequisite to obtaining a DEA registration. The Disposal Act authorized the development of regulations to permit LTCFs to dispose of controlled substances on behalf of ultimate users who reside or have resided in their facilities. The DEA is permitting hospitals/clinics with an on-site pharmacy and retail pharmacies to become authorized collectors with authority to install and maintain collection receptacles at LTCFs, and declines to extend this authority to the LTCFs themselves. 21 CFR 1317.40.

[7] **Issue:** Several commenters urged the DEA to create a new status that permits non-registrant organizations to become authorized collectors for the sole purpose of collecting controlled substances from ultimate users and others authorized to dispose of controlled substances on behalf of ultimate users. One commenter asked that the DEA allow non-profit, non-registrant organizations to register as authorized collectors with a reduced fee.

Response: The DEA is not developing a new category of registrant specifically for collecting pharmaceutical controlled substances from ultimate users. Any entity that wishes to collect controlled substances from ultimate users must do so in accordance with this rule, which includes provisions for specified existing registrant categories to modify their registration to become authorized as collectors. Any person not already registered with the DEA, wishing to become authorized as a collector must first satisfy all of the requirements for registration

identified in the CSA and its implementing regulations. Non-registrant organizations may partner with law enforcement and with registrants that are collectors. 21 CFR 1317.65.

[8] **Issue:** One commenter asked the DEA to clarify how a local government may register with the DEA to become an authorized collector.

Response: As discussed above, the DEA is not creating a new registration category for the exclusive purpose of collecting controlled substances from ultimate users. Persons registered with the DEA as manufacturers, distributors, reverse distributors, NTPs, hospitals/clinics with an on-site pharmacy, or retail pharmacies may apply to modify their registration to become an authorized collector in the manner proscribed by this final rule. 21 CFR part 1301. Any person not already registered with the DEA, wishing to become authorized as a collector must first satisfy all of the requirements for registration identified in the CSA and its implementing regulations. These requirements include being authorized to handle controlled substances by the State in which the applicant is located unless exempt by statute or regulation. The DEA encourages entities that are not registrants to partner with authorized collectors or law enforcement. 21 CFR 1317.65. For example, local governments may partner with authorized mail-back collectors to provide mail-back packages to the public.

[9] **Issue:** One commenter asked the DEA to clarify that no Federal or State government entity may require registrants to amend their DEA registration to become authorized collectors.

Response: The Disposal Act specifically prohibits the DEA from requiring any entity to establish or operate a delivery or disposal program. 21 U.S.C. 822(g)(2). The prohibition does not extend to every Federal and State agency and the DEA does not have the authority to institute such a prohibition.

D. *Locations Where Authorized Collectors May Maintain Collection Receptacles or Host Take-Back Events (1 issue)*

[1] **Issue:** Six commenters asked the DEA to permit retail pharmacies to manage collection receptacles at establishments other than the retail pharmacy's registered location, such as community centers. Commenters stated other locations may be more convenient for ultimate users and would thus maximize participation. Two commenters asked the DEA to allow collection receptacles at unregistered locations such as permanent household hazardous waste collection sites.

Response: The DEA acknowledges that in some locations, and under certain circumstances, alternative settings may be more convenient for ultimate users, but that is not the only consideration. The DEA believes that in order to adequately ensure the safety and welfare of the public, collection receptacles must be located inside the DEA-registered location of authorized collectors. 21 CFR part 1317.75. Authorized collectors, as registrants, are readily familiar with the security procedures and other requirements to handle controlled substances. Most publicly-accessible locations where controlled substances are not typically handled, such as community centers and hazardous waste collection sites, are not targets for theft in the same manner as those locations where pharmaceutical controlled substances are regularly handled. Thus, those locations are unlikely to be familiar with, or to have in place, the security controls necessary to ensure the security of collected substances and prevent diversion of controlled substances. However, law enforcement may continue to conduct take-back events, and other persons may partner with law enforcement to conduct such take-back events at various locations. 21 CFR 1317.65.

E. *Registration Requirements for Authorized Collectors (5 issues)*

[1] **Issue:** Several commenters asked the DEA to clarify whether or not registration modifications for authorized collectors may be conducted online.

Response: Registration modifications may be conducted online. For the final rule, the DEA is modifying the text of § 1301.51 to clarify that online modifications are indeed permitted. Registrants may go to www.DEAdiversion.usdoj.gov to modify their registration when they start or stop collection activities.

[2] **Issue:** Three commenters stated that it is overly burdensome to require authorized collectors to modify their registration each time they start or stop collection activities. These commenters asked that the DEA provide additional details regarding the registration modification process.

Response: The DEA carefully reviewed the registration requirements and did not find indications to suggest that registration modifications will be overly burdensome. The rule requires that a registrant must apply to modify their DEA registration prior to initiating any collection activities. 21 CFR part 1301. Authorization as a collector is subject to renewal in the same manner as registration. The DEA will consider an authorized collector to be conducting collection activities until the registration is modified, revoked, surrendered, suspended, or otherwise terminated. If an authorized collector stops collection activities, he/she must modify his/her registration to indicate such. The requirement to modify a registration requires a simple written notification to the DEA. This written notification can be easily and quickly conducted online in a few minutes. 21 CFR part 1301. The registrant may go online and select the option to indicate that the registrant has ceased collecting. Registrants without ready access to the online notification method can easily and quickly communicate such information to the DEA in writing via the mail, which the DEA will process promptly upon receipt.

[3] **Issue:** One commenter suggested that the DEA relax requirements for registration modifications regarding LTCF collection receptacles. This commenter was concerned that registration modifications may outpace the DEA's resources.

Response: The DEA evaluated this request and determined that the registration requirements regarding LTCF collection receptacle management are necessary to ensure accountability and prevent diversion; the related procedures are the minimum necessary to ensure that authorized collectors maintain the receptacles in a manner that is consistent with the applicable regulations. 21 CFR part 1301.

[4] **Issue:** One commenter asked the DEA to clarify whether or not an entity may apply for registration as a reverse distributor with the sole intent of providing destruction services for collected substances.

Response: Any entity may apply for registration as a reverse distributor pursuant to and in accordance with 21 U.S.C. 822–823, and 21 CFR part 1301. Reverse distributors are not required to conduct all activities that they are authorized to perform.

[5] **Issue:** Two commenters asked the DEA to clarify whether a destruction facility must be registered with the DEA.

Response: Pursuant to this rule, a destruction facility is not required to register with the DEA simply because a registrant utilizes that facility to destroy controlled substances in a manner consistent with this rule and all other applicable Federal, State, tribal, and local laws and regulations. At this time, the DEA does not believe it is appropriate to require these entities to be registered because the destroying registrant maintains possession and control of the substances (and therefore retains responsibility and accountability) until the substances are rendered non-retrievable. 21 CFR part 1301. All handling, monitoring, reporting, recordkeeping, and

witnessing with regard to the destruction of pharmaceutical controlled substances must be performed by registrants or their employees. The DEA has omitted the language that was proposed for § 1317.15(c)(4) in order to prevent confusion.

F. *Law Enforcement (7 issues)*

[1] **Issue:** Several commenters asked the DEA to expand the definition of "law enforcement officer" to include law enforcement components of Federal agencies and civilian law enforcement officers.

Response: The final rule definition is expanded from the proposed rule to specifically include officers of the law enforcement components of Federal agencies, and police officers of the Veterans Health Administration and the Department of Defense. The NPRM proposed a definition of "law enforcement officer" to include persons who are employees of a "law enforcement *agency*." The DEA is modifying this definition in the final rule to specifically include employees of law enforcement *components* of Federal agencies. Any person who meets the criteria for "employee" and "law enforcement officer" outlined in the final rule will be a qualified officer for the purposes of disposal of pharmaceutical controlled substances, regardless of whether the person is considered a "civilian" law enforcement officer. 21 CFR part 1300.

[2] **Issue:** Four commenters stated it would be overly burdensome to require law enforcement to have a collection receptacle that fits the specifications in the NPRM. These commenters stated that the collection receptacle would pose logistical issues, and that the volume of drugs collected would likely exceed the volume that the receptacle could contain. Commenters also noted that it is unnecessary to mandate that law enforcement utilize collection receptacles at take-back events.

Response: Law enforcement are not required to have a collection receptacle that meets all of the specifications in the rule, and the text of the rule is amended to clarify that the specifications

apply to authorized collectors and *not* law enforcement. The only suggested requirements for the physical construction of collection receptacles maintained by law enforcement are that they be securely placed and maintained at the law enforcement's physical location. 21 CFR 1317.35. Also, law enforcement are not required to utilize collection receptacles at take-back events. The text of the final rule states, "[e]ach take-back event should have at least one receptacle for the collection of permitted substances..." 21 CFR 1317.65. Thus, law enforcement should have some sort receptacle at take-back events.

[3] **Issue:** Commenters expressed concern that law enforcement may not have the facilities to store the collected substances until they are shipped to a destruction facility.

Response: The rule suggests that law enforcement store collected substances in a manner that is consistent with its standard procedures for storing illicit controlled substances. The language used in the text of the rule, "should," is suggestive. Law enforcement are encouraged to follow the guidance in 21 CFR 1317.35; however, they are not required to do so. It should be noted that the requirements in 21 CFR 1317.65 pertaining to law enforcement presence at take-back events are mandated; however, the DEA only suggests procedures for the storage and transportation of pharmaceutical controlled substances collected at take-back events.

[4] **Issue:** One commenter asked the DEA to permit entities other than law enforcement to conduct take-back events.

Response: If an authorized collector or other entity wishes to conduct a take-back event, the event must be held in partnership with law enforcement, as provided in the rule. 21 CFR 1317.65. Take-back events are intended to be limited-duration events that may take place at an unregistered location that is easily accessible to the public, such as a community center or town center. Given the likelihood of publicity and low physical security at such locations, the DEA

believes that it is imperative to ensure active law enforcement participation for the safety of the event participants and the community, as well as to help deter theft and diversion of pharmaceutical controlled substances.

[5] **Issue:** Commenters urged the DEA to relax the "authorized employee" requirement for civilian law enforcement officers. These commenters stated that the DEA should treat civilian law enforcement officers as "authorized employees" for the purposes of this rule. They stated that these officers and employees currently assist with take-back events, and if they were no longer permitted to, there would be a staffing shortage to assist with take-back events. Additionally, several commenters encouraged the DEA to allow civilian law enforcement employees to handle collected substances if they meet the same requirements as an employee or handle the substances in a manner consistent with law enforcement protocols.

Response: In the NPRM, "authorized employee" referred to those registrant personnel who would be permitted to directly participate in the disposal process. "Authorized employee" did not pertain to law enforcement officers or to take-back events. In the final rule the definition is modified, but it still only pertains to those persons who may be permitted to directly participate in the disposal process. 21 CFR part 1300. With respect to law enforcement and take-back events, as discussed above, any person who meets the criteria for "employee" and "law enforcement officer" outlined in the final rule will be a qualified officer for the purposes of disposal of pharmaceutical controlled substances, regardless of whether the person is considered a "civilian" law enforcement officer. The DEA declines to expand the law enforcement authority to specifically include civilian law enforcement employees. Only employed law enforcement officers, as defined by this final rule, may handle pharmaceutical controlled substances at take-back events. As discussed in the NPRM and previous responses to this issue,

the DEA believes that this level of security is necessary to prevent theft and diversion and to ensure the safety of the public due to the highly publicized nature of take-back events and the fact that such events are likely to occur at locations with minimal security. The DEA does not believe that this requirement will hinder the success of take-back events. As previously discussed, only one law enforcement officer must oversee the take-back event, and at the discretion of the law enforcement agency or law enforcement component of a Federal agency, this officer may also be the law enforcement officer who maintains control and custody of the collected substances. 21 CFR 1317.65. There are no prohibitions against other persons assisting law enforcement officers conduct the take-back event.

[6] **Issue:** One commenter asked the DEA to address what rights Military Provost Marshal Officers have with respect to collecting controlled substances from ultimate users.

Response: Under § 1317.35 of the new regulation, Federal law enforcement may continue to conduct take-back events and mail-back programs, and operate collection receptacles as further detailed in the regulation. If the Office of the Provost Marshal is considered "Federal law enforcement," it would be eligible to conduct such collection activities. Federal law enforcement can, and in some cases must, appoint a law enforcement officer to oversee those activities. The appointed officer would then have the authority granted by his/her agency.

[7] **Issue:** One commenter asked the DEA to clarify how law enforcement may transport and deliver collected substances to a destruction facility (i.e., whether they may ship such substances using a common carrier) and how law enforcement can comply with Department of Transportation (DOT) requirements when transporting substances that may contain hazardous materials.

Response: The DEA has no expertise or authority to interpret or apply the DOT laws, regulations, or guidelines regarding transportation of pharmaceutical controlled substances that may constitute hazardous materials. As such, interested persons are encouraged to contact the DOT directly with their specific circumstances, and such persons can obtain more information at www.phmsa.dot.gov/hazmat. However, the DEA understands that the DOT's Hazardous Materials Regulations apply to entities that place hazardous materials in commercial transportation, and not government vehicles operated by government personnel solely for non-commercial purposes. If more detailed guidance is necessary, the DEA encourages law enforcement and other entities to consult the DOT for guidance on transporting collected substances that may contain hazardous materials. For additional commentary on hazardous material disposal please see comment section "Q." entitled "Hazardous Materials Transportation and Hazardous Waste Destruction."

G. *Collection Receptacle Design, Inner Liners, Placement, and Security (24 issues)*

Clarification of Terms

[1] **Issue:** One commenter noted that the DEA interchangeably used the terms "container" and "shell" when referring to the outer collection receptacle.

Response: The DEA is modifying the final rule to consistently use the term "container" when referring to the outer portion of collection receptacles. This change is purely for stylistic consistency and makes no substantive change to the rule.

Collection Receptacle Design

[2] **Issue:** The DEA specifically requested comments regarding the value of the use of a uniform symbol to be placed on collection receptacles. The DEA received 22 comments regarding the use of a uniform symbol. Five commenters supported the use of a uniform symbol, and 17

commenters opposed the use of a uniform symbol. One commenter suggested that the symbol be yellow. Four commenters noted that the use of such a symbol is unnecessary given the requirement to clearly mark and label the receptacles. Three commenters expressed concern that the use of such symbols would result in the receptacles becoming targets for diversion. One commenter was not opposed to the use of a uniform symbol but does not believe it is essential. One commenter indicated that the use of a uniform symbol should be contingent upon the location and security of the collection receptacle.

Response: The DEA appreciates all of the comments submitted in response to this request. After careful consideration, the DEA declines to include a uniform symbol requirement in this final rule. However, the DEA may consider requiring a uniform symbol on collection receptacles after a sufficient time to observe the effects of the existing requirement to clearly mark and label collection receptacles.

[3] **Issue:** Eleven commenters stated that any signage indicating what ultimate users may deposit into the collection receptacle should be in plain language. These commenters noted that most ultimate users cannot distinguish between controlled substances and non-controlled substances. Other commenters stated that no sign should be required at all, and others suggested the use of pictograms instead of words. Others raised concerns that signage will draw attention to the receptacles, thus increasing risk for theft and diversion.

Response: The final rule does not require any specific language, design, or color choice for the display on the collection receptacle as long as the sign indicates that only schedules II–V controlled substances and non-controlled substances *are* acceptable. 21 CFR 1317.75. As explained above, comingling is permitted but not required. 21 CFR 1317.75. Plain language, pictograms, or a combination of the two, may be used, as long as it is clear that schedule I

controlled substances, controlled substances not lawfully possessed by the ultimate user, and illicit or dangerous substances are not permitted to be placed in the container. The DEA believes that some notice regarding what substances may be disposed in collection receptacles is necessary in order to provide guidance to the public and to discourage the use of receptacles for disposing trash or other items. While the diversion risks presented by the requirement for signage is mitigated by physical security requirements (*e.g.*, that the receptacle be securely fastened to a permanent structure), authorized collectors should be mindful that the selected signage not transform the receptacle into a target for theft or diversion.

[4] **Issue:** Four commenters suggested that the collection receptacle sign encourage ultimate users to remove medication from its container before placing the medication in the collection receptacle. Several of the commenters who had participated in authorized pharmaceutical controlled substance take-back programs noted that the packaging for medication is voluminous, and that including such packaging will be burdensome since it will necessitate changing inner liners more frequently.

Response: The DEA appreciates these commenters' concerns. Although collectors may encourage ultimate users to remove substances from their containers before depositing them into a collection receptacle or mail-back package, the DEA declines to require it. The DEA has declined to mandate whether substances must be disposed of, with or without packaging, because such requirements would not necessarily affect security or increase the risks of diversion, and as such, should be left to the individual collectors and other relevant authorities who best know the needs and requirements of their programs and locations.

[5] **Issue:** Other commenters indicated that some hazardous waste disposal regulations require the disposal of medication containers, which may not fit into the receptacles.

Response: As discussed in the immediately preceding comment, the DEA is neither requiring nor prohibiting medication containers to be disposed of with pharmaceutical controlled substances. Moreover, there is no indication that the vast majority of medications will not fit into the "small opening" that the collection receptacles specifications require. For additional commentary on hazardous waste disposal please see comment section "Q.", entitled "Hazardous Materials Transportation and Hazardous Waste Destruction."

[6] **Issue:** The DEA received comments that the inner liner should be a large plastic tub or bucket within a receptacle that can be easily removed and the collected items either dumped into smaller containers or sorted before being secured into storage for disposal or prior to destruction.

Response: The DEA carefully considered the specifications of both the inner liner and the outer container of the collection receptacle. To prevent diversion and protect the public health and safety, the DEA drafted this rule with the precisely considered objective of limiting the number of people who handle the collected substances. The DEA's extensive experiences in regulating and enforcing the closed system of distribution established by the CSA have demonstrated that a key factor in reducing diversion risk is limiting the handling of controlled substances. In the context of disposal, this means prohibiting the sorting of collected substances once they are deposited into a collection receptacle.

[7] **Issue:** One commenter stated that the collection receptacle design specifications will require current collection programs for non-controlled substances to install new collection receptacles if those programs wish to additionally collect pharmaceutical controlled substances. This commenter stated that such installations will be burdensome and will discourage participation for these programs.

Response: The DEA deeply appreciates the concern and activism of local communities and other groups currently conducting non-controlled substance drug take-back programs and their wish to expand collection activities to pharmaceutical controlled substances. Programs such as these are an important and vital component of the communities they serve. The DEA understands that publication of this final rule may necessitate the need for some programs to implement new procedures and install new equipment in order to additionally collect pharmaceutical controlled substances. The DEA has not established the new requirements lightly or without considerable deliberation as to its impacts on existing programs. However, the risk of diversion for non-controlled substances is relatively low compared to the much higher risk of diversion, and the corresponding and associated risks to public health and safety, for pharmaceutical controlled substances. The DEA has been charged by Congress with the enforcement of the controlled substance laws of the United States, and must ensure that pharmaceutical controlled substances are properly secured and not easily susceptible to theft or diversion. Accordingly, the collection receptacle design specifications outlined in § 1317.75 will be implemented as proposed.

[8] **Issue:** A commenter asked the DEA to permit the use of similar receptacles that may already exist and were designed for the deposit and storage of medical waste.

Response: The DEA is not prohibiting the use of collection receptacles that currently exist on the market as long as such receptacles meet all of the design specifications outlined in § 1317.75 of this rule.

[9] **Issue:** Five commenters stated that the requirement for a collection receptacle to be fastened to a permanent structure is burdensome. Several commenters pointed out that many pharmacies do not own the property that is their DEA-registered location, and such fixtures and installments

are prohibited. One commenter pointed out that this requirement would be particularly burdensome for small, rural pharmacies. Another commenter asked if the requirement applies if the collection receptacle is located in a locked room, inaccessible to the public.

Response: The DEA appreciates the willingness of pharmacies to aid in the societal goal of helping to combat unauthorized access to and abuse of pharmaceutical controlled substances. The DEA understands that there may be logistical concerns for some retail pharmacies that wish to maintain a collection receptacle at their registered location. However, the DEA believes that permanently-secured, fixed containers are the minimum required to prevent diversion and theft of collected substances. The requirement that collection receptacles be securely fastened to a permanent structure applies to all authorized collectors' collection receptacles, no matter the location of the registrant. 21 CFR 1317.75. Although the final rule does not expressly prohibit collection receptacles from being placed in a locked room that is inaccessible to the public, the final rule does mandate that collection receptacles at authorized collectors' registered locations must be accessible to ultimate users, and others authorized to dispose of controlled substances on behalf of ultimate users, as they are the only people who may deposit pharmaceutical controlled substances into a collection receptacle (e.g., ultimate users cannot transfer pharmaceutical controlled substances to pharmacy staff). 21 CFR 1317.30. The DEA encourages retail pharmacies leasing their commercial space to work with their landlords to allow for the installation of collection receptacles under the conditions established by this rule.

[10] **Issue:** Nine commenters stated that requiring an outer container with an inner liner is unnecessary and burdensome. These commenters proposed that the collection receptacle be designed in such a way that it can be returned to the reverse distributor as a complete unit.

Response: The DEA appreciates the value in utilizing temporarily secured containers that can be sealed and shipped for destruction; however, the DEA believes that such systems present an unreasonable risk of diversion because, even when secured, such containers can be relatively easily removed when compared to a securely fastened and locked outer container. Relatedly, the DEA is requiring that collection receptacles be "substantially constructed," which is intended to ensure that the construction is such that unauthorized access to the contents of the receptacle is not easily obtained. 21 CFR 1317.75. Accordingly, the DEA is requiring that collection receptacles have a substantially-constructed outer container and removable inner liners. 21 CFR 1317.60 and 1317.75.

[11] **Issue:** Three commenters stated that the collection receptacle should not be required to have a traditional lock, but that its opening be designed so that that the contents cannot be removed.

Response: In implementing the Disposal Act to provide secure and responsible disposal methods for pharmaceutical controlled substances by ultimate users, the DEA must ensure that collected substances are properly secured and not easily susceptible to theft or diversion. The requirements pertaining to collection receptacles were carefully considered and designed to limit the handling of the controlled substances, from ultimate user to destruction. These considerations dictated the size of the opening. However, the NPRM and the final rule allow for flexibility regarding a traditional lock, and require that "the small opening in the outer container of the collection receptacle shall be locked *or made otherwise inaccessible to the public* when an employee is not present (e.g., when the pharmacy is closed)." 21 CFR 1317.75(f).

[12] **Issue:** One commenter suggested that the DEA conduct a national pilot program prior to implementation of the final rule to ensure that collection receptacle requirements are feasible and effective.

Response: The DEA believes that the need to implement this rule in order to allow secure convenient options for disposal outweighs the delay and limited benefit that may be obtained by implementing any pilot programs or other testing or research. Through various outreach efforts, including the public meeting the DEA held in January 2011, comments from industry, and information obtained from pilot programs, the DEA believes that it has effectively researched and analyzed the various aspects of this rule. Also, the DEA believes that implementation of this rule is important to helping reduce the amount of unwanted pharmaceutical controlled substances available for theft, diversion, and accidental ingestion.

[13] **Issue**: One commenter asked the DEA to allow a Special Agent in Charge (SAC) to approve container and inner liner designs.

Response: As discussed in the NPRM, the DEA determined that the elimination of individual SAC approval for various aspects of disposal or destruction is necessary in order to ensure clear and consistent requirements throughout the United States, thus reducing the potential for confusion regarding requirements for ultimate users and authorized collectors. Specific approval of individual collection receptacles and inner liner designs is not required. All collection receptacles and inner liner designs must meet the specifications outlined in this final rule. 21 CFR 1317.60 and 1317.75.

[14] **Issue:** One commenter suggested that national pharmacy organizations educate the public on proper disposal methods and various disposal options. This commenter suggested that such organizations post information online and disseminate leaflets at retail establishments.

Response: With regard to patient information regarding disposal, the DEA is not requiring any entity to educate the public on proper disposal methods and their various disposal options. However, the DEA anticipates that many entities will voluntarily choose to do so. The DEA applauds and encourages voluntary, educational outreach to the public on issues related to the abuse potential and proper disposal of pharmaceutical controlled substances, whether it be through law enforcement, community groups, or professional organizations.

Collection Receptacle Inner Liners

[15] **Issue:** Several commenters asked for clarification regarding inner liner tracking requirements. Specifically, commenters asked how unique identification numbers should be assigned, how tracking systems are to be implemented, and what entity will be responsible for placing identification numbers on inner liners. One commenter suggested that the DEA regulate the manufacture of inner liners or require that inner liners be sequentially numbered.

Response: The rule outlines the design requirements and the recordkeeping requirements for inner liners. The purpose of a unique identification number is to provide for complete and accurate records that can be inventoried to ensure that each liner is accounted for from receipt, to installation, removal, storage, transfer, and destruction. 21 CFR part 1304. The unique identification numbers therefore must be unique to the individual collector. 21 CFR 1317.60. The DEA does not intend to require any particular method for assigning such numbers and is modifying the text of proposed § 1317.60(e) by indicating that only inner liners must bear a permanent, unique identification number. The company manufacturing the inner liners may assign the numbers. The DEA does not have authority to directly regulate the manufacturers of the inner liners.

[16] **Issue:** One commenter suggested that the inner liner be clear so that it can be visually inspected for non-compliant items.

Response: Due to associated increased risks for diversion, the DEA determined that the contents of the inner liners must not be viewable once the inner liner is sealed. 21 CFR 1317.60. The DEA appreciates the concerns regarding certain non-compliant items being placed in collection receptacles; however, for reasons discussed in previous comments, no one is permitted to handle the contents of inner liners. 21 CFR 1317.75. The DEA would like to point out that the text of the rule does not prohibit items from being observed *prior* to being placed in the collection receptacle, which could be an effective way to ensure that such non-compliant items are not placed in the collection receptacle.

[17] **Issue:** Several commenters indicated that the requirement to store sealed inner liners in the same manner as schedule II controlled substances will be overly burdensome and will reduce the amount of space available for storing schedule II inventory at retail pharmacies. These commenters suggested that the DEA allow the authorized collector to transfer collected substances in inner liners to a secure warehouse facility for storage until they can be picked up or shipped.

Response: The DEA appreciates these concerns but declines to permit authorized collectors to transfer collected substances to warehouse facilities for storage. Filled inner liners must be stored only at primary registered locations (and at LTCFs in accordance with § 1317.80(c)) and may not be transported to off-site warehouses. The basis for this requirement is that the risk of diversion increases each time inner liners change hands or are transported. However, as previously discussed, this final rule expands the NPRM requirement and authorizes practitioners

to store collected substances at their registered location in either a securely locked, substantially constructed cabinet or a securely locked room with controlled access. 21 CFR 1317.05.

[18] **Issue:** Four commenters stated that the DEA should permit schedule I controlled substances to be disposed of via collection receptacles, mail-back packages, or take-back events.

Response: The Disposal Act addresses the issue of unused prescription drugs, and it allows the DEA to provide ultimate users with a secure and responsible method to dispose of pharmaceutical controlled substances. This rule does not address the disposal of illicit controlled substances, *e.g.*, those substances controlled in schedule I of the CSA. Schedule I controlled substances, by definition, have no accepted medical use in treatment in the United States, and may not be lawfully prescribed or otherwise distributed to any person. In fact, any transfer of a schedule I controlled substance by an ultimate user is a violation of the CSA, unless the ultimate user is participating in an investigational use of drugs pursuant to 21 U.S.C. 355(i) and 360b(j), and the delivery is conducted in accordance with 21 CFR 1317.85.

Collection Receptacle Placement and Safety

[19] **Issue:** Ten commenters expressed concern regarding security in retail pharmacies with collection receptacles. Several commenters asked the DEA to provide guidance for proper security measures. One commenter asked for clarification on an authorized collector's liability should a receptacle become subject to diversion or if improper substances are deposited.

Response: The DEA appreciates the concerns of the commenters and has carefully considered the risks and benefits associated with collection receptacles located in authorized retail pharmacies. The DEA's rationale for allowing collection at authorized retail pharmacies was described in the NPRM. As previously noted, the DEA is not requiring any pharmacy to provide a collection receptacle. Each registrant is free to weigh the risks and benefits in determining

whether or not to seek status as an authorized collector. The DEA proposed the rule with the security requirement for permanently-secured, fixed containers based on a determination that this was the minimum required to help reduce the risk of diversion and theft of pharmaceutical controlled substances. 21 CFR 1317.75. At retail pharmacies, the location of collection receptacles within the immediate proximity of a designated area where controlled substances are stored and at which an employee is present is anticipated to provide an additional layer of security due to the increased visibility of the receptacles. 21 CFR 1317.75. While potential violations of the CSA and its implementing regulations are investigated and assessed independently, this final rule imposes the minimum required procedures to prevent and detect diversion. Even so, each authorized collector's circumstances are unique. All registrants should be mindful of their responsibility to provide effective controls and procedures to guard against theft and diversion under 21 CFR 1301.71(a), and their duty to report thefts and significant losses of controlled substances under 21 CFR 1301.74 and 1301.76.

[20] **Issue:** One commenter suggested that the inner liners be nondescript and free of any markings that would indicate their contents. This commenter was concerned that any markings on the inner liners would increase diversion risks and make them potential targets for drug seekers.

Response: The DEA appreciates the commenter's concern for potential diversion risks that inner liners might pose, and made the determination to require them only after careful consideration of the associated risks and benefits of their use, and alternatives to their use. The DEA is requiring the size of the inner liner to be clearly marked on the outside of the liner, and for the inner liner to bear a unique identification number in order to help ensure accountability, and to identify and prevent diversion. 21 CFR 1317.60. Given the totality of information

reviewed, the DEA concluded that a requirement for the contents to be non-viewable once the inner liner is sealed will help reduce diversion risks and deter drug seekers.

[21] **Issue:** One commenter stated that requiring contents of the inner liner to be non-viewable could lead to diversion as staff could record controlled substances as being disposed of without actually placing them into the receptacle.

Response: The rule prohibits authorized collectors' staff from handling collected substances, even for the purpose of depositing them into the collection receptacle. Ultimate users, and those who are authorized to handle controlled substances on behalf of ultimate users for the purpose of disposal, are the only persons who may deposit pharmaceutical controlled substances into a collection receptacle. 21 CFR 1317.30. Therefore, the DEA does not envision a circumstance where pharmaceutical controlled substances might be recorded as having been disposed of, but were in actuality diverted as a result of pharmacy staff never having placed the substances into the collection receptacle.

[22] **Issue:** One commenter indicated that the use of an inner liner that is removable and sealable immediately upon removal without emptying or touching the contents is impractical because the contents may spill or fall out and then must be handled.

Response: The DEA carefully considered the design and security requirements for inner liners and determined that the collection receptacle option will help to minimize the risk of diversion while ensuring safety and convenience for ultimate users and collectors. As discussed in the NPRM, inner liners that allow opportunities for collectors to sort or otherwise handle the collected substances would decrease security and increase the risk of diversion. The DEA does not believe that overfill or spillage from the inner liners will be a concern as the requirement that inner liners fit within the outer container of the collection receptacle is designed to prevent such

occurrences. However, security requirements, such as the presence of two employees to remove or supervise the removal of an inner liner, help reduce the risk of theft and diversion if such instances do occur. 21 CFR 1304.22, 1317.60, and 1317.75. If spillage occurs, a registrant's responsibility to provide effective controls and procedures to guard against theft and diversion of controlled substances would require the registrant to take corrective action to prevent spillage from recurring.

[23] **Issue:** Several commenters asked the DEA to identify the maximum allowable capacity for a receptacle and the maximum duration that controlled substances may be stored in the receptacle.

Response: There is no maximum or minimum capacity for collection receptacles at this time. Although there is no maximum duration that the collected substances may remain in the collection receptacle at this time, authorized collectors are reminded of their responsibility to provide effective controls and procedures to guard against theft and diversion, 21 CFR 1301.71(a), and their duty to report thefts and significant losses of controlled substances under 21 CFR 1301.74 and 1301.76.

[24] **Issue:** Several commenters asked the DEA to allow "disposal companies," distributors, and reverse distributors to manage and maintain collection receptacles at the registered locations of authorized collector retail pharmacies and at LTCFs on behalf of the authorized collector retail pharmacies. These commenters also asked if such entities may establish a fee system for such services.

Response: Distributors and reverse distributors will not be permitted to manage or maintain collection receptacles at retail pharmacies or LTCFs. 21 CFR 1317.40 and 1317.80. The DEA determined that no entities other than retail pharmacies and hospitals/clinics with an on-site

pharmacy will be permitted to manage collection receptacles at LTCFs. 21 CFR 1317.40 and 1317.80. As discussed in the NPRM, this rule establishes a checked system of transfers where each registrant who handles collected substances serves as a source of verification for the other registrants that handle the same substances, thus ensuring that the collected substances reach their intended destination with accountability and a reduced risk of diversion. In order to maintain this system, all collected substances must be handled in the manner described in this rule, including the requirement that the handling of a collection receptacle inner liner be restricted to employees of the authorized collector as provided, with the limited exception for LTCFs. 21 CFR 1317.80. Such requirements ensure that persons handling collected substances during the disposal process are accountable to their employer, and the number of entities handling the collected substances is reduced while also providing a secure system of checks that increases the level of accountability.

H. *Mail-Back Programs (11 issues)*

[1] **Issue:** Thirteen commenters stated that the on-site destruction requirement for mail-back programs is severely limiting due to the limited number of commercial incinerators. These commenters urged the DEA to allow collectors to receive mail-back packages whether or not they have a means of on-site destruction. Several commenters also asked the DEA to allow collectors to use a third party to destroy mail-back packages.

Response: As discussed in the NPRM, an on-site method of destruction for mail-back packages is the minimum necessary to prevent diversion of controlled substances destined for destruction. 21 CFR 1317.05. Importantly, an on-site method of destruction reduces the accumulation of controlled substances in a single location, and minimizes the transfer of controlled substances between various locations. This is intended to help minimize the risk of diversion. For each of

the three methods of ultimate user disposal included in this rule, the DEA has attempted to minimize the number of entities that handle the collected substances in order to minimize the risk of diversion, which increases each time a controlled substance is transferred to a new person. It is emphasized that authorized collectors may partner with reverse distributors and other authorized registrants with on-site methods of destruction to promote mail-back programs, e.g., empty mail-back packages may be disseminated at hospitals/clinics and retail pharmacies and mailed back to a reverse distributor with an on-site method of destruction.

[2] **Issue:** One commenter strongly supports the requirement that authorized collectors who conduct a mail-back program use an on-site method of destruction; however, other commenters expressed concern that the requirement would discourage authorized collectors from conducting mail-back programs. Several commenters noted that very few destruction facilities currently exist and there was concern that such facilities do not have proper security to handle controlled substances.

Response: As indicated in the previous response, mail-back programs have the potential to provide a secure and responsible means of disposal without geographical restriction within the United States. As such, the existence of a small number of appropriate destruction sites should not impact ultimate users' ability to participate or the potential for mail-back programs to develop. In other words, a single destruction site can support many different mail-back programs and an unlimited number of mail-back packages may be provided to ultimate users at various locations throughout the United States to be mailed back to a single destruction site. Also, as discussed in the NPRM, the DEA hopes that the rule will encourage innovation and expansion of destruction methods beyond incineration so that additional entities may provide destruction services for mail-back programs in the future.

[3] **Issue:** A few commenters expressed concern that no entities will undertake the implementation of a mail-back program because of the related expense, noting that the requirement that mail-back packages be pre-addressed with pre-paid postage will be very costly. A commenter also asked the DEA to clarify whether unregistered retail pharmacies working with a registered authorized collector would be permitted to make mail-back packages available to patients.

Response: As discussed in the NPRM, authorized collectors who conduct mail-back programs are encouraged to collaborate to operate mail-back programs by partnering with other entities to assist with the dissemination of mail-back packages to ultimate users, in order to minimize costs. Additionally, pre-paid postage will ensure that the package is not returned to sender, which will help reduce its handling and therefore, the diversion risks. Pre-addressed envelopes will help ensure that the package is delivered to the authorized location.

[4] **Issue:** One commenter asked the DEA to clarify whether there are specific testing requirements in regard to the packaging standards (e.g., water/spill proof, tear resistant, sealable, etc.). One commenter asked the DEA to clarify the distinction between packages damaged as part of normal transport and packages damaged by other means, such as tampering.

Response: The DEA is not requiring specific testing requirements to ensure packages meet the standards provided in § 1317.70 (e.g., water/spill proof, tear resistant, sealable, etc.). However, the packages must be consistent with these standards. Collectors authorized to receive mail-back packages must make a determination based on the facts and circumstances as to whether or not an apparently damaged package became so through normal transportation or through tampering or other intentional means.

[5] **Issue:** Commenters expressed concern that the requirement for mail-back collectors to issue mail-back packages with unique identification numbers is burdensome and does not seem to provide any useful information since ultimate users are not required to notify collectors that they have mailed a package, and it is likely that many packages will not be used. Five commenters asked the DEA to explicitly state that authorized collectors who conduct mail-back programs will not be responsible for reconciling mail-back packages that were never returned.

Response: The DEA believes that recording the unique identification numbers of mail-back packages in accordance with § 1317.70 is a reasonable recordkeeping requirement designed to help identify and prevent diversion; this information can aid investigations and is useful for that purpose alone. The DEA recognizes that disseminated packages may go unused, and this alone should not form the basis for unreasonable scrutiny of authorized collectors. Additionally, at this time, authorized collectors are not responsible for tracking mail-back packages that were disseminated but never returned.

[6] **Issue:** One commenter disagreed with the DEA's assessment that mail-back programs are more susceptible to diversion and therefore require stricter controls.

Response: The DEA carefully considered the diversion risks in mail-back programs. Based on the DEA's experience, the DEA believes that the risks of diversion associated with mail-back programs are great because of necessary actions including the handling of the packages, mail sorting, and mail delivery by non-registrants. The DEA believes that the security measures established by this rule are the minimum required to reduce the risk of diversion inherent to mail-back programs.

[7] **Issue:** One commenter expressed concern that mail-back packages would be subject to greater risks of diversion in rural areas.

Response: The DEA appreciates the commenter's concern. The DEA has considered the diversion risks for mail-back programs, including packages originating in rural areas. It may be true that mail-back packages originating in some rural areas may be subject to an increased risk of diversion due to fewer people being able to readily witness theft from a mailbox. However, it may also be true that risks of diversion from mail-back programs might be lower in rural areas due to less traffic (pedestrian, vehicular, or equine), resulting in fewer opportunities for tampering with or theft of mail-back packages. Regardless, the DEA believes that the relative risks of diversion of mail-back packages in rural areas are mitigated by the required security procedures and are outweighed by the benefits of providing ultimate users a means to dispose of unused, unwanted, or expired pharmaceutical controlled substances.

[8] **Issue:** The United States Postal Service (USPS) has raised a number of issues relating specifically to the mail-back program, and also to the disposal regulations in general. The USPS asked the DEA to make several changes to the terminology used in the proposed rule, so that the DEA regulations will be consistent with standard USPS products and services. The USPS also requested that the DEA clarify that all registrants must comply with USPS laws and regulations, including applicable USPS requirements for packaging and mailing pharmaceuticals.

The USPS asked the DEA to consistently refer to "mail-back packages" as "mailing packages" rather than "mailers" as the USPS refers to "mailers" as persons or entities entering a mailing. The USPS also asked the DEA to remove any references to "business reply mail" that are inconsistent with the USPS's use of the term. The USPS asked that proposed § 1317.85 specify that ultimate users may return recalled controlled substances to the manufacturer or other authorized registrant by U.S. Mail. The USPS also asked the DEA to clarify that inner liners are requirements for collection receptacles—not mail-back packages.

The USPS also requested that the DEA state that collectors operating a mail-back program must exclusively use the United States Postal Service. The USPS also asked the DEA to make all references to "mail system" in the preamble refer exclusively to the United States Postal Service. The USPS asked that they not be prohibited from transporting controlled substances to a reverse distributor on behalf of law enforcement, especially in light of the fact that law enforcement may operate mail-back programs.

Response: The DEA appreciates the time taken by the USPS to review the proposed rule and submit thoughtful comments with their concerns and suggestions. In addition, the DEA acknowledges that the USPS understands these regulations and has experience responsibly handling controlled substances. The DEA is modifying some of the terminology that was used in the NPRM, per the USPS's concerns and suggestions. Rather than use the term "mailing packages," all references to "mailers" are changed to "mail-back packages." The DEA believes this will better avoid the confusion regarding "mailers" being defined as persons or entities that enter a "mailing." The reference to "business reply mail" is also removed. The DEA declines to specify that "mail" or "mail system" refers exclusively to the USPS; however, the USPS is a shipping option.

Additionally, in § 1317.85, ultimate users still have the options to return a recalled controlled substance as is currently allowed under § 1307.12 of the existing regulations. The text of the rule clearly states that all persons and entities must comply with applicable Federal laws and regulations, which includes USPS laws and regulations. Also, inner liners are requirements for collection receptacles—not mail-back packages. The mail-back package specifications are outlined in § 1317.70.

While the USPS asked that the text of the regulation specifically state that mail-back packages may be sent via the U.S. Postal Service as well as by common or contract carrier, the DEA declines to make this change. The DEA considers the USPS to be a common or contract carrier for purposes of the CSA.

[9] **Issue:** One commenter asked the DEA to clarify whether the regulation that requires mail-back programs to include only mail-back packages mailed from within the United States will preclude USPS-serviced mail-back programs in any of the areas in which it operates (e.g., the Caribbean District, other territories such as Guam, and United States military installations).

Response: The term "import" means "any bringing in or introduction of" a controlled substance into any area. Pursuant to 21 U.S.C. 952, it is unlawful to import controlled substances into the customs territory of the United States (the 50 States, the District of Columbia, and Puerto Rico), except under specific circumstances not relevant to ultimate user disposal. Thus, an ultimate user located outside of the customs territory of the United States is not permitted to send a mail-back package into the customs territory of the United States.

[10] **Issue:** One commenter asked the DEA to clarify whether authorized collectors operating mail-back programs may use carrier services that allow packages to be held at a carrier facility until the packages can be picked up.

Response: Although some changes to business operations may need to occur in order for an authorized collector to effectively establish and maintain a mail-back program, the requirements established by this rule are the minimum required to detect and prevent diversion. As described in this rule, mail-back packages must be pre-addressed to the authorized mail-back location with the on-site destruction method, and thus, the packages must be delivered to the authorized mail-back location rather than picked up by the collector. 21 CFR 1317.70. The pre-addressed

delivery location must be capable of receiving such deliveries on a regular basis without interruption. Otherwise, the opportunities for diversion increase as the packages are delayed or stored during transit.

[11] **Issue:** One commenter suggested that the DEA establish a national mail-back program.

Response: This rule authorizes certain collectors to conduct mail-back programs. 21 CFR 1317.40 and 1317.70. There is no limitation regarding the geographic coverage of mail-back programs within the United States if the programs comply with all applicable Federal, State, tribal, and local laws and regulations. At this time, the DEA does not have the resources to operate a national mail-back program.

I. *Take-Back Events (6 issues)*

[1] **Issue:** One commenter indicated it would be difficult for ultimate users to participate in take-back events, particularly in rural areas.

Response: The DEA has attempted to expand the variety of disposal options while also ensuring secure and responsible drug disposal, and the DEA anticipates that the expansion to include certain hospitals/clinics to become authorized as collectors will provide more disposal options for ultimate users, including those in rural areas. Additionally, the DEA encourages those persons living in rural areas who are unable to utilize a collection receptacle or attend a take-back event to dispose of unwanted pharmaceutical controlled substances in the same manner in which the pharmaceutical controlled substances were received, i.e., if the substances were delivered by a mail-order pharmacy, the DEA encourages the pharmacy to include a mail-back package for safe disposal; or, if the substances were dispensed at a pharmacy, the DEA encourages pharmacies to have a collection receptacle available for safe disposal. Nonetheless, the DEA recognizes that some ultimate users may not have convenient access to any of the

disposal options available in this rule. Until the availability of these disposal options increases, ultimate users who wish to dispose of unwanted pharmaceutical controlled substances may continue to dispose of them in manners consistent with all applicable Federal, State, tribal, and local laws and regulations. The DEA's Office of Diversion Control website provides information regarding safe disposal of pharmaceutical controlled substances, including guidance from the FDA and the EPA. Ultimate users can find this information at www.DEAdiversion.usdoj.gov.

[2] **Issue:** Several people asked the DEA to clarify the role of law enforcement at take-back events. One commenter asked the DEA to relax the two-employee requirement for law enforcement officers handling collected substances. Another commenter stated that law enforcement officer supervision, rather than direct participation, should suffice.

Response: Law enforcement must appoint at least one law enforcement officer employed by the agency to oversee collection at the take-back event. 21 CFR 1317.65. "Oversee" has its common, everyday meaning: to supervise, manage, watch over, and direct in an official capacity. The direct participation this rule mandates is that a law enforcement officer must maintain custody and control of the collected substances from the time they are collected to the point in time that they are securely transferred, stored, or destroyed. 21 CFR 1317.65. This rule does not require two law enforcement officers to be present at take-back events; however, law enforcement may determine that two or more law enforcement officers are necessary at a particular take-back event due to safety and security concerns. In the alternative, law enforcement may determine that the same law enforcement officer may oversee the take back event and also maintain custody and control of the collected substances from the time the substances are collected from the ultimate user or person authorized to dispose of the ultimate

user decedent's property until secure transfer, storage, or destruction has occurred, as outlined in § 1317.65(b). Although the participation of law enforcement is required at take-back events, the DEA is not requiring law enforcement to hold or participate in take-back events. As discussed in the NPRM, law enforcement must determine how often available resources allow them to hold take-back events.

[3] **Issue:** A few commenters requested that the DEA allow other authorized collectors, such as retail pharmacies and reverse distributors, to become authorized to hold take-back events. One commenter stated that law enforcement officers' presence should be optional if there is a collection receptacle at the event that meets the specifications in the rule.

Response: If an authorized collector or other entity wishes to conduct a take-back event, the event must be held in partnership with law enforcement. 21 CFR 1317.65. Take-back events are intended to be limited-duration events that may take place at an unsecure location that is easily accessible to the public, such as a community center or town center. Given the likelihood of publicity and limited physical security at such locations, the DEA believes that it is important to ensure active law enforcement participation for the safety of the event participants and the community. The DEA believes that active law enforcement participation will help deter theft and reduce diversion risks. The presence of a collection receptacle at a take-back event does not preclude the need for law enforcement presence at the collection site because the publicity for the event increases the receptacle's visibility for drug seekers, thus increasing diversion risks.

[4] **Issue:** A number of entities expressed concern that the implementation of this rule will result in the cessation of DEA-sponsored national take-back events. These commenters felt that take-back events will be too costly for communities and law enforcement, and commenters suggested that the DEA continue take-back events and provide a transition plan from the national take-back

events until implementation of the rule.

Response: The DEA-sponsored national take-back events were initiated as a means of providing safe and convenient disposal of pharmaceutical controlled substances by ultimate users until alternative options could be implemented. The DEA is committed to continuing national take-back events until the effective date of this final rule. The DEA believes that implementation of disposal methods is best tailored to local communities by local communities. The DEA encourages public and private partnerships to optimize the expanded disposal options in a cost-efficient manner.

[5] **Issue:** One commenter expressed concern that existing take-back events would likely be unable to continue under this rule. This commenter was concerned that the prohibition of sorting would cause a burden since non-controlled substances and packaging could not be sorted from controlled substances. This commenter stated that it will be overly burdensome for programs to handle all collected substances as schedule II controlled substances.

Response: The DEA does not intend for this rule to require changes to existing non-controlled substance take-back programs. The security measures required by this rule are the minimum necessary to ensure a safe and secure means of disposal of pharmaceutical controlled substances. It should be noted however, that law enforcement are not required to follow the physical security requirements for handling, sorting, or storing collected controlled substances. 21 CFR 1317.35. The physical security requirements applicable to law enforcement in the final rule at §§ 1317.35 and 1317.65 state that law enforcement "should" take certain measures; and that law enforcement "shall" appoint a law enforcement officer to oversee a take-back event and law enforcement officers "shall" maintain custody and control of the collected substances. Additionally, this rule provides a number of previously unavailable means of ultimate user

disposal that are likely to decrease the frequency of and need for community take-back events. The DEA would like to clarify that comingling of controlled and non-controlled substances is permitted, but not required, and co-sponsors of take-back events may specify that only controlled substances will be accepted. Another method to alleviate the burdens would be to provide a separate receptacle for non-controlled substances at the take-back event. Additionally, as discussed in response to previous comments, this rule does not require that collected substances be in their original packaging, and law enforcement may discourage or prohibit ultimate users from disposing of original packaging into the collection receptacle for controlled substances at take back-events.

[6] **Issue:** One commenter indicated that municipalities and other organizations should be permitted to "take the lead" in organizing and conducting take-back events in conjunction with, and in the presence of, law enforcement. Other commenters raised concerns that such events conducted in partnership with local government and community groups would no longer be allowed, and that the requirements would prevent controlled substance take-back events from being held concurrently with other take-back events, such as for the disposal of hazardous waste and non-controlled substances.

Response: The rule permits any entity to partner with law enforcement to hold a pharmaceutical controlled substances take-back event. 21 CFR 1317.65(a). Municipalities or other organizations may partner with law enforcement as long as such events are conducted in accordance with all applicable laws and regulations pertaining to the disposal of pharmaceutical controlled substances. The DEA emphasizes that take-back events are intended to be one-time or periodic events held in a community center or other convenient and accessible location, and that there is no prohibition against holding such events in conjunction with events for the

disposal of other substances, such as hazardous waste or non-controlled pharmaceuticals.

J. *Prohibition on Handling, Sorting, and Inventorying Inner Liner Contents and Mail-Back Package Contents (8 issues)*

[1] **Issue:** One commenter adamantly stated that collected substances should not be sorted under any circumstances. This commenter expressed concerns about diversion risks and the brokering of unused controlled substances.

Response: The DEA agrees that the diversion risks of handling, sorting, or inventorying collected substances outweigh any perceived benefits. The DEA has carefully considered all of the various commenters' concerns on the prohibition of handling, sorting, and inventorying inner liner contents and mail-back package contents, and will retain these prohibitions. As provided in §§ 1317.60(c) and 1317.70(f), inner liners shall be sealed *immediately* upon removal from the permanent outer container; sealed inner liners and returned mail-back packages shall not be opened, x-rayed, analyzed, or otherwise penetrated. Accordingly, their contents shall not be sorted or inventoried subsequent to being placed into a collection receptacle or mail-back package. To clarify this, § 1317.75(c) was modified to add the prohibition against individually handling substances after they have been deposited into a collection receptacle. These specific security measures are designed to help prevent and reduce the opportunities for diversion (including the re-introduction of tainted pharmaceutical controlled substances into the stream of commerce).

[2] **Issue:** Twenty-four commenters stated that pharmacists and other volunteers should be permitted to sort collected substances, particularly in the presence of law enforcement officers at take-back events. One commenter stated that the DEA should recognize the accountability,

expertise, and experience of healthcare professionals, and the DEA should utilize these experts in an effort to broaden medication disposal efforts.

Response: The DEA appreciates the valuable expertise and experience of healthcare professionals, including pharmacists. The DEA has carefully considered the comments in response to the NPRM, and the remarks at the January 2011 public meeting. The DEA believes that the disposal methods outlined in this rule will provide ultimate users and their authorized representatives with expanded options to safely and securely dispose of unwanted, unused, and expired pharmaceutical controlled substances. Pursuant to § 1317.65, law enforcement may continue to conduct take-back events when a law enforcement officer maintains control and custody of collected substances at take-back events and only the ultimate user transfers controlled substances to law enforcement control and custody. However, non-law enforcement personnel may assist the law enforcement officer, and the final rule does not prohibit healthcare professionals from voluntarily polling ultimate users about the substances they are discarding or from assisting ultimate users to separate pharmaceutical controlled substances from non-controlled substances during the disposal process, and inventorying the non-controlled substances.

Furthermore, nothing in this rule prohibits law enforcement from partnering with authorized collectors or other entities to inventory or sort substances that have been collected by law enforcement provided that the collected substances remain under the control and custody of law enforcement. This final rule in § 1317.65(b) requires that law enforcement maintain control and custody of the collected substances from the time the substances are collected until secure transfer, storage, and destruction has occurred. Therefore, if law enforcement opts to inventory or sort collected substances within their possession, law enforcement should provide adequate

security to prevent diversion or theft of controlled substances within their possession and control as a result of, or during, inventorying or sorting.

[3] **Issue:** Thirty-eight commenters stated that the DEA should permit collectors or certain non-registered persons to handle, sort, and inventory collected substances for data collection and research purposes. Many of these commenters urged the DEA to provide an exception to allow pharmacists and volunteers to inventory and sort controlled substances under the supervision of law enforcement officers. Numerous commenters stated that inventorying collected substances is crucial to determining a root cause analysis of medication waste. Others stated that such information could help guide prescribing practices and be used in educational settings. Several commenters stated that inventorying collected substances is necessary to determine outcome measures for grants for disposal programs. Also, several commenters stated that the DEA should provide an exception for Institutional Review Board-approved research projects.

Response: The DEA understands and appreciates these comments. As discussed in the preceding response, law enforcement has the discretion to partner with other entities to conduct a take-back event pursuant to § 1317.65(a). There are no restrictions on how law enforcement handles the collected substances so long as they maintain control and custody of the substance. Accordingly, law enforcement may inventory and sort substances that law enforcement collects. The diversion-related concerns present when authorized registrants collect controlled substances from ultimate users is not present when law enforcement collects substances from ultimate users. Taking into account the totality of the various risks and benefits, the DEA believes that this final rule imposes the minimum necessary controls to allow a secure and responsible means by which ultimate users can dispose of pharmaceutical controlled substances. Relying on its experience, and as discussed in the NPRM, the DEA finds that any potential benefits of allowing authorized

collectors or unregistered persons to independently inventory or sort controlled substances after receipt from the ultimate user do not outweigh the risks of diversion, except when the controlled substances remain in the control and custody of law enforcement, as mentioned in the previous response.

Data collection is not impossible under the rule even though collected substances cannot be sorted or inventoried after they have been deposited into a collection receptacle or received by a collector through a mail-back package (unless the collection is conducted by law enforcement and the substances are within the custody and control of law enforcement). For example, authorized collectors may seek information voluntarily from ultimate users regarding the substances the ultimate user is disposing. And, data such as the weight of the inner liners, the number of ultimate users attending a take-back event, and the number of mail-back packages received in relation to the number of packages disseminated, can be useful measures. The rule only prohibits authorized collectors from physically handling the substances, such as taking the substances from the ultimate user, or sorting substances after the ultimate user has deposited them into a receptacle or mail-back package. 21 CFR 1317.70 and 1317.75.

[4] **Issue:** Twenty-two commenters stated that contents should be sorted to ensure adequate storage space. Several commenters stated that packaging and pill bottles should be sorted since they are voluminous. Other commenters stated that non-controlled substances should be sorted from controlled substances.

Response: Pursuant to §§ 1317.70(b) and 1317.75(b), comingling of controlled and non-controlled substances is permitted, but it is not required. In addition, this rule does not require pharmaceutical controlled substances collected from ultimate users to be collected and stored in the original packaging, and collectors may institute procedures to prevent inadvertently

collecting packaging. Authorized collectors may address adequacy of space issues by choosing not to collect comingled pharmaceutical controlled substances and non-controlled substances, refusing to accept the original controlled substance packaging, or by increasing destruction frequencies. In addition, the DEA has expanded the available storage options for practitioners in this final rule by allowing practitioners to store sealed inner liners and returned mail-back packages in a securely locked room with controlled access. 21 CFR 1317.05.

[5] **Issue:** A commenter noted that authorized collectors should have direct supervision over the substances that are placed into collection receptacles to prevent undesirable materials from being deposited into collection receptacles.

Response: Each potential authorized collector must weigh all of the potential risks and benefits in deciding whether to implement and manage any ultimate user disposal program, including any necessary steps to prevent the unwanted collection of regulated hazardous waste or otherwise undesirable materials, in a manner consistent with this rule and all other applicable Federal, State, tribal, and local laws and regulations. Authorized collectors may view what ultimate users deposit into collection receptacles, and they may ask what substances are being deposited. Although the actual disposal of a pharmaceutical controlled substance into a collection receptacle must be performed by an ultimate user in accordance with § 1317.30, the authorized collector maintains ultimate control over that receptacle and should institute necessary measures to protect against the collection of unwanted substances so long as such measures are consistent with this rule and all other applicable Federal, State, tribal, and local laws and regulations.

[6] **Issue:** Several commenters asked that the DEA permit pharmacy staff to deposit collected substances into collection receptacles. These commenters asked the DEA to consider situations where the pharmacy is completely blocked from the public (such as with a bullet-proof barrier).

Response: For the reasons discussed in the NPRM and in previous comment responses, the DEA declines to allow pharmacy staff to handle pharmaceutical controlled substances collected from ultimate users. The registered location of any retail pharmacy that wishes to become an authorized collector must satisfy the specifications for collection receptacles and inner liners. 21 CFR 1317.60 and 1317.75. If a retail pharmacy desires to be an authorized collector, that pharmacy shall only allow ultimate users (and others authorized to dispose of controlled substances on behalf of ultimate users) to deposit the pharmaceutical controlled substances directly into the collection receptacles in accordance with § 1317.30. The requirements of the collection receptacles were carefully considered and designed to limit the number of hands that handled the pharmaceutical controlled substances in order to prevent diversion and diversion opportunities, as well as to prevent the re-introduction of tainted pharmaceutical controlled substances into the closed system of distribution.

[7] **Issue:** Twenty commenters suggested that the DEA permit some sort of inspection for inner liner and mail-back package contents to ensure that unacceptable contents are removed, such as x-raying and scanning. These commenters were particularly concerned about mercury-containing thermometers, iodine-containing medications, medical sharps, compressed cylinders, and other hazardous waste. Other commenters expressed concern that by allowing comingling of substances in collection receptacles, employees may be subjected to hazardous conditions if unsafe or hazardous materials are deposited.

Response: The DEA understands and appreciates these concerns of the commenters; however, the DEA has concluded that allowing inspection of inner liners and mail-back packages presents an unacceptable risk of diversion. These issues were closely reviewed prior to the NPRM and re-reviewed in association with these comments. Whether an authorized collector comingles

ultimate users' pharmaceutical controlled substances with non-controlled substances is within the discretion of that authorized collector. This rule does not mandate comingling. 21 CFR 1317.75. Each potential authorized collector must weigh all of the potential risks and benefits in deciding whether to implement and manage any ultimate user disposal program, including any necessary steps to prevent the unwanted collection of regulated hazardous waste or otherwise undesirable materials, in a manner consistent with this rule and all other applicable Federal, State, tribal, and local laws and regulations. As discussed in response to previous comments, collectors may control the substances collected, and they may view substances before they are deposited into collection receptacles. For additional commentary on hazardous waste disposal, please see comment section "Q.", entitled "Hazardous Materials Transportation and Hazardous Waste Destruction."

[8] **Issue:** Some commenters urged the DEA to require authorized collectors to provide clear instructions on what may and may not be placed in mail-back packages in order to reduce instances in which hazardous materials/waste may be inadvertently destroyed in a manner that is not consistent with environmental or other applicable laws or regulations due to the prohibition against opening or inspecting the contents of mail-back packages.

Response: The rule includes a requirement for the collector to provide packages with instructions indicating what substances are permitted to be included in the package. 21 CFR 1317.70. The rule does not require specific language for such instructions, which must ultimately be determined by the collector in a manner consistent with the rule.

K. *Long-Term Care Facilities (LTCFs) (21 issues)*

Definitions and Terms Specific to LTCFs

[1] **Issue:** Commenters asked the DEA to clarify the meaning of "LTCF" with regard to assisted living facilities, hospice facilities, and residential care in private homes, as the meaning of LTCF often varies by State.

Response: LTCF is defined at § 1300.01(b) and "means a nursing home, retirement care, mental care or other facility or institution which provides extended health care to resident patients."

[2] **Issue:** Commenters asked the DEA to clarify the meaning of "have resided" with regard to a LTCF's ability to dispose of controlled substances on behalf of residents.

Response: The phrase "have resided," is utilized in the Disposal Act, but was not defined by Congress. The DEA has not determined a need to apply a technical definition for this phrase apart from its ordinary meaning. The DEA understands the ordinary meaning of "have resided" to be typically understood as persons who have died or otherwise recently departed a location without manifesting intent to return. Thus, for example, as discussed in response to issue [7] below, when a LTCF resident is transferred to another facility, the resident "has resided" at the LTCF, and the LTCF may dispose of the former resident's pharmaceutical controlled substances in an authorized collection receptacle. 21 CFR 1317.30.

Registration of Collection Receptacles at LTCFs

[3] **Issue:** Commenters asked the DEA to clarify whether an authorized LTCF location where an authorized collector maintains a collection receptacle would be considered a "registered location" of the retail pharmacy.

Response: The location of the collection receptacle is both a registered location and a controlled premise. It is a registered location of the authorized hospital/clinic or retail pharmacy because the authorized collector may only install and manage a collection receptacle at a LTCF pursuant to the authority granted by the DEA, and they are limited at that location to conducting only

those activities that are specifically authorized and required under this rule as necessary to the installation and maintenance of that authorized collection receptacle. LTCFs with authorized collection receptacles are "controlled premises" pursuant to 21 U.S.C. 880(a) and 21 CFR 1316.02(c); accordingly, the DEA may enter LTCFs and conduct administrative inspections in furtherance of, and in carrying out, the responsibilities charged to the DEA by the CSA pursuant to 21 U.S.C. 880(b) and 21 CFR 1316.03.

Disposal Methods and Procedures at LTCFs

[4] **Issue:** A commenter asked the DEA if LTCFs may use an on-site method of destruction. Three commenters specifically asked if LTCFs may continue their current drug disposal method of "sewering." Other commenters asked the DEA to clarify how existing methods of disposal utilized by LTCFs will be impacted by this rule and to provide for an interim method of disposal for LTCFs.

Response: Although the DEA appreciates the commenters' concerns, the DEA cannot comment on each potential method of disposal occurring at LTCFs prior to these regulations. The implementation of authorized disposal methods for ultimate users is strictly voluntary and, with the exception of law enforcement-sponsored programs, generally such programs have no lawful means of existence prior to the effective date of this rule. It is important to note that this rule provides additional options for disposal and does not prohibit any methods currently used by LTCFs that are consistent with Federal, State, tribal, and local laws and regulations. For example, LTCFs are not prohibited by this final rule from destroying patients' unwanted pharmaceutical controlled substances at the LTCF, on behalf of the resident patients, in accordance with applicable Federal, State, tribal, and local laws and regulations, including environmental laws and regulations. However, as explained further below, the DEA has

considered the diversion risks and determined that the installation and maintenance of collection receptacles by authorized hospitals/clinics and retail pharmacies is the most secure and responsible means by which registrants may collect and dispose of LTCF residents' pharmaceutical controlled substances.

As stated in § 1317.90(a), the requirement to render controlled substances "non-retrievable" applies only to DEA registrants that destroy controlled substances. The "non-retrievable" language does not apply to ultimate users. As discussed in the NPRM, the DEA does not believe that "sewering" would render a pharmaceutical controlled substance "non-retrievable." However, such a requirement would not apply to a LTCF unless the LTCF is itself a registrant and destroying its own pharmaceutical controlled substance stock pursuant to § 1317.05(a).

[5] **Issue:** Many commenters indicated that the DEA should provide LTCFs with additional options for disposal of controlled substances on behalf of residents. Approximately fifteen commenters asked the DEA to expand which registrants are permitted to manage collection receptacles at LTCFs. Seven commenters asked the DEA to permit LTCFs to use mail-back packages. Several commenters stated that LTCFs should be allowed to use the same disposal options that this rule affords ultimate users.

Response: As previously discussed, this rule in § 1317.40 expands the types of registrants that may be authorized as collectors, and permitted to manage and maintain collection receptacles at LTCFs. In addition to retail pharmacies (including "closed-door pharmacies" that service LTCFs), hospitals/clinics with an on-site pharmacy may maintain collection receptacles at LTCFs. Furthermore, the options available to all ultimate users to dispose of their pharmaceutical controlled substances are also available to LTCF residents. As ultimate users

(defined in 21 U.S.C. 802(27) as persons who have lawfully obtained, and who possess, a controlled substance for their own use or for the use of a member of their household), LTCF residents may avail themselves of all disposal methods made available by this rule to ultimate users, including participation in authorized mail-back programs. For example, on behalf of an LTCF resident, an LTCF employee may place the resident's unwanted pharmaceutical controlled substances in a mail-back package, seal it, and deposit it into the facility's outgoing mail system. Care should be taken to ensure that LTCF residents' use of mail-back programs does not result in the accumulation of pharmaceutical controlled substances in a single location susceptible to internal or external diversion threats.

The DEA has carefully considered the risks and benefits of collection activities at LTCFs. Among the DEA's specific considerations were that LTCFs typically have large volumes of controlled substances on-site and that they are typically not registered with the DEA. The DEA also specifically considered the risks and benefits associated with LTCF personnel disposing of pharmaceutical controlled substances on behalf of persons who reside or have resided at that LTCF. The DEA determined that in order to adequately protect the public health and safety, and to prevent diversion, the collection of such substances must be limited to certain registrants that are well-equipped to handle the unique circumstances surrounding the disposal of controlled substances at LTCFs. After careful deliberation, the DEA determined such registrants should be limited to retail pharmacies and hospitals/clinics with an on-site pharmacy. 21 CFR 1317.40. In making its determination, the DEA took consideration of the fact that hospitals/clinics with on-site pharmacies, and retail pharmacies, routinely dispense large volumes of controlled substances in a public setting. Additionally, many hospitals/clinics with on-site pharmacies and retail pharmacies have experience working closely with LTCFs or have well-established, on-going

relationships with LTCFs. For example, many retail pharmacies and hospitals/clinics directly deliver pharmaceutical controlled substances to LTCF residents, some retail pharmacies have developed expertise in dispensing substances at LTCFs via an automated dispensing system (ADS) (i.e., mechanical systems that perform operations or activities relative to the dispensing of medications), and some LTCFs share common management or ownership with hospitals/clinics.

The DEA recognizes that other types of registrants also have relationships with LTCFs, and considered authorizing other types of registrants to install and manage collection receptacles at LTCFs. However, after careful consideration, the DEA determined that the presence of certain factors that increase opportunities for diversion in the specified circumstances weigh against further expanding the types of registrants that may collect at LTCFs.

Specifically, the DEA declines to allow reverse distributors to install and maintain collection receptacles at LTCFs because reverse distributors are at the end of the supply chain. It would be contrary to the public health and safety and pose an increased risk of diversion to authorize a reverse distributor to independently install and maintain a collection receptacle at an LTCF, remove the inner liner, transport collected substances to the final destruction location, and ensure they are destroyed. One of the principal factors considered by the DEA in coming to this conclusion is the fact that in such a situation, the reverse distributor would be the sole registrant to maintain the only records of installation, removal, and destruction. Such an authorization would be contrary to the closed system of distribution where each registrant who handles controlled substances serves as a source of verification for the other registrants that handle the same substances, thus ensuring that controlled substances reach their intended destination with accountability and a reduced risk of diversion. The regulations implemented by this final rule specifically utilize this system of checks for collection activities at LTCFs. Retail pharmacies

and hospitals/clinics with an on-site pharmacy are registrants. As established in this final rule, when retail pharmacies and hospitals/clinics maintain collection receptacles at an LTCF, they may not transport sealed inner liners. Rather, they are expected to transfer sealed inner liners to another registrant for destruction pursuant to § 1317.05(c)(2)(iv). Two-registrant integrity allows the DEA to verify and cross-check each registrants' records. Conversely, LTCFs and destruction facilities are generally not registrants. Therefore, if a reverse distributor were authorized to install and maintain collection receptacles at LTCFs, and also pick-up, transport, and destroy sealed inner liners from LTCFs, the DEA would be unable to verify the reverse distributor's removal or destruction records with another registrant's records. Allowing this would not meet the two-registrant integrity requirement that is the minimum required to ensure accountability, particularly when collected substances are destined for destruction.

As discussed in responses to other comments, because LTCFs are generally not registrants, the DEA is unable to allow such facilities to be authorized collectors for the purpose of disposing ultimate user-collected substances, or handle disposed substances on behalf of another registrant. We note that although LTCFs may not use mail-back packages or administer a mail-back program, ultimate users who reside in LTCFs may use mail-back packages under this rule. 21 CFR 1317.30 and 1317.70.

[6] **Issue:** One commenter asked the DEA to allow a LTCF resident, or the resident's legal representative, to dispose of controlled substances through all available means, whether the resident is alive or deceased.

Response: All means of disposing of pharmaceutical controlled substances are available to ultimate users and persons lawfully entitled to dispose of an ultimate user decedent's property, including those ultimate users who reside, or have resided, in a LTCF. 21 CFR 1317.30.

[7] **Issue:** Commenters also asked the DEA to address how LTCFs should handle situations in which a resident is transferred to a hospital and the resident leaves unwanted medication at the LTCF.

Response: Pursuant to the Disposal Act, Congress provided the DEA authority to authorize LTCFs only to "dispose of controlled substances on behalf of ultimate users who reside, or have resided," at the LTCF. 21 CFR 1317.30. When a LTCF resident is transferred to a hospital or other facility, the resident "has resided" at the LTCF, and if the medication is intentionally left at the LTCF, it is "unwanted," and the resident has discontinued use. Accordingly, the LTCF may dispose of the former resident's pharmaceutical controlled substances by depositing the substances into an authorized collection receptacle immediately, but no longer than three business days after discontinuation of use. 21 CFR 1317.80.

[8] **Issue:** Several commenters indicated that the three-day disposal provision for LTCFs is overly restrictive and potentially costly for residents. These commenters stated that three days is too short a time span and will result in residents being forced to purchase additional medications when there is a short break in use as a result of illness, hospitalization, or a trial dosage reduction. One commenter stated that three days is not a long enough time period to determine if the patient may need the medication again in the future.

Response: The DEA declines to extend the timeframe for LTCFs to dispose of pharmaceutical controlled substances on behalf of LTCF residents. As previously discussed, LTCFs are required to dispose of pharmaceutical controlled substances "immediately, but no longer than three business days after the discontinuation of use" in § 1317.80(a). With respect to "discontinuation of use," the final rule modifies § 1317.80(a) to include a permanent discontinuation as directed by the prescriber, as a result of the resident's transfer from the LTCF, or as a result of death. The

DEA cannot readily foresee a circumstance where a short break in use as a result of illness, short-term hospitalization, or a trial dosage reduction would be considered a discontinuation of use. Also, if the prescriber has not yet determined whether or not a medication is needed in the future, then it is likely that there has not yet been a "discontinuation of use."

Collection Receptacle Maintenance at LTCFs

[9] **Issue:** Fifteen commenters indicated that the requirement to have two employees of the authorized collector retail pharmacy remove and install inner liners is burdensome, and it will discourage retail pharmacies from installing and maintaining collection receptacles at LTCFs. The commenters suggested that the DEA allow LTCF personnel to remove, store, and replace the inner liners. A commenter suggested that LTCF personnel be permitted to sort out non-controlled substances to reduce the amount of material collected in the receptacles.

Response: As explained above, the DEA is amending the final rule to allow flexibility in the requirement that two employees of the authorized collector be present for the installation and removal of inner liners at LTCF collection receptacles. As amended, the final rule in § 1317.80(c) provides that installation, storage, and removal may also be performed by one employee of the authorized collector and one supervisor-level employee of the LTCF (e.g., a charge nurse, supervisor, or similar employee) designated by the hospital/clinic or retail pharmacy authorized to collect at that location. Hospitals/clinics and retail pharmacies that choose the flexibility allowed by using a supervisor-level employee from the LTCF are reminded that they are still ultimately responsible for the security of the collected substances, as well as keeping complete and accurate records and fulfilling reporting requirements. The contents of the inner liners may not be sorted once deposited into a receptacle, pursuant to § 1317.75(c), but, as previously stated, § 1317.75(b) states that comingling of controlled and non-controlled

substances is permitted but not required. Therefore, the authorized collector or the LTCF may choose to limit the collected substances to pharmaceutical controlled substances to maximize available space in the collection receptacle. This can be easily accomplished at LTCFs because trained medical personnel will be depositing substances into collection receptacles and should be well-equipped to sort controlled substances from non-controlled substances before depositing the substances into a collection receptacle. Also, as previously discussed, inner liners may be stored at LTCFs in accordance with § 1317.80(d). Another available option to manage volume and the prohibition of on-site storage is for an authorized collector to maintain more than one collection receptacle at an LTCF.

[10] **Issue:** Commenters asked the DEA to clarify whether reverse distributors are permitted to pick up collection receptacle inner liners from an authorized LTCF location.

Response: In accordance with § 1317.05(c)(2)(iv), reverse distributors may pick up inner liners from collection receptacles located at authorized LTCFs, and reverse distributors may receive the inner liners that are sent to the reverse distributor's registered location from the LTCF by common or contract carrier. However, the inner liner must be removed from the collection receptacle under the supervision of either two employees from the hospital/clinic or retail pharmacy that is managing the receptacle, or one employee from the managing hospital/clinic or retail pharmacy and one supervisor-level employee of the LTCF (e.g., a charge nurse, supervisor, or similar employee) designated by the authorized collector, pursuant to § 1317.80(c).

[11] **Issue:** Several commenters expressed concern regarding the transportation and storage of substances collected from LTCFs, specifically with regard to the safety of employees who transport collected substances from LTCFs and logistical difficulties (e.g., storage space) that

may result in fewer retail pharmacies willing to install and maintain collection receptacles at LTCFs.

Response: As previously discussed, hospitals/clinics and retail pharmacies may store sealed inner liners at the LTCF in a securely locked, substantially constructed cabinet, or a securely locked room with controlled access for up to three business days pursuant to § 1317.80(d). However, the DEA encourages LTCFs and authorized collectors managing collection receptacles at LTCFs to exhaust other, more secure, alternatives, including: arranging regularly scheduled pick-ups by reverse distributors or common or contract carriers to coincide with removal of the inner liner or delivery of controlled substances to the LTCF; operating multiple collection receptacles at a LTCF to help minimize overflow; and pursuing ultimate user disposal options through members of the patients household or other persons lawfully entitled to dispose of a LTCF patient's property. The DEA believes these alternatives are better options than storage at LTCFs. LTCFs are generally unregistered locations with large quantities of highly pilferable controlled substances in high doses. The DEA carefully weighed the benefits with the risks of allowing storage at LTCFs, including the potential for creating a new avenue of diversion at a location over which the DEA has limited regulatory oversight. However, in consideration of the circumstances unique to LTCFs, and to ease the burden on LTCFs and authorized collectors, the DEA is permitting in this final rule sealed inner liners to be stored at LTCFs in accordance with § 1317.80(d).

The DEA has also relaxed the rule, in § 1317.80(c), to allow flexibility in the two-person integrity requirement with respect to collection at LTCFs by allowing authorized hospitals/clinics and retail pharmacies to designate a supervisory-level employee of the LTCF as one of the authorized persons to conduct or oversee the installation, removal, storage and transfer

inner liners. However, the authorized collector may opt to have two or more of its own employees perform or oversee these activities. In addition, authorized collectors that are practitioners may not themselves transport collected substances to a destruction location. 21 CFR 1317.05. Rather, the practitioner may destroy the collected substances by delivering the sealed inner liners to a reverse distributor or distributor's registered location by common or contract carrier, or a reverse distributor or distributor may pick-up sealed inner liners at the LTCF. 21 CFR 1317.05.

[12] **Issue:** Commenters indicated that the installation and maintenance of collection receptacles by retail pharmacies at LTCFs will likely result in considerable costs, burdens, and other liabilities, and, as such, few retail pharmacies will be willing to install and maintain collection receptacles at LTCFs, and few LTCFs will want to bear the costs.

Response: The DEA carefully considered the costs associated with all aspects of disposal, along with all other considerations such as convenience, safety, and the risk of diversion, including the security and design of collection receptacles. As discussed in the preamble to this rule, participation in any disposal program for ultimate users is voluntary and the DEA is not authorized to impose the burden of costs upon any specific entity. As such, each registrant that may become authorized as a collector must individually weigh the associated benefits and burdens in determining whether to do so. In order to accommodate LTCF residents, the DEA has expanded the authorized collectors that may maintain collection receptacles at LTCFs to include certain hospitals/clinics and retail pharmacies. 21 CFR 1317.40. The DEA has also relaxed the two-person integrity requirements with respect to LTCFs, and is allowing for storage of sealed inner liners at the LTCF in order to reduce the burdens on hospitals/clinics and retail

pharmacies. 21 CFR 1317.80. These are the minimum requirements to ensure that safety and security of LTCF residents, and to deter and detect diversion.

[13] **Issue:** Several commenters expressed concerns over liability when a collection receptacle is installed at a LTCF because the collector pharmacy is fully responsible for the receptacle but does not have constant, direct supervision over it. The commenters did not specify what type of liability (e.g., criminal, civil, administrative, etc.) was concerning, however, the commenters suggested that the DEA provide the authorized collector retail pharmacies a release from responsibility when installing and maintaining a collection receptacle at a LTCF.

Response: It would be contrary to the public health and safety to authorize an entity to collect pharmaceutical controlled substances from ultimate users, and also absolve that entity from any responsibility for such collection. In any event, the DEA does not have authority to provide a general release from liability to all hospitals/clinics and retail pharmacies that apply for, and are authorized to, install and maintain a collection receptacle at a LTCF as part of their registered activities. Part of the purpose in authorizing only certain hospitals/clinics and retail pharmacies to install and maintain collection receptacles at LTCFs is to ensure that a responsible registrant under the regulatory authority of the DEA is charged with ensuring the secure and responsible collection of pharmaceutical controlled substances at LTCFs. As such, with regard to authorized collection receptacles at LTCFs, all responsibility for such receptacles, including compliance with the CSA and DEA regulations, rests with the hospital/clinic or retail pharmacy authorized to install and maintain the collection receptacle. The DEA designed the physical security controls and other accountability measures (e.g., recordkeeping, two-person integrity, regular monitoring by LTCF personnel) for collection receptacles at LTCFs in an effort to minimize the risk of diversion in circumstances where constant, direct supervision by the hospital/clinic or retail

pharmacy is not feasible. In the event an authorized collector knows or has reason to know diversion from collection receptacles is occurring, the authorized collector must take steps to prevent the diversion, including reporting to the appropriate authorities pursuant to §§ 1301.74 and 1301.76. Such action stems from the responsibility to provide effective controls and procedures to guard against theft and diversion as required by § 1301.71(a).

Security at LTCFs

[14] **Issue:** One commenter asked the DEA to clarify the required security measures for collection receptacles at LTCFs. Two commenters asked the DEA to outline what LTCF staff must do to monitor the collection receptacle.

Response: The required security measures outlined in §§ 1317.60 and 1317.75 that apply to all collection receptacles also apply to those located at LTCFs unless stated otherwise in the rule. The rule provides that a collection receptacle must be located in an area that is regularly monitored by LTCF personnel. 21 CFR 1317.75(d)(2)(iii). "Regularly monitored" has its ordinary meaning. The goal of this requirement is to prevent diversion; accordingly, specific examples would depend on individual circumstances. However, a sub-basement or other seldom-used storage area would not be considered to be regularly monitored by LTCF personnel because those areas are not routinely accessed by LTCF personnel in the course of conducting the everyday the business of the LTCF. The requirement that the receptacle be "regularly monitored" is designed to prevent diversion opportunities, and to ensure that diversion would be detected as soon as possible. Only authorized collectors may install, manage, and maintain collection receptacles at LTCFs, therefore, only the authorized collectors may remove, seal, transfer, and store or supervise the removal, sealing, transfer, and storage of sealed liners. 21 CFR § 1317.80(b). The authorized collector is responsible for ensuring the regular monitoring of

LTCF personnel and ensuring the appropriate security procedures are in place at LTCFs in the event of suspected tampering or diversion. If tampering or diversion is suspected, LTCF personnel should notify law enforcement authorities and the authorized collector, as the circumstances warrant.

[15] **Issue:** Eight commenters expressed concern for the safety of residents of LTCFs. These commenters are concerned that collection receptacles in LTCFs may affect resident safety due to these locations becoming a potential target for drug seekers. Five commenters suggested that the DEA increase penalties for offenses related to collected substances at LTCFs. One commenter encouraged the DEA not to authorize the installation of collection receptacles at LTCFs because their presence may compromise the safety of staff and residents.

Response: Congress authorized the DEA to implement regulations authorizing LTCFs to dispose of controlled substances on behalf of ultimate users who reside, or have resided, at such LTCFs. The DEA has considered the risks associated with authorizing the installation and maintenance of collection receptacles at LTCFs, as discussed in the NPRM, and determined that the security measures described in this rule, in § 1317.75, are the minimum required to ensure the safe and secure disposal of pharmaceutical controlled substances at LTCFs. If authorized collectors or LTCFs believe the presence of a collection receptacle endangers the safety or security of the LTCF residents under particular circumstances, they should take additional measures as appropriate to ensure the safety of the residents and staff, and to ensure the security of the collected substances. And, if those other alternatives have failed to abate the observed dangers, the authorized collector can choose to discontinue placing a collection receptacle at a particular LTCF.

The CSA already provides for administrative, civil, and criminal sanctions for individuals and registrants that violate the CSA. The DEA is without authority to mandate enhanced penalties for violations of the CSA that involve LTCFs.

[16] **Issue:** Two commenters expressed concern about security issues due to potential stockpiling of unwanted controlled substances at LTCFs. These commenters listed the following reasons as the bases for their concerns: the three business day disposal requirement, the lack of guidance on the frequency at which inner liners must be removed, the two employee requirement for installing and removing inner liners, and lack of a realistic alternative for disposal if no retail pharmacy manages a collection receptacle at the facility. These commenters stated that stockpiling would increase diversion risks and would be a liability for the LTCF.

Response: As discussed in the NPRM and in response to comments in this final rule, these new regulations *expand* the options available to ultimate users (including LTCF residents) to dispose of excess pharmaceutical controlled substances. A resident, a member of the resident's household, and an individual lawfully entitled to dispose of the decedent resident's property all may dispose of a resident's pharmaceutical controlled substances using any of the several methods of disposal mentioned here. 21 CFR 1317.30.

If there is a collection receptacle at the LTCF, the collected substances should not accumulate under the procedures outlined in this rule. One of the primary goals of the procedures outlined in these new regulations is to prevent the accumulation of collected substances while awaiting destruction. For example, LTCFs are required to deposit pharmaceutical controlled substances into collection receptacles "*immediately*, but no longer than three business days after the discontinuation of use," pursuant to § 1317.80(a). Although the DEA has not specifically proposed regulations regarding the frequency at which the inner

liners of collection receptacles must be replaced, an authorized collector that maintains a collection receptacle at a LTCF should coordinate with that LTCF in order to ensure that the inner liners are replaced at a frequency suitable to ensure continuous safe and secure disposal by the LTCF. This type of coordination is part of an authorized collector's responsibility to provide effective controls and procedures to guard against theft and diversion as required by § 1301.71(a). Controls against diversion are ineffective when stockpiling of unused pharmaceutical controlled substances at a LTCF is the result of an authorized collector's failure to adequately maintain a collection receptacle. It is emphasized that there is no limit on the number of collection receptacles that an authorized collector may install and maintain at a LTCF. Accordingly, the number of receptacles may be increased to account for volume and/or pick-up schedules.

As previously discussed, this rule allows but does not require authorized collectors to store sealed inner liners at a LTCF for up to three business days in a securely locked, substantially constructed cabinet or a securely locked room with controlled access, pursuant to § 1317.80(d). However, the DEA encourages collectors to schedule inner liner removals and installations to coincide with existing LTCF visits when possible, for example, arranging a routine system in which medication deliveries coincide with the removal and transfer of sealed inner liners for appropriate destruction, thereby making sealed inner liner storage unnecessary.

Other Concerns Regarding LTCF Drug Disposal

[17] **Issue:** One commenter expressed concern that the DEA's assumption that controlled substances in LTCFs have been dispensed to, and are thus the property of, a resident may result in the reluctance of LTCFs to use automated dispensing systems to dispense to an ultimate user as needed.

Response: Congress has defined "dispense" to mean the delivery of a controlled substance to an ultimate user by, or pursuant to the lawful order of, a practitioner. 21 U.S.C. 802(10). The DEA is bound to this definition. Accordingly, once a pharmaceutical controlled substance has been dispensed to a patient, including a resident of a LTCF, the substance is the property of the patient or ultimate user. The use of an automated dispensing system (ADS) does not change the analysis. An ADS is conceptually similar to a vending machine. A pharmacy stores bulk drugs in the machine in separate bins or containers and programs and controls the ADS remotely. Only authorized staff at the LTCF would have access to its contents, which are dispensed on a single-dose basis at the time of administration pursuant to a prescription. The ADS electronically records each dispensing, thus maintaining dispensing records for the pharmacy. Because the controlled substances are not considered dispensed until the system provides them, substances in the ADS are counted as pharmacy stock. Even though ADSs in LTCFs are used to dispense medications for administration on an as-needed basis (i.e., one dose at a time) in accordance with a practitioner's prescription, the substance is the property of the LTCF resident once dispensed. Even though a pharmaceutical controlled substance is the property of the ultimate user once dispensed from the ADS, the LTCF may dispose of the medication on behalf of an ultimate user who resides, or has resided at an LTCF by depositing the medication into an authorized collection receptacle located in the LTCF. 21 CFR § 1317.80. Controlled substances held within the ADS that have not been dispensed to a patient are considered inventory or stock of the registrant and therefore must be disposed of by the registrant in accordance with 21 CFR § 1317.05.

[18] **Issue:** Commenters indicated that LTCFs may be serviced by multiple pharmacies which could result in controlled substances from multiple servicing pharmacies being disposed of in a

single receptacle installed by one such pharmacy and asked the DEA to clarify how to manage such situations (e.g., how other pharmacies would contribute to the efforts of collection; whether drugs dispensed by other pharmacies can be disposed of in the receptacle). Commenters also asked the DEA to clarify the process and requirements for the collection receptacle when the LTCF changes ownership or pharmacy service.

Response: This rule allows certain hospitals/clinics and retail pharmacies to become collectors at LTCFs pursuant to § 1317.40, after properly modifying their registrations, in accordance with part 1301. This rule does not require authorized collectors to have any pre-existing or other relationships with the LTCF. Depending on the circumstances, there may be more than one authorized collection receptacle at a single LTCF. Other than the regulations specific to the installation and maintenance of collection receptacles and all related laws and regulations, the DEA is not, at this time, regulating the relationship between the authorized collector and the LTCF, or between multiple authorized collectors that have relationships with the LTCF, and the DEA is not prohibiting collectors from refusing to collect any certain specified pharmaceutical controlled substances. However, conduct that implements exclusionary or anti-competitive actions at an LTCF that adversely affects competing registrants will be referred to the appropriate authorities for action. It is important to remind authorized collectors with collection receptacles at LTCFs that they are solely responsible for the security, integrity, and maintenance of their own collection receptacles and they must be vigilant and ensure complete accountability for any pharmaceutical controlled substances they collect at LTCFs. If a LTCF changes ownership and changes its name, the authorized collector must modify its registration in accordance with § 1301.51(b)(2) to reflect the new name of the LTCF.

[19] **Issue:** One commenter specifically suggested that the DEA restrict collection receptacles at LTCFs to the collection of controlled substances and to require signage indicating such in order to ensure compliance with State Medicaid program directives requiring the recovering of non-controlled drugs for potential credit or restocking.

Response: The DEA is modifying the final rule in §§ 1317.70(b) and 1317.75(b) to clearly indicate that comingling of controlled and non-controlled substances is permitted but not required. The DEA's authority is limited to controlled substances. As such, the DEA cannot promulgate regulations requiring signage pertaining to compliance with State Medicaid programs or any other programs outside the DEA's scope of authority, but collectors are free to post signage pertaining to non-controlled substances. Moreover, collectors may post any information they deem appropriate for the safe and secure disposal of controlled substances. All collections that may include pharmaceutical controlled substances, whether comingled or not, must be consistent with this rule, and all other applicable Federal, State, tribal, and local laws and regulations.

[20] **Issue:** Two commenters referenced prescription labeling requirements that prohibit the transfer of controlled substances to a person other than to whom it was prescribed. The commenters asked for clarification regarding such transfers and transfers to a person lawfully entitled to dispose of an ultimate user decedent's property. The commenters indicated that such transfers could be considered dispensing and therefore outside of the authority of the LTCF employee. Additional concerns included State laws that prohibit LTCFs from giving back unused controlled substances to the resident or another person and those that require such substances to be destroyed at the facility.

Response: Pursuant to 21 U.S.C. 825(c), FDA regulations require that when a schedule II, III,

or IV controlled substance is dispensed to or for a patient, the label include a warning that Federal law "prohibits the transfer of the drug to any person other than the patient for whom it was prescribed." 21 CFR 290.5. This is not a regulation within the DEA's authority; however, the regulation does not appear to be inconsistent with the Disposal Act. As described in detail in the NPRM, the CSA expressly provides that it is unlawful to distribute a controlled substance except as provided. The CSA permits an ultimate user who has lawfully obtained a pharmaceutical controlled substance to deliver the controlled substance to another person for the purpose of disposal only if that person is authorized to receive such substance and in accordance with the implementing regulations. The CSA further provides that if a person dies while lawfully in possession of a pharmaceutical controlled substance, any person lawfully entitled to dispose of the decedent's property may deliver the substance to another person for the purpose of disposal under the same conditions described above. Pursuant to the Disposal Act, a LTCF may dispose of a resident's pharmaceutical controlled substances in accordance with these regulations. When a LTCF deposits a pharmaceutical controlled substance into a collection receptacle in accordance with these regulations, it is not "dispensing." As discussed, "dispense" means the delivery of a controlled substance to an ultimate user by, or pursuant to the lawful order of, a practitioner. 21 U.S.C. 802(10).

With regard to State laws, the DEA cannot comment on the laws of each individual State because these laws are outside of the DEA's purview. The DEA is tasked by Congress with implementing Federal laws related to controlled substances. However, nothing contained within the DEA regulations should be construed as authorizing or permitting any person to do any act he/she is not authorized or permitted to do under other Federal laws or under the law of the State in which he/she desires to perform such act, nor shall compliance with the DEA's regulations be

construed as compliance with other Federal or State laws. 21 CFR 1307.02.

[21] **Issue:** One commenter asked the DEA to discuss whether the HHS reviewed the rule with regard to their "anti-kickback" statute. This commenter expressed concern over whether or not the HHS would permit a retail pharmacy that dispenses to a particular LTCF to provide collection services to the same LTCF free of charge.

Response: All collection and disposal of controlled substances must be conducted in accordance with all applicable laws and regulations, including HHS regulations. This rule neither imposes requirements or regulations for the funding of disposal programs, nor imposes requirements or regulations regarding fees that registrants may charge to operate disposal programs.

L. *Disposing on Behalf of Ultimate Users (Other than Residents of LTCFs) (3 issues)*

[1] **Issue:** Commenters asked the DEA to clarify how hospitals, schools, summer camps, or other entities may dispose of controlled substances that unintentionally end up in their possession (e.g., when persons abandon controlled substances and return is not possible). Also, several commenters asked the DEA to explain how controlled substances may be disposed of when the ultimate user or other authorized person is unable to dispose of them due to death or incapacitation.

Response: The DEA has limited authority regarding who may deliver pharmaceutical controlled substances for the purpose of disposal. Pursuant to the Disposal Act, Congress granted the DEA authority to authorize three groups of people to deliver controlled substances for the purpose of disposal. First, an "ultimate user" who has lawfully obtained a pharmaceutical controlled substance may deliver the substance to another person who is authorized to accept it for the purpose of disposal. The CSA defines "ultimate user" as "a person who has lawfully obtained, and who possesses, a controlled substance for his own use or for the use of a member of his

household or for an animal owned by him or by a member of his household." 21 U.S.C. 802(27). Second, if a person dies while lawfully in possession of a pharmaceutical controlled substance, any person lawfully entitled to dispose of the decedent's property may deliver the substance to another person for the purpose of disposal. 21 CFR 1317.30. Third, LTCFs may dispose of pharmaceutical controlled substances on behalf of ultimate users who reside or have resided at such facilities. 21 U.S.C. 822(g). The DEA has no authority to expand the types of individuals and entities lawfully permitted to deliver pharmaceutical controlled substances for the purpose of disposal. The DEA has carefully considered its statutory authority, diversion risks, public safety, convenience for ultimate users, and the interests of the public. The DEA believes that this rule provides safe and convenient disposal options for ultimate users and other authorized persons. The DEA understands that there may be circumstances where there is no authorized person to dispose of the controlled substances, such as when controlled substances are abandoned at a school or summer camp, and return to the ultimate user is not feasible. In such instances, the affected entities should contact local law enforcement or their local DEA office for guidance on proper disposal procedures.

[2] **Issue:** The DEA received a number of comments regarding the lack of provisions for hospice and other homecare programs to dispose of controlled substances on behalf of patients. According to the commenters, many hospices have written policies and procedures in place for the management and disposal of controlled substances in the patient's home. Given the available options for ultimate user disposal, commenters expressed concern that hospices may no longer be able to assist families in disposing of a deceased patient's drugs. Commenters suggested that the DEA allow hospice staff to dispose of a decedent's controlled substances by sewering or landfill disposal.

Response: The DEA appreciates the difficulties facing home hospice staff with regard to the disposal of pharmaceutical controlled substances. The Disposal Act provides that "if a person dies while lawfully in possession of a controlled substance for personal use, any person lawfully entitled to dispose of the decedent's property may deliver the controlled substance to another person for the purpose of disposal under the same conditions as provided" for ultimate users. 21 U.S.C. 822(g)(4). Otherwise, home hospice and homecare personnel are not authorized to receive pharmaceutical controlled substances from ultimate users for the purpose of disposal. In addition, an ultimate user includes "a person who has lawfully obtained, and possesses, a controlled substance for his own use or *for the use of a member of his household*." 21 U.S.C. 802(27). Accordingly, a member of the hospice patient's household may dispose of the patient's pharmaceutical controlled substances, but the home hospice or homecare provider cannot do so unless otherwise authorized by law (for example, under state law) to dispose of the decedent's personal property.

This rule provides a number of options for ultimate users and persons lawfully entitled to dispose of a deceased ultimate user's property to safely and securely dispose of pharmaceutical controlled substances, yet the DEA does not require ultimate users to utilize these options. However, it is unlawful for ultimate users to transfer pharmaceutical controlled substances to unauthorized persons, and it is unlawful for unauthorized persons to receive such substances. It is also unlawful for any person to possess a controlled substance unless authorized to do so under the CSA (i.e., an ultimate user, an entity registered with the DEA, or an entity exempt from registration with the DEA). 21 U.S.C. 844(a). Home hospice and other homecare providers are encouraged to assist their patients, and their patients' families, in disposing of pharmaceutical controlled substances in accordance with the CSA and its implementing regulations. While

education is paramount, home healthcare agencies are also encouraged to partner with authorized collectors to promote or jointly conduct mail-back programs.

[3] **Issue:** One commenter asked the DEA to clarify the authority for a hospice employee to utilize a LTCF's collection receptacle for the disposal of controlled substances of a LTCF resident who is also a patient of the hospice.

Response: This rule does not specifically address hospice care or hospice employees, who are typically not registrants. As discussed, it is unlawful to possess a controlled substance unless authorized to do so under the CSA. 21 U.S.C. 844(a). The DEA has, however, provided options for the disposal of pharmaceutical controlled substances by a LTCF on behalf of a person who resides, or has resided, at the LTCF, regardless of whether or not that person is also receiving hospice care. The Disposal Act authorized the Attorney General to allow LTCFs to dispose of controlled substances on behalf of ultimate users who reside, or have resided, at the LTCF, in a manner determined by the Attorney General. 21 U.S.C. 822(g)(3). LTCF is defined as "a nursing home, retirement care, mental care, or other facility or institution which provides extended health care to resident patients." 21 CFR part 1300. Congress specifically allowed the Attorney General to consider permitting LTCFs to dispose of pharmaceutical controlled substances on behalf of LTCF residents. This allowance did not extend to other persons who are simply attending to a person who is resident of the LTCF. As such, a hospice employee is not authorized to dispose of pharmaceutical controlled substances on behalf of a person who resides or has resided at a LTCF.

M. *Registrant Return, Recall, and Transfer (3 issues)*

[1] **Issue:** One commenter urged the DEA to retain the existing regulations in part 1307. This commenter stated that part 1307 adequately addresses registrant return, recall, and transfer. The

commenter stated that part 1307 functions properly; thus, there is no need to change it, and the commenter expressed concern that the new regulations will disrupt existing business practices. The commenter was particularly concerned that most controlled substances returned to distributors are re-salable and "not intended for disposal." Other commenters indicated confusion with regard to registrants seeking assistance from a SAC when disposing of controlled substances.

Response: The DEA first notes that the terms "disposal" and "destruction" are not interchangeable in the context of the rule. As described in the NPRM at footnote 4 and in this final rule at footnote 4, the terms "disposal," "dispose," and "disposition" appear several times in the CSA but are not defined. In the NPRM and this final rule, the DEA uses the terms "disposal" and "dispose" to refer generally to the wide range of activities that result in controlled substances being unavailable for further use or one entity ridding themselves of such substances (e.g., returns). Within the CSA, a controlled substance can be "disposed of" by destruction, return, recall, sale, or through the manufacturing process. As such, the modified regulations regarding registrant disposal codify existing practice, expand available options, and implement consistent procedures among registrants in accordance with their authorized business activities. This required deleting the existing regulations at § 1307.21 which authorized the SACs to individually authorize disposal. The new rule eliminates the authority of the SACs to individually authorize disposal methods for non-practitioners, and retains this option for practitioners. 21 CFR 1317.05. Otherwise, the new regulations maintain existing disposal practices for registrant inventory and authorize: prompt on-site destruction; prompt delivery of controlled substances to a reverse distributor; and prompt delivery (for the purposes of return and recall) to the person from whom the controlled substance was obtained, the manufacturer, or a registrant authorized to accept

returns on the manufacturer's behalf. Additionally, non-practitioners may promptly transport the controlled substances to a reverse distributor, a destruction location, or the location of any person authorized to receive the controlled substances for the purpose of return or recall. 21 CFR 1317.05. The DEA appreciates that by eliminating the option for a SAC to authorize specific disposal procedures on a case-by-case basis for non-practitioners, some reverse distributors may need to alter their disposal practices. Although this change may impact current business practices, as discussed in the NPRM, nationwide consistency is necessary in the disposal pharmaceutical controlled substances.

[2] **Issue:** One commenter asked the DEA to clarify what method of return is permitted other than via a freight forwarding facility pursuant to § 1317.10.

Response: With regard to the use of freight forwarding facilities pursuant to 21 CFR 1317.10(c), use of the word "may" indicates that the use of freight forwarding facilities is permitted but not required. Other authorized methods of transferring pharmaceutical controlled substances for the purpose of return or recall are outlined in § 1317.05(a)(3) and (4) for practitioners, and in 21 CFR 1317.05(b)(3) and (4) for non-practitioners.

[3] **Issue:** One commenter stated that it will be difficult for reverse distributors to adjust current business operations to meet the 14-day destruction requirement for recalled controlled substances, because product returns may be received from thousands of customers across the country. Additionally, this requirement may not be consistent with other agencies' regulations and policies governing manufacturers' voluntary recalls and other product recalls.

Response: As explained further below, the 14-day destruction requirement (which this final rule extends to 30 days) does not apply to recalled pharmaceutical controlled substances. 21 CFR 1317.15.

N. *Destruction (19 issues)*

Non-Retrievable Destruction Standard

[1] **Issue:** Forty commenters asked the DEA to outline performance standards and parameters for the "non-retrievable" destruction standard. Although many commenters applauded the DEA for proposing a standard that will permit future innovation, many commenters felt that innovation may be hindered by the uncertain terms. Commenters asked the DEA to list currently-approved methods, and to outline how the DEA will evaluate new technology intended to render controlled substances "non-retrievable."

Response: In the NPRM, the DEA indicated that incineration and chemical digestion are some examples of current technology that may be utilized to achieve the non-retrievable standard. The preamble of the NPRM states that sewering (disposal by flushing down a toilet or sink) and landfill disposal (mixing controlled substances with undesirable items such as kitty litter or coffee grounds and depositing in a garbage collection) are examples of current methods of disposal that do not meet the non-retrievable standard. The term non-retrievable is defined in the rule and is results-oriented because the DEA's concern is that the substance be permanently rendered to an unusable state. The performance standard is that the method renders the substance so that it cannot be transformed to a physical or chemical condition or state as a controlled substance or controlled substance analogue. 21 CFR part 1300. The DEA will not be routinely engaged in evaluating new technologies intended to render controlled substances "non-retrievable." Much like the DEA does not evaluate, review, or approve the specific processes or methods utilized to produce, synthesize or propagate a controlled substance, the DEA will not evaluate, review, or approve the processes or methods utilized to render a controlled substance non-retrievable, as long as the desired result is achieved.

[2] **Issue:** Twenty commenters asked the DEA to include the language regarding sewering and landfill disposal in the text of the regulation. These commenters applauded the DEA for stating that sewering and landfill disposal do not meet the "non-retrievable" standard; however, these commenters asked the DEA to include this same language in the text of the regulation.

Response: The DEA has determined that the most effective way of ensuring that the non-retrievable standard of destruction remains current with continuously changing technology is to provide a required end result rather than specify what means achieve or fail to achieve that result. A substance is rendered non-retrievable when its physical or chemical state is permanently and irreversibly altered and it may be unique to a substance's chemical or physical properties; the same means of destruction may not render every controlled substance non-retrievable. 21 CFR part 1300. Thus, the DEA declines to amend the text of the regulation to include such a broad prohibition. In consideration of the Disposal Act's goal to decrease the amount of pharmaceutical controlled substances introduced into the environment, the DEA emphasizes that sewering and landfill alone do not meet the non-retrievable standard. Once a controlled substance is rendered non-retrievable, it is no longer subject to the requirements of the DEA regulations.

[3] **Issue:** Several commenters requested that the DEA review and approve new destruction methods prior to allowing their use.

Response: As discussed in the immediately preceding responses, the DEA will not be engaged in reviewing or approving new destruction methods prior to allowing their use.

[4] **Issue:** One commenter suggested that the DEA provide a transition period to allow for additional research into the means by which a non-retrievable state may be achieved. This commenter proposed a timeframe, such as five years, to allow appropriate technology to develop.

This commenter also suggested that the DEA permit sewering and landfill disposal in the interim.

Response: The DEA believes that technology by which pharmaceutical controlled substances may be rendered non-retrievable currently exists, thus providing existing opportunities for compliance with this rule and negating the need for a transition period beyond the effective date of this rule.

[5] **Issue:** Several commenters suggested that the DEA collaborate with the United States Environmental Protection Agency (EPA) to develop best practices for achieving a non-retrievable state using environmentally responsible methods.

Response: The DEA appreciates the environmental concerns surrounding the destruction of pharmaceutical controlled substances. The DEA has worked with, and is continuing to work with, the EPA regarding secure and responsible drug disposal, particularly for pharmaceutical controlled substances that may also be considered hazardous wastes. Additionally, the DEA has clearly stated in the rule that all methods of destruction must comply with all applicable Federal, State, tribal, and local laws and regulations, including EPA regulations.

[6] **Issue:** A commenter asked the DEA to clarify whether or not the non-retrievable standard of destruction applies to substances disposed from households, and this commenter stated that the DEA should develop and endorse a practical solution for in-home disposal.

Response: Ultimate users may continue to dispose of their own pharmaceutical controlled substances in the manner recommended by other Federal and State agencies, such as the FDA, Office of National Drug Control Policy (ONDCP), and EPA. The non-retrievable standard is only applicable to inventoried controlled substances (i.e., a registrant's stock) and collected controlled substances (i.e., substances collected from ultimate users by authorized collectors) to

be disposed of by registrants, pursuant to § 1317.90. The non-retrievable standard does not apply to non-registrants.

[7] **Issue:** Several commenters asked the DEA to clarify whether or not controlled substances that were rendered "non-retrievable" will be regulated by the DEA.

Response: As provided in the definition, a controlled substance is considered non-retrievable when it cannot be transformed to a physical or chemical condition or state as a controlled substance or controlled substance analogue. 21 CFR part 1300. Once a substance is rendered non-retrievable, it is no longer subject to the requirements of the DEA regulations. The DEA believes that further regulations regarding substances that have been rendered non-retrievable are currently unnecessary because a non-retrievable substance cannot be abused and diversion to illicit use is futile.

Incineration and Chemical Digestion Destruction Methods

[8] **Issue:** Several commenters asked the DEA to specifically recommend incineration as the preferred method to achieve a non-retrievable state.

Response: The DEA believes that any actual or perceived endorsement or recommendation of a specific destruction method, beyond the provision of examples of current methods in the preamble, could suppress exploration and implementation of new technologies as people may assume that the endorsed or recommended methods are required at the exclusion of other methods. As such, the DEA is specifying a required result—non-retrievable—rather than a required method for achieving that result. 21 CFR 1317.90.

On-Site Destruction Methods

[9] **Issue:** Several commenters asked the DEA to clarify what "on-site destruction" means.

Response: As provided in § 1300.05(b) of the final rule, on-site destruction means that the controlled substances are destroyed on the physical premises of the destroying registrant's registered location. Collectors that are authorized to conduct mail-back programs must have and utilize an on-site method of destruction, pursuant to 21 CFR 1317.05(c)(1). The requirement for an on-site method of destruction does not apply to non-registrants.

[10] **Issue:** Commenters also expressed concern that distributors are unlikely to have an existing on-site method of destruction because they are not typically licensed as waste handlers and suggested that the DEA provide alternatives to on-site destruction for hospitals and other medical facilities.

Response: This rule does not require any distributor or other registrant to utilize an on-site method of destruction except under certain circumstances in order to conduct a voluntary activity (e.g., receipt of mail-back packages as an authorized collector in accordance with § 1317.05(c)(1)).

[11] **Issue:** One commenter asked the DEA to consider the use of collection receptacles with deactivation technology.

Response: This rule does not prohibit on-site destruction of pharmaceutical controlled substances by authorized collectors with "deactivation" capability so long as such destruction is consistent with the standards set forth in the rule and the destruction results in a non-retrievable state. 21 CFR 1317.90.

Other Destruction-Related Concerns

[12] **Issue:** Approximately 20 commenters stated that the 14-day destruction requirement is impractical. These commenters suggested that the DEA allow more time since there are a limited number of commercial incinerators in the United States. Several commenters stated that

reverse distributors must accumulate large amounts of controlled substances in order to obtain favorable pricing. Other commenters stated that the requirement will make it difficult for reverse distributors to properly process and record all transactions, and it will impose substantial financial and operational restrictions on reverse distributors as most reverse distributors do not have on-site destruction and may need to travel long distances to reach an appropriate destruction facility.

Response: The DEA has carefully and thoroughly considered these concerns, and the final rule in § 1317.15(d) extends the destruction requirement timeframe from 14 calendar days to 30 calendar days and eliminates the "as soon as practicable" standard with respect to this destruction requirement. The DEA remains concerned about increased diversion risks due to pharmaceutical controlled substances remaining at a single location for extended periods of time. As discussed in detail in the NPRM, prescription drug abuse is an American epidemic, and it is America's fastest growing drug problem. When large volumes of pharmaceutical controlled substances accumulate, they become an attractive target for drug seekers and drug abusers. Accordingly, regardless of the applicable timeframe to destroy controlled substances, reverse distributors are reminded that they must be vigilant and adhere to the requirements in the CSA and the implementing regulations. Finally, these registrants are reminded of their responsibility to provide effective controls and procedures to guard against theft and diversion, and their responsibility to notify the DEA of any theft or significant loss of any controlled substances within one business day of discovery. 21 CFR part 1301. The DEA continuously monitors compliance with the CSA and applicable regulations to ensure that controlled substances are not diverted to illicit purposes. If necessary, the DEA may consider revising the requirements applicable to reverse distributors' destruction activities, or imposing additional security

requirements.

[13] **Issue:** Several commenters asked the DEA to clarify the day the clock starts for the 14-day destruction requirement.

Response: As discussed above, the final rule extends the timeframe from 14 days to 30 days. Day 1 is the day the substances are physically acquired through pick-up or delivery. 21 CFR 1317.15.

[14] **Issue:** One commenter asked the DEA to clarify whether or not the 14-day destruction requirement applies to law enforcement.

Response: This destruction requirement does not apply to law enforcement. Law enforcement guidelines are outlined in § 1317.35.

[15] **Issue:** One commenter suggested that the DEA apply the 14-day destruction requirement to all authorized collectors that destroy or cause the destruction of controlled substances, not just reverse distributors.

Response: As previously discussed, the final rule extends the destruction requirement timeframe from 14 days to 30 days. 21 CFR 1317.15. This requirement applies to reverse distributors destroying any controlled substance, as well as distributors when destroying sealed inner liners acquired from authorized collectors for destruction. Pursuant to § 1317.05(c), authorized collectors that maintain mail-back programs or collection receptacles must promptly destroy mail-back packages and inner liners, without adhering to a certain number of days in order to provide them some flexibility depending upon their particular circumstances.

[16] **Issue:** Two commenters stated that all management and disposal of controlled substances should be restricted to DEA-registered hazardous waste disposal companies.

Response: The DEA believes that restricting the management and disposal of controlled substances as suggested would severely burden registrants without adding benefit. Pursuant to this rule, a destruction facility is not required to register with the DEA simply because a registrant utilizes that facility to destroy pharmaceutical controlled substances in a manner consistent with this rule and all other applicable Federal, State, tribal, and local laws and regulations. The DEA does not find it necessary to register these entities because the destroying registrant maintains possession and control of the substances (and therefore retains responsibility and accountability) until the substances are rendered non-retrievable. This is because all handling, monitoring, security, recordkeeping, and witnessing with regard to the pharmaceutical controlled substances is performed or supervised by registrants.

[17] **Issue:** One commenter indicated that the DEA should provide for broader Federal approval for methods of destruction rather than allowing for regionally-based guidance through the relevant SAC.

Response: As discussed, this rule expands the options available to registrants for proper disposal, but does not require any particular method of destruction, so long as the substances are rendered non-retrievable. This rule does not authorize SACs to specifically authorize any particular method of destruction, but it does allow a practitioner to seek guidance from the relevant SAC regarding the disposal of controlled substances. 21 CFR 1317.05.

[18] **Issue:** Several commenters asked for clarification regarding the means by which an authorized collector may promptly destroy collected substances, and whether chemical treatment of controlled substances until such time as controlled substances can be retrieved for destruction would be considered prompt destruction.

Response: As discussed, the DEA is not requiring any particular method or means of

destruction. All controlled substances destined for destruction must be rendered non-retrievable in order to be destroyed in a manner consistent with this rule. 21 CFR 1317.90. If chemical treatment renders a substance non-retrievable, it has been properly destroyed and is no longer subject to the DEA's regulations.

[19] **Issue:** One commenter suggested that the DEA require controlled substances to be partially destroyed prior to disposal in collection receptacles, such as by grinding them up and mixing them with kitty litter.

Response: With regard to mixing pharmaceutical controlled substances with other substances prior to depositing them in a collection receptacle, this rule neither prohibits nor requires such activity. Some authorized collectors may find it desirable to direct ultimate users to mix pharmaceutical controlled substances with non-hazardous items, such as kitty litter, prior to depositing in receptacles; however, the DEA declines to mandate such a requirement for all authorized collectors. The security controls required by this rule are the minimum required to ensure the safe and secure disposal of pharmaceutical controlled substances.

O. *Economic Concerns (18 issues)*

Continuation of Existing Programs

[1] **Issue:** Eighteen commenters with experience operating a disposal program stated that following the new regulations will be prohibitively costly, and their current program will be forced to stop collection activities. These commenters stated that they sort controlled substances from non-controlled substances and packaging. According to these commenters, controlled substances represent a small fraction of their total volume of collected substances, and the sorting prohibition will substantially increase costs.

Response: As explained above, comingling of controlled and non-controlled substances is

permitted by the rule in § 1317.75, but it is not required, and this rule does not require pharmaceutical controlled substances collected from ultimate users to be collected and stored in the original packaging. Authorized collectors may choose to address adequacy of space issues by choosing not to collect comingled controlled substances and non-controlled substances and by excluding packaging materials from being deposited into the collection receptacle. Also, law enforcement continues to have autonomy regarding their collection activities, and this rule does not prohibit law enforcement from handling collected substances. Prior to the effective date of this rule, it is unlawful for ultimate users to transfer controlled substances to any entity (excluding law enforcement), except in the limited circumstances allowed under 21 CFR 1307.21(a)(2).

[2] **Issue:** Several commenters stated that they would have to hire additional help for their program to continue, and that they would no longer be able to rely on volunteers or other personnel that did not meet the NPRM's "authorized employee" definition.

Response: As discussed, in § 1300.05(b) the final rule modifies the proposed definition of "authorized employee" to omit the word "authorized." In this final rule, the DEA is adopting the general common law of agency's definition of the term "employee." Any person who meets certain criteria may have access to or influence over collected substances on behalf of an authorized collector. Also, under this rule, volunteers may assist with disposal programs or take-back events as long as they do not have access to or influence over the collected controlled substances.

Two Employee Requirement

[3] **Issue:** Approximately 30 commenters felt that it would be infeasible for two employees to oversee disposal procedures due to limited personnel. Commenters suggested allowing an

"authorized employee" of another registrant, such as a reverse distributor, to satisfy the second "authorized employee" requirement. One commenter stated that the DEA should clarify that under proposed § 1317.75(g), installation and removal of inner liners may be performed by a law enforcement officer instead of two employees.

Response: The DEA believes that the two-employee integrity requirement is a necessary security measure to effectively guard against diversion and to ensure that the controlled substances are handled, transferred, and recorded in a manner that is consistent with all applicable laws and regulations. The DEA carefully considered the various concerns and took steps to alleviate some of these concerns. First, as just discussed, the final rule modifies the proposed definition of "authorized employee" to instead adopt the common law of agency's definition of the term "employee," thus including employees that were excluded by the definition proposed in the NPRM (*e.g.*, part-time employees and off-duty law enforcement officers). 21 CFR part 1300. Second, as previously discussed, the final rule relaxes the two employee requirement for collection receptacles located at LTCFs in § 1317.80(c). The DEA is making this exception because of the unique circumstances faced by LTCFs, as recognized by the Disposal Act, and in keeping with the DEA's historically accommodating regulations with respect to LTCFs (e.g., §§ 1306.11(f) and 1306.13(b) regarding faxing schedule II prescriptions and dispensing partial prescriptions). The DEA believes that the above changes will alleviate some of the concerns expressed by the commenters while maintaining the necessary security to reduce diversion risks.

[4] **Issue:** Twenty-seven commenters stated that the requirement to have two employees from the pharmacy present to remove and install a collection receptacle's inner liner is excessive and too costly. Several commenters noted that this requirement alone will dissuade retail pharmacies

from managing collection receptacles. Several commenters stated that small pharmacies may not have two employees working during the same shift, or even have two people employed full-time by the pharmacy. Two commenters suggested requiring a dual-lock system on collection receptacles, where the collector registrant retains one key and a reverse distributor retains the other.

Response: The DEA carefully considered the commenters' concerns, and amended the text of the rule to address this issue. In the context of this issue, the two-employee requirement only applies to installation and removal of the inner liners which does not need to be accomplished by two employees on the same shift. Also, dual-locks on collection receptacles at retail pharmacies are not a reasonable alternative because collectors are authorized only at *their own* registered location or controlled premise. If a retail pharmacy employee retained one key in a dual-lock system, and a reverse distributor retained the other key, then the reverse distributor would be handling collected substances at the retail pharmacy's registered location or controlled premise, an activity that is not permitted. Reasonable alternatives include installing and removing an inner liner during a shift change, or other times when there is more than one employee present. The final rule also modifies the proposed definition of "authorized employee," by adopting the common law of agency's definition of "employee" and correspondingly eliminating the requirement that employees authorized to conduct disposal activities be employed full-time by the authorized collector. 21 CFR part 1300. The DEA believes that the two-employee integrity requirement is a necessary security measure to effectively guard against diversion and to ensure that the controlled substances are handled, transferred, and recorded in a manner that is consistent with all applicable laws and regulations.

[5] **Issue:** Several commenters stated that the requirement that two employees from a retail pharmacy be present to install and remove inner liners at LTCFs is prohibitively burdensome. Several commenters stated that most retail pharmacies do not have a vehicle for this purpose, and it is a liability to have pharmacy employees traveling to LTCFs to change inner liners. Two commenters suggested that the requirement should be one employee from the pharmacy and one employee from the LTCF.

Response: The DEA carefully considered alternatives that will provide convenient options for the unique population of LTCF residents, but will also provide safe and secure disposal. As amended, the final rule in § 1317.80(c) provides that inner liner installations, storage, removals, and transfers at LTCFs may be performed either by two employees of the authorized collector, or by one employee of the authorized collector and a supervisor-level employee of the LTCF designated by the authorized collector. The DEA believes that this modification is important to encourage hospitals/clinics and retail pharmacies to maintain collection receptacles for LTCF residents, by easing the burdens on authorized collectors who maintain collection receptacles at LTCFs--the only collectors who maintain collection receptacles at locations away from their primary registered locations. Additionally, the DEA recognizes that some authorized collectors do not have a vehicle specifically for the purpose of travelling to LTCFs, or currently allow employees to travel. The DEA notes that no particular vehicle is required to transport employees of the authorized collector to the LTCF, and, as discussed above, the DEA encourages authorized collectors managing a collection receptacle at a LTCF to coordinate removal of inner liners with the delivery of controlled substances dispensed to LTCF residents.

[6] **Issue:** Fifteen commenters stated that it will be economically burdensome to have two employees of the reverse distributor accompany the collected substances to the point of

destruction to witness the destruction. These commenters noted that waste management companies often travel hundreds of miles to reach a destruction facility. The commenters stated that it is unreasonable to have two employees of the reverse distributor accompany the collected substances and witness the destruction, and some commenters suggested that the DEA permit other security mechanisms, such as GPS devices and security cameras, to serve in lieu of the second employee.

Response: The DEA believes that the two-employee integrity requirement is a necessary security measure to effectively guard against diversion and to ensure that the collected substances are handled, transferred, and recorded in a manner that is consistent with all applicable laws and regulations. 21 CFR 1317.95. The DEA notes that the DEA registrants who expressed concern regarding this requirement already adhere to it in their current business practices. However, the DEA has thoroughly and carefully considered the commenters' concerns and considered the following alternatives to the two-person integrity requirement: (1) requiring destruction facilities to register with the DEA; (2) requiring the transferring registrant (*e.g.*, retail pharmacies, hospitals/clinics, etc.) to accompany the controlled substances to the point of destruction; (3) requiring on-site destruction; (4) requiring additional recordkeeping and witnessing at the point of destruction by the non-registrant destruction facility; and (5) requiring GPS devices or security cameras to serve in lieu of the second employee. The DEA did not elect these alternatives because the DEA is without sufficient authority to impose them, or the alternatives were impractical, excessive, did not provide adequate security, would result in voluminous, difficult to maintain and verify records, and/or would reduce the disposal options available to ultimate users.

The two-person integrity requirement is of paramount importance when transporting controlled substances to the point of destruction because these persons are uniquely entrusted with ensuring the substances are destroyed and not diverted to illicit purposes. Registrants that destroy on-site also face diversion risks and security concerns and must adhere to the two-person integrity requirement when destroying controlled substances. These diversion risks and security concerns increase substantially in the case of reverse distributors because they routinely acquire from other registrants large volumes of controlled substances destined for destruction, and they routinely transport those substances to a remote, un-registered location for destruction, yet there is no independent mechanism to ensure or verify that the substances within their possession are actually destroyed and not diverted.

Furthermore, as explained previously, in every other transfer of controlled substances in the closed system of distribution, there are two registrants on each side of the transfer to ensure accountability and identify and prevent diversion. When controlled substances are transferred for destruction, there may not be a registrant verifying the destruction of the controlled substances. Adherence to the two-employee integrity requirement will provide accountability for the controlled substances during the destruction process, preventing possible loss, possible theft, and diversion of the controlled substances.

Similarly, the DEA declines to allow GPS devices or security cameras to serve in lieu of a second employee. These types of security measures can be compromised, and do not provide the same level of deterrence or risk mitigation as the presence of a second person because they are strictly after-the-fact methods of diversion control as opposed to providing security throughout the transportation and destruction process. GPS devices cannot provide information as to whether or not controlled substances were removed from the transporting vehicle, and

cameras cannot observe transportation and destruction from all angles. For example, a single driver being monitored by GPS and video could drive to the destruction facility on the approved route, remove the controlled substances from the vehicle, move with the controlled substances out of the view of the camera, and place the controlled substances into a separate vehicle or hidden spot off camera rather than destroying them. In such a scenario, neither the GPS, nor the camera would indicate any sort of diversion, whereas a second person would be present throughout transportation and destruction to serve as a deterrent and ensure that the controlled substances were actually destroyed.

For these reasons, the DEA believes that the two-person integrity requirement is the most reasonable, secure, and economic substitute for another registrant serving as an independent verification method at the end of the closed system of distribution.

Implementation Costs

[7] **Issue:** One commenter indicated that the enhanced security procedures proposed for the disposal process will be overly burdensome and costly. This commenter recommended that the DEA meet with industry stakeholders to identify options that will allow innovation while maintaining security.

Response: The security requirements in this rule are the minimum needed to protect the public health and safety, to ensure accountability, and to reduce the risk of diversion during the disposal process. In addition, there were multiple opportunities for industry stakeholders (and any other interested persons) to participate in the rulemaking process for this rule through participation in the public meeting held in January 2011, and the submission of written comments during the open comment period. The DEA carefully considered discussion from the meeting, as well as the written comments submitted in response to the NPRM.

[8] **Issue:** Eleven commenters stated that the regulations proposed in the NPRM are too costly, and the costs will discourage potential collectors from participating. Several commenters expressed concern about the costs associated with retail pharmacies managing collection receptacles, particularly at LTCFs.

Response: As provided in the Disposal Act and discussed in the NPRM, the DEA cannot require any entity to establish or maintain a disposal program. Based on information received from the public and industry during the public meeting in 2011, as well as information received in response to the NPRM, the DEA believes that many entities are eager to voluntarily establish disposal programs. Entities may choose to establish disposal programs for various reasons, including for profit, to build goodwill in the community, to attract customers, to advertise businesses, and to preserve the environment.

[9] **Issue:** Several commenters provided feedback regarding costs related to voluntary implementation and maintenance of disposal programs, although none provided any actual data that could be applied to the cost analysis except for a suggestion that the DEA review information from a report on waste collection, and one commenter that provided an estimate without any supporting data. Generally, commenters indicated that the proposed methods of collection would have associated costs incurred through recordkeeping, purchase of inner liners, changes in procedures, increases in destruction costs, and development of mail-back packages and collection receptacles. Commenters encouraged the DEA to further explore the potential costs of the proposed options as well as additional alternatives.

Response: The DEA appreciates the commenters' concerns regarding potential costs associated with the implementation and maintenance of disposal programs. The DEA has updated its economic analysis to address, directly, the costs of this rule with respect to those registrants that

do choose to establish a collection program. Such implementation, however, is strictly voluntary; thus, any entity that does not wish to incur the related costs may choose not to participate. Additionally, as described in the NPRM, the DEA anticipates that a variety of interest groups, corporations, community groups, and other entities will work together to provide secure and responsible disposal options pursuant to this rule.

[10] **Issue:** One commenter suggested that the DEA provide an exception for analytical labs from the requirements of proposed § 1317.95(c) (§ 1317.95(d) in the final rule), which requires that two employees handle the destruction of controlled substances, in instances where the testing renders a substance non-retrievable.

Response: The DEA declines to provide a blanket exception for analytical laboratories for the described situation. The DEA believes that such instances as described by the commenter will be incidental to testing. If the testing is specifically designed to develop new methods of destruction or destruction is otherwise not incidental to testing, all destruction must be in accordance with the provisions in subpart C of this rule.

[11] **Issue:** One commenter expressed concern that this rule will impose obligations on authorized collectors that are inconsistent with obligations imposed by other agencies, particularly the FDA, EPA, and DOT. The commenter stated that the potential liability stemming from such conflicts will discourage participation.

Response: The DEA has worked directly with other Federal agencies regarding the implementation of this rule, including the EPA and DOT. The DEA believes that authorized collectors may comply with this rule and other agency regulations. Authorized collectors should contact applicable agencies for further guidance if they believe that their specific circumstances may lead to conflicts.

Funding and Incentives

[12] **Issue:** One commenter asked the DEA to allow private/public partnerships for collection receptacles, mail-back programs, and take-back events.

Response: This rule does not dictate what funding sources are permitted or prohibited. Entity partnerships are not prohibited as long as the authorized collector follows all procedures outlined in this rule.

[13] **Issue:** Ten commenters expressed concern that there is no mandate, funding, or incentive for collectors to participate. Two commenters suggested that the DEA establish incentives to encourage participation, or require all pharmacies to install and maintain collection receptacles. Several commenters indicated that without a clear source of funding, cost mitigation, or participation incentive, it is unlikely that registrants will voluntarily accept the financial burdens associated with the provision of collection opportunities.

Response: The DEA appreciates the suggestions and concerns of the commenters regarding funding for voluntary controlled substances collection programs. The DEA points out that the Disposal Act did not authorize the DEA to assign responsibility of funding to any entity, and the Disposal Act specifically required the DEA to promulgate the implementing regulations in such a way that participation would not be mandatory. The DEA's intent in soliciting comments regarding this rule's potential economic impact was to gain knowledge regarding potential costs—not which entities should fund disposal programs. The DEA has attempted to provide regulations that minimize the financial burden while retaining a level of security to ensure public safety and reduce diversion risks. This rule does not address the responsibility of costs associated with any collection program. The DEA recognizes that collection programs will have associated costs and each entity that chooses to establish and maintain such a program must

determine how to manage such costs.

Other Economic Concerns

[14] **Issue:** A number of commenters urged the DEA not to impose additional fees on registrants that choose to become authorized collectors. These commenters asked the DEA to clarify whether or not there will be any cost to modify a registration to become an authorized collector. One commenter suggested that the DEA offer a reduced fee for non-profit organizations to become registered as reverse distributors.

Response: Section 1301.51(c) states that no fee will be required to modify a registration to become authorized as a collector. Pursuant to 21 U.S.C. 886a, fees charged by the DEA under its diversion control program must be set at a level that ensures the recovery of the full costs of operating the various aspects of the program. The DEA last modified the registration fees on April 16, 2012. 77 FR 15234. If the DEA determines in the future that such fees should be modified in order to ensure the recovery of the full costs of the diversion control program, including those contained in this rule, the DEA will propose a modified fee schedule pursuant to the notice-and-comment rulemaking process. The DEA currently provides limited exceptions and exemptions from registration fees to very specific groups and entities as identified in part 1301. At this time, the DEA does not anticipate expanding such exceptions and exemptions as a result of or in conjunction with the implementation of this rule.

[15] **Issue:** A few commenters noted that DEA's Economic Impact Analysis estimated the universe of potential respondents to include distributors, reverse distributors, manufacturers, and retail pharmacies, without considering hospitals, surgery centers, dental clinics, veterinary practices, or physicians' offices.

Response: The DEA's analysis included a universe of potential respondents comprised of only

those entities that may be affected by the rule—those registrants that are eligible to become authorized collectors (i.e., distributors, reverse distributors, manufacturers, NTPs, and hospitals/clinics with an on-site pharmacy, and retail pharmacies).

[16] **Issue:** Two commenters stated that the DEA did not appropriately calculate the costs associated with the proposed rule. One commenter stated that the DEA should acknowledge the costs associated with recordkeeping requirements, purchasing inner liners, purchasing mail-back packages, procedural changes, and increased destruction costs.

Response: As discussed previously, the economic analysis of the final rule takes into account costs associated with voluntary performance of collection activities even though the provisions that facilitate non-registrant disposal are completely voluntary, not mandated. Any collector, reverse distributor, distributor, or law enforcement that chooses to engage in the voluntary activities described in this section, does so based on its own evaluation of costs and benefits (tangible and intangible).

[17] **Issue:** One commenter stated that the economic impact analysis is inadequate because it does not acknowledge that parts of this rule are an "indirect" mandate for LTCFs. This commenter referred to incidents where LTCFs will have no other options for controlled substance disposal if patients are unable to dispose of the medication and there is no other person authorized to dispose of the controlled substances.

Response: In response to this comment, the final rule modifies the language of § 1317.80(a), as proposed, which appeared to prohibit LTCFs from using any disposal method other than a collection receptacle. Under the final rule, LTCFs *may* dispose of controlled substances on behalf of an ultimate user who resides, or has resided, at such LTCF. 21 CFR 1317.30 and 1317.80. The DEA notes that the decision to implement and manage a collection program for

ultimate user disposal is voluntary. It should be noted that LTCF residents are ultimate users themselves and they, members of their households, and persons lawfully entitled to dispose of a decedent's personal property, may avail themselves of all disposal methods made available by this rule. 21 CFR 1317.30.

[18] **Issue:** One commenter stated that the DEA did not consider veterinary practices, prisons, or clinics when calculating the economic impact analysis.

Response: In the proposed rule, the DEA considered veterinary practices, prisons, and clinics in the accompanying calculations concerning economic impact to the extent that these entities would be registered as practitioners or non-practitioners. For the final rule, the DEA calculated the economic impact on these entities to the extent that they could become collectors. Not all registrants are eligible to become authorized collectors. Of this specified list of entities inquired about by the commenter, only a small subsection, specifically hospitals/clinics with on-site pharmacies, may become authorized as collectors in accordance with this final rule. 21 CFR 1317.40 and 1317.70.

P. *Recordkeeping and Reporting (8 issues)*

[1] **Issue:** One commenter asked the DEA to clarify whether or not the recordkeeping requirements in the rule apply to all registrants or only authorized collectors.

Response: The new recordkeeping requirements contained in this rule are applicable to all registrants, including authorized collectors. To clarify this important distinction, the DEA moved the recordkeeping provisions in proposed part 1317 to part 1304.

[2] **Issue:** Several commenters urged the DEA to remove the inventory and recordkeeping requirements for mail-back packages and inner liners. The commenters believe that such recordkeeping will be challenging and provide limited benefits. One commenter suggested that

the DEA instead adopt tracking procedures currently used in some non-controlled substance collection programs.

Response: As described in the NPRM, inventory and recordkeeping requirements for collected substances are necessary for a number of reasons, including accountability of collected substances within the possession and control of authorized collectors. The inventory and recordkeeping requirements included in this rule are generally consistent with those otherwise required of registrants, thus minimizing burden. The DEA believes that these inventory and recordkeeping requirements are necessary to help minimize the risk of diversion and to identify diversion of controlled substances destined for destruction.

[3] **Issue:** One commenter suggested that the DEA eliminate ARCOS reporting requirements for reverse distributors regarding collected substances from ultimate users. Another commenter asked the DEA to clarify what information is required for ARCOS reporting.

Response: In this final rule, § 1304.33(g) (relocated from proposed § 1317.50) exempts reverse distributors and distributors that acquire controlled substances from collectors or law enforcement from reporting to ARCOS with respect to pharmaceutical controlled substances collected through mail-back programs and collection receptacles.

[4] **Issue:** One commenter asked the DEA to clarify what records reverse distributors must keep when receiving collected substances from law enforcement.

Response: The recordkeeping requirements in §1304.22(e)(4) that apply to controlled substances acquired by registrants that reverse distribute from collectors also apply to those acquired from law enforcement. The final rule also adds a new paragraph in § 1304.11(e)(3)(iii) specifying the information relating to controlled substances acquired from collectors and law enforcement that a registrant that reverse distributes must maintain in its inventories. Under the

revised § 1304.03(a), these provisions relating to reverse distributors apply to any entity that reverse distributes, as defined in § 1300.01(b), whether or not it is registered with the DEA as a reverse distributor. Finally, the requirement in § 1304.21(e) to maintain a DEA Form 41 applies to the destruction of a sealed inner liner or mail-back package by a registrant that reverse distributes.

[5] **Issue:** Commenters asked the DEA to clarify who is responsible for tracking the mail-back packages, and how mail-back packages that were disseminated but not returned to the authorized collector will be reconciled with the inventory.

Response: There is currently no requirement for the authorized collector to reconcile the inventory in order to determine which packages were not returned. As discussed in the NPRM, the DEA does not believe that requiring authorized collectors to institute a tracking or notification system for ultimate users is necessary at this time, although such systems are not prohibited so long as the collector does not require the ultimate user to provide personally identifiable information, as specified in § 1317.70(d).

[6] **Issue:** Commenters asked the DEA to eliminate the following recordkeeping requirements for inner liners: tracking unused inner liners on hand, recording the acquisition date, recording the installation date, and the requirement that two employees witness the removal and installation of inner liners.

Response: As previously discussed, the DEA believes that all of the inventory and recordkeeping requirements in part 1304 are the minimum necessary to ensure accountability and identify diversion.

[7] **Issue:** Two commenters asked the DEA if reporting to the FDA is sufficient to satisfy the DEA's reporting requirements for cases of controlled substance recalls.

Response: No. Regardless of any other Federal, State, tribal, or local agency requirements, each registrant must maintain records and make reports to the DEA in a manner consistent with the requirements of chapter II of title 21 of the CFR.

[8] **Issue:** One commenter asked the DEA to clarify the recordkeeping requirements of § 1317.50(b)(2)(iii)—specifically, the requirement to record the registration number of the collection location when the collection occurs at a LTCF, which typically does not have a registration number.

Response: The final rule moves the referenced requirements to new § 1304.22(f). The record should include the approved collection location address of the LTCF and the authorized collector's registration number.

Q. *Hazardous Materials Transportation and Hazardous Waste Destruction (3 issues)*

[1] **Issue:** Approximately 20 commenters expressed concern that the requirements outlined in this rule for the transportation of collected substances conflict with current regulations under the DOT's Pipeline and Hazardous Materials Safety Administration (PHMSA). One concern involved the comingling of collected substances that the DOT considers "hazardous materials" with nonhazardous materials or hazardous materials of a different class. Other concerns included how inner liners from collection receptacles that contain hazardous materials should be labeled and packaged for transport, and other notice requirements for hazardous waste under the DOT's PHMSA.

Response: All drug disposal activities must be conducted in a manner consistent with this rule and all other applicable Federal, State, tribal, and local laws and regulations. Compliance with the destruction requirements outlined in subpart C of this rule does not exempt any entity from complying with other Federal, State, tribal, or local laws or regulations. It is not within DEA's

expertise or authority to opine what pharmaceutical controlled substances could be hazardous materials subject to DOT regulations. However, the DEA consulted with the DOT during various stages of this rulemaking. The DEA has been informed that if collected substances include hazardous materials, the transportation of those materials is subject to all applicable DOT regulations, including the "Hazardous Materials Regulations" (HMR). The DEA encourages entities to consult www.phmsa.dot.gov/hazmat for information regarding the HMR. In particular, the DEA encourages entities to contact the DOT's PHMSA regarding its "Approvals and Permits Program." PHMSA issues approvals and special permits to entities that apply for authorization to use agency approved alternatives to the HMR. Interested entities may consult www.phmsa.dot.gov/hazmat/regs/sp-a. for more information. The DEA has worked with the DOT to facilitate this process in an effort to ensure maximum participation in the collection of controlled substances for secure and responsible disposal, and the DEA will continue to work with the DOT to facilitate registrant compliance with all applicable laws and regulations. For these purposes, it should be noted that sealed collection receptacle inner liners may be transported inside of a shipping container that is labeled and packaged for transport with the necessary notice requirements applicable to hazardous waste under the DOT's PHMSA.

[2] **Issue:** One commenter asked whether or not law enforcement must comply with the DOT's PHMSA requirements for transporting collected substances that may contain hazardous materials.

Response: It is not within the DEA's expertise or authority to opine on the applicability of DOT regulations. However, the DEA believes that the DOT's Hazardous Materials Regulations apply to entities that place hazardous materials in commercial transportation, and not government vehicles operated by government personnel solely for non-commercial purposes. However, State

and local governments may have different regulations that do apply to government entities or law enforcement. The DEA encourages these entities to consult the DOT as well as their State and local governments for specific guidance on transporting collected substances that may contain hazardous materials.

[3] **Issue:** Commenters asked the DEA whether or not collected substances must be destroyed as hazardous waste under the EPA's Resource Conversation and Recovery Act (RCRA).

Response: It is not within the DEA's expertise or authority to opine what pharmaceutical controlled substances could be hazardous waste subject to EPA regulations. The DEA does not have the authority to regulate hazardous waste and thus cannot advise on whether or not collected substances must be destroyed as hazardous waste pursuant to RCRA. However, the DEA has worked with the EPA at various stages of this rulemaking, and the DEA continues to work with the EPA to ensure the secure and responsible disposal of controlled substances, including those that may be considered hazardous waste. The DEA believes that there is a small portion of pharmaceuticals that are regulated as hazardous waste, and an even smaller portion of pharmaceuticals that are regulated as both controlled substances and hazardous waste. However, pharmaceutical controlled substances that are collected directly from ultimate users via mail-back programs or collection receptacles may fall under RCRA's Household Hazardous Waste Exemption; if so, EPA RCRA regulations would not apply in those instances. The DEA acknowledges that some state and local regulations may be more stringent.

The DEA is working with the EPA to ensure that this final rule will enable LTCF residents to responsibly, securely, and safely dispose of controlled substances that may also be considered hazardous waste. Collected substances from LTCFs may pose a unique challenge since the EPA currently uses a bifurcated system to determine whether pharmaceutical waste

from LTCFs must be treated as hazardous waste under the RCRA. If the waste is generated by the resident, it does not have to be treated as hazardous waste and is exempt under the Household Hazardous Waste Exemption. If the waste is generated by the LTCF, it must be treated as hazardous waste unless it is otherwise exempt. Hazardous waste generated by LTCFs may be exempt if the LTCF is a "conditionally-exempt small quantity generator." To qualify under such exemption, the LTCF must generate less than or equal to 100 kilograms of non-acute hazardous waste, *and* less than or equal to one kilogram of acute hazardous waste on a monthly basis. The DEA believes that most LTCFs may qualify under this conditional exemption. Also, the DEA acknowledges that many pharmaceuticals that are recognized as acute hazardous waste (e.g., blood thinners) are non-controlled substances. The DEA hopes that authorized collectors and LTCFs will collaborate to minimize the impact that disposing of such pharmaceuticals may have on collection efforts by separating these non-controlled substances from controlled substances to be deposited into collection receptacles.

The EPA is aware of the concerns regarding collected substances at LTCFs, and according to the Fall 2013 Regulatory Agenda, the EPA is currently drafting regulations to address hazardous waste pharmaceuticals, including the small group of pharmaceutical controlled substances that the EPA classifies as hazardous waste under the RCRA, when discarded. According to the Regulatory Agenda, the EPA's proposal, "Management Standards for Hazardous Waste Pharmaceuticals," may propose to "revise the regulations to improve management and disposal of hazardous waste pharmaceuticals," and clarify regulation of reverse distribution. The abstract for the proposal may be viewed at www.reginfo.gov. Interested persons are encouraged to follow the progress of this pending regulatory action.

The DEA encourages authorized collectors and others to seek guidance directly from the EPA, and the DEA encourages such persons to consult www.epa.gov for more information. All drug disposal and destruction must be conducted in a manner consistent with this rule and all other applicable Federal, State, tribal, and local laws and regulations.

R. *Transporting Collected Substances (3 issues)*

[1] **Issue:** One commenter indicated that transporting collected substances directly to the destruction location will be virtually impossible because drivers must stop for rest breaks.

Response: The DEA recognizes that transportation to destruction facilities may occur over long distances. The requirement to transport collected substances directly to the destruction facility means that the collected substances should be constantly moving towards their final destruction destination and unnecessary or unrelated stops, and stops of an extended duration should not occur. The final rule in §§ 1317.05(b)(4) and 1317.95(c)(1) is modified to specify this requirement, which is designed to reduce the opportunities for diversion.

[2] **Issue:** Several commenters were concerned that this rule will change their existing transport procedures that were already approved by their local SAC.

Response: In promulgating this rule, the DEA carefully considered the impact of these changes to existing procedures and is requiring the minimum procedures necessary to ensure safe and secure means of transporting controlled substances. The rule provides a nationwide standard, and allows non-practitioners the flexibility to determine the best method of transportation considering their own individual circumstances while also ensuring accountability and reducing theft and diversion risks. Any previous waivers, Memorandums of Understanding, or Memorandums of Agreement issued in accordance with § 1307.21 shall be superseded by this final rule once it becomes effective. However, practitioners may seek assistance from their local

SAC pursuant to § 1317.05(a)(4).

[3] **Issue:** Other commenters sought guidance on whether or not the DEA will limit the quantity of controlled substances that may be transported, and whether or not there will be additional requirements for interstate transport of collected substances.

Response: This final rule does not impose any transportation quantity limits or any requirements specific to interstate transport of controlled substances.

S. *Miscellaneous Comments (2 issues)*

[1] **Issue:** Approximately eight commenters asked the DEA to expand the rule to include procedures for controlled substances that have been "partially administered" or "partially dispensed." These commenters referred to institutional settings where transdermal patches are used, as these used patches may contain residual amounts of controlled substances.

Response: As previously discussed, destruction of the residual amounts of controlled substances administered by a practitioner to a patient that remain in the delivery apparatus (in this instance, the transdermal patch) must continue to be recorded in accordance with existing § 1304.22(c). In accordance with the revised § 1304.21, these destructions are not required to be recorded on DEA Form 41. All disposals of inventory must be accomplished in accordance with § 1317.05(a), and all other applicable recordkeeping and inventory requirements.

[2] **Issue:** One commenter indicated that §§ 1317.15 and 1317.95 may conflict in that § 1317.15 allows for storage by a reverse distributor while § 1317.95 does not.

Response: The DEA has reviewed the relevant portions of this rule and determined that §§ 1317.15 and 1317.95 do not conflict. Section 1317.15 encompasses the wider topic of reverse distributor activities, including the acquisition and storage of controlled substances from other registrants, whereas § 1317.95 deals exclusively with the actual destruction process and the

procedures that are required for destruction once substances are in the possession and control of the reverse distributor (including securely stored substances).

IV. Regulatory Analyses

Regulatory Flexibility Act

The Administrator, in accordance with the Regulatory Flexibility Act of 1980 (RFA) (5 U.S.C. 601-612), has reviewed this rule and by approving it certifies that it will not have a significant economic impact on a substantial number of small entities. In developing this rule, the DEA considered numerous alternatives for each requirement and method of collection and evaluated the impact of this rule on small entities. The DEA has concluded that the rule will not have a significant economic impact on a substantial number of small entities. The DEA updated the economic impact analysis after considering comments made by the public in response to the NPRM. The updated economic impact analysis of the final rule may be viewed in the rulemaking docket at www.regulations.gov.

In developing this rule, the DEA considered several options for both registrant and non-registrant disposal and reverse distributor destruction requirements. The DEA analyzed alternative methodology approaches keeping in mind its obligations under the CSA. The DEA considered three options for non-registrant disposal: (1) "Single Collection," which would permit non-registrants to utilize only one method of collection to dispose of their lawfully possessed controlled substances; (2) "Open Collection," which would authorize any person to collect controlled substances from ultimate users for disposal, regardless of their status as a registrant; and (3) "Multiple Collection," which would authorize non-registrants to utilize more than one method of collection to transfer controlled substances for the purpose of disposal to law enforcement and certain registrants. In addition, the DEA considered two options for registrant

disposal: (1) "Retain Existing Regulations," which would make no changes to the existing registrant disposal regulations (§§ 1307.12 and 1307.21); and (2) "Establish Consistent National Standards," which would eliminate existing regulations on the disposal of controlled substances (§§ 1307.12 and 1307.21) and promulgate a new part that would comprehensively outline the process and procedure for the disposal of controlled substances by registrants and non-registrants.

Finally, the DEA considered four options for reverse distributors: (1) "On-site Requirement," which would require reverse distributors to have and utilize an on-site method of destruction; (2) "Prompt Requirement," which would require reverse distributors, like all other registrants, to promptly destroy controlled substances; (3) "No Requirement," which would retain the current destruction standard and would not put a deadline on when reverse distributors must destroy controlled substances acquired for destruction; and (4) "No Later Than 30 Calendar Day Requirement," which would require reverse distributors to destroy controlled substances received for the purpose of destruction no later than 30 calendar days from receipt. The DEA performed a qualitative analysis of each of these alternatives and selected the "Multiple Collection" option for non-registrant disposal, the "Establish Consistent National Standards" option for registrant disposal, and the "No Later than 30 Calendar Day Requirement" option for reverse distributors.

In accordance with the RFA, the DEA evaluated the impact of this rule on small entities. While all 1.5 million DEA registrants must comply with the rule as it relates to the disposal of pharmaceutical controlled substances, only a small subset of the registrants are associated with activities where the rule imposes new mandatory requirements or provides options for voluntary activities. Therefore, the DEA examined the impact of two mandatory provisions in the rule: the

30-day destruction requirement for reverse distributors and the two employee transportation requirement for manufacturers, distributors, and reverse distributors. Additionally, the DEA estimated the level of voluntary participation in collection activities in accordance with the rule and the resulting cost impact.

The mandatory provisions and voluntary participation activities are estimated to affect 53,533 entities (439 manufacturers, 585 distributors, 55 reverse distributors, 656 narcotic treatment programs (NTPs), 3,068 hospitals/clinics, 29,582 pharmacies, and 19,148 long term care facilities (LTCFs). Of the 53,533 affected entities, 50,714 (423 manufacturers, 555 distributors, 38 reverse distributors, 610 NTPs, 1,346 hospitals/clinics, 29,328 pharmacies, and 18,414 long term care facilities), or 94.7% are estimated to be small entities.

Both the 30-day destruction and the two employee transportation requirements associated with the mandatory portions of the rule will apply to the 55 reverse distributors that receive controlled substances from other registrants for disposal, of which 38 were estimated to be small entities. The potential increase in destruction, transport, travel, and labor cost associated with these two requirements was analyzed for each of the 38 small entities. Additionally, reverse distributors with on-site destruction facilities may receive authorization to voluntarily operate a mail-back program. The DEA estimates that the three small reverse distributors with on-site destruction facilities will each operate a mail-back program. The DEA does not estimate that any reverse distributors will operate collection receptacles at their registered locations because of the small numbers of employees that work at those locations. However, reverse distributors will be impacted by the destruction of controlled substances from collection receptacles that are transferred to them for destruction. The total estimated cost of the mandatory portions and voluntary participation aspects of the rule was compared to the estimated annual revenue for

each of the small reverse distributors. The economic impact of the mandatory portion and voluntary participation aspects of this rule is estimated to be significant, greater than one percent of annual revenue, for two (5%) of 38 affected small businesses.

The two-person transportation requirement associated with the mandatory portions of the rule also affects 423 small manufacturers and 555 small distributors that transport to reverse distributors or to an unregistered, off-site location for destruction. The potential increase in labor cost associated with the two-person requirement was analyzed for manufacturers and distributors. Additionally, a small number of manufacturers and distributors are estimated to volunteer to operate collection receptacles at their registered locations primarily for use by their employees. However, the DEA believes that manufacturers and distributors will not operate collection receptacles at their registered locations unless they believe there will be a benefit to them for the service. The economic impact of the mandatory portion and voluntary participation aspects of this rule is estimated to be significant for none (0.0%) of the 423 small manufacturers and none (0.0%) of the 555 small distributors.

The rule also permits certain other registrant categories to voluntarily conduct collection activities. The DEA estimates some retail pharmacies, hospitals/clinics with on-site pharmacies, and NTPs will voluntarily participate as collectors by operating collection receptacles at their locations. Some retail pharmacies and hospitals/clinics with an on-site pharmacy are also estimated to operate collection receptacles at LTCFs. The level of participation and operating costs were estimated to determine the number of small entities with impact greater than 1% of revenue.

In summary, the DEA estimates that zero (0.0%) of the 423 small manufacturers, zero (0.0%) of the 555 small distributors, two (5.0%) of 38 small reverse distributors, 62 (10.2%) of

the small NTPs, zero (0.0%) of the 1,349 small hospitals/clinics, 810 (2.8%) of the 29,328 small pharmacies, and zero (0.0%) of the 18,414 small long term care facilities may be significantly impacted by this rule (that is, where the annual cost is estimated to be greater than 1% of annual revenue). But DEA emphasizes that these estimates are entirely dependent on the level of voluntary participation by these entities. All of the provisions relating to collection activities by manufacturers, distributors, NTPs, hospitals/clinics, pharmacies, and LTCFs are completely voluntary and these entities would be free to choose whether or not to participate based on their own review of the cost to them and the anticipated benefits in providing collection receptacles.

In total, the DEA estimates that 874 (1.7%) of the 50,714 affected small entities may be significantly affected by this rule. The DEA's assessment of economic impact by size category indicates that the rule will not have a significant effect on a substantial number of these small business entities.

In accordance with the RFA (5 U.S.C. 605(b)), the Administrator hereby certifies that this rulemaking has been drafted consistent with the RFA, that a regulatory analysis on the effects or impacts of this rulemaking on small entities has been done, and that the rule will not have a significant economic impact on a substantial number of small entities.

Executive Orders 12866 and 13563

This rule was developed in accordance with the principles of Executive Orders 12866 and 13563. Based on the completed economic analysis, the DEA does not anticipate that this rulemaking will have an annual effect on the economy of $100 million or more or adversely affect, in a material way, the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, or tribal governments or communities. An economic analysis of the final rule can be found in the rulemaking docket at

www.regulations.gov. Public comment was received in public meetings held on January 19–20, 2011, and through a solicitation for comment in the NPRM to help inform and develop these rules. Although not an economically significant rule, this rule on the disposal of controlled substances has been reviewed by the Office of Management and Budget (OMB).

The DEA has determined that reverse distributors currently destroy controlled substances within the "No Later than 30 Calendar Day" requirement the majority of the time. However, it is recognized that there may be instances when reverse distributors do not currently meet this requirement. Additionally, many manufacturers, distributors, and reverse distributors currently employ two persons to transport controlled substances for destruction. However, it is recognized that there may be instances when manufacturers, distributors, and reverse distributors do not currently meet this requirement. For these instances, the DEA estimated the cost to accommodate the requirements and has determined the cost is not a significant economic impact.

Moreover, the DEA estimated a range of costs of voluntary participation for manufacturers, distributors, reverse distributors, narcotic treatment programs, hospitals/clinics with an on-site pharmacy, and retail pharmacies that may participate to collect ultimate user pharmaceutical controlled substances.

In summary, the DEA estimates that the annual total cost to the economy as a result of the rule is $2,719,319 for the mandatory provisions of this rule and the total annualized cost of the mandatory provisions and the voluntary participation aspects of the rule ranges from $44,896,787 to $73,222,427. The DEA estimates the highest cost in any given year occurs in the first year, ranging from $45,282,242 to $99,075,339. Accordingly, the DEA does not anticipate that this rulemaking will have an annual effect on the economy of $100 million or more or adversely affect in a material way the economy, a sector of the economy, productivity,

competition, jobs, the environment, public health or safety, or State, local, or tribal governments or communities.

Since the aspects of the rule that facilitate non-registrant disposal are completely voluntary (not mandated), manufacturers, distributors, reverse distributors, narcotic treatment programs, hospitals/clinics with an on-site pharmacy, and retail pharmacies may become collectors if they choose to engage in the voluntary activities based on its own evaluation of costs and benefits (tangible and intangible). For the purposes of this analysis, the DEA assumes that an entity will volunteer to perform the activities to facilitate non-registrant disposal only if there is a net zero or positive benefit to the entity. For example, a pharmacy may derive tangible benefits, such as additional revenue from increased retail traffic to the pharmacy. Collectors may also derive tangible benefits such as public safety and good will from their collection activities. Any collector that chooses to engage in these voluntary activities can decide to cease these activities at any time. Therefore, for the purposes of this analysis, the DEA estimates that the cost of the voluntary participation aspects of this rule are offset by the benefits of the voluntary participation aspects of this rule and have a net zero economic impact. The total cost of the mandatory provisions and voluntary participation aspects of the rule ($73,222,427 at the highest voluntary participation rate) is compared to the benefit of this rule. In evaluating the costs and benefits of the rule, the annual cost of the rule is compared with the anticipated reduction in the growth rate of costs associated with diversion of controlled substances into the illicit market. The cost-benefit analysis uses the costs associated with the nonmedical use of prescription opioids, $8.6 billion in 2001[7] and $53.4 billion in 2006.[8] These are conservative estimates of the rapidly growing total cost associated with diversion of controlled substances into the illicit

[7] Clin. J. Pain (The Clinical Journal of Pain), Volume 22, Number 8, October 2006.
[8] Clin. J. Pain (The Clinical Journal of Pain), Volume 27, Number 3, March/April 2011.

market. Although there is a lack of evidence to quantify the cost savings or public health impacts of the rule, the DEA believes that this rule reduces the growth in the cost of the diversion of controlled substances into the illicit market by at least $44.9 to $73.2 million annually and, therefore, this rule will have positive net economic benefits, including benefits related to the health and safety of the citizens and residents of the United States.

Paperwork Reduction Act

Pursuant to § 3507(d) of the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501 *et seq*.), the DEA has identified the following collections of information related to this rule and has submitted these collection requests to the OMB for review and approval. This rule implements the Disposal Act, in addition to reorganizing and consolidating existing regulations on disposal into a comprehensive regulatory framework for the destruction of controlled substances. In accordance with the CSA, which establishes a closed system of distribution for all controlled substances, registrants are required to make a biennial inventory and maintain, on a current basis, a complete and accurate record of each controlled substance manufactured, received, sold, delivered, or otherwise disposed of. 21 U.S.C. 827(a) and 958. These records must be in accordance with and contain such relevant information as may be required by regulations promulgated by the DEA. 21 U.S.C. 827(b)(1).

In this rule, the DEA revises existing, and adds a minimum amount of new, registrant recordkeeping requirements. These requirements are consistent with requirements already required by statute and regulation.

Title: Implementation of Registrant Recordkeeping Requirements Pursuant to the CSA, 21 U.S.C. 827

The records that registrants are required to maintain pursuant to law are a vital

component of the DEA's enforcement and control responsibilities—such records alert the DEA to problems of diversion and ensure that the system of controlled substances distribution is open only to legitimate handlers of such substances.

The DEA is revising the information that reverse distributors are currently required to record for clarity and consistency, and adding a minimum amount of new requirements. For all controlled substance records, reverse distributors will be required to maintain their existing business records so that the record of receipt is maintained with the corresponding record of return or destruction. By maintaining all relevant business records together, the DEA will be able to trace each substance received by a reverse distributor from its acquisition to its disposition, whether by destruction or return to the manufacturer.

The DEA estimates that there will be 60 respondents to this information collection and that their estimated frequency of response will vary because, in accordance with 21 U.S.C. 827 and 958, registrants make an initial and biennial inventory and maintain, on a current basis, a complete and accurate record of each controlled substance manufactured, received, sold, delivered, or otherwise disposed of. Under existing law, reverse distributors are required to maintain, for at least two years, inventory records and records of controlled substances received, delivered, destroyed, or returned to the manufacturer. The annual hour burden for recordkeeping for reverse distributors is estimated to increase by 34 hours due to the requirements in this final rule, and the annualized cost to respondents is estimated to be $719. The DEA is also modifying information that registrants are required to record in the return and recall process. The DEA is eliminating the previous rule on return and recall, § 1307.12, and implementing separate rules on the return and recall of controlled substances for registrants and non-registrants in part 1317. The return and recall recordkeeping requirements reflect these changes.

The DEA estimates that the universe of potential respondents to this information collection will be 1,511,389 respondents (all registrants may transfer controlled substances for return or recall). The DEA estimates that the frequency of response will vary, because, in accordance with 21 U.S.C. 827(a), registrants must make an initial and biennial inventory and maintain, on a current basis, a complete and accurate record of each controlled substance manufactured, received, sold, delivered, or otherwise disposed of. Because registrants are already required to maintain records in accordance with 21 U.S.C. 827(a)–(b), the DEA anticipates that the annual hour burden will not be increased by this rule.

The DEA is implementing new recordkeeping requirements for registrants that collect controlled substances from ultimate users and other non-registrants in accordance with the new authority provided in the Disposal Act. The implementation of the Disposal Act regulations will provide ultimate users, LTCFs, and other non-registrants safe and convenient options to transfer controlled substances for the purpose of disposal: take-back events, mail-back programs, and collection receptacles. Registered manufacturers, distributors, reverse distributors, narcotic treatment programs, hospitals/clinics with an on-site pharmacy, and retail pharmacies may obtain authorization from the DEA to be a collector pursuant to § 1317.40. A collector is a registered manufacturer, distributor, reverse distributor, narcotic treatment program, hospital/clinic with an on-site pharmacy, or retail pharmacy that is authorized under this rule to receive a pharmaceutical controlled substance from an ultimate user for the purpose of destruction, as defined in part 1300. The DEA is requiring information that collectors must record based on the particular ultimate user collection method implemented (i.e., mail-back program or collection receptacle).

The DEA estimates that the universe of potential participants to this information

collection will be 87,736 respondents (Manufacturers—536, Distributors—829, Reverse Distributors—60, Narcotic Treatment Programs—1,332, Hospitals/Clinics—15,953, Retail Pharmacies—69,026).[9] However, the DEA estimates that the participants to this information collection will be 54,457 respondents (Manufacturers—107, Distributors—166, Reverse Distributors—10, Narcotic Treatment Programs—999, Hospitals/Clinics—2862, Retail Pharmacies—34,513, and an additional 15,800 hospitals/clinics and retail pharmacies operating collection receptacles at LTCFs). The DEA estimates that the frequency of response will vary, because, in accordance with 21 U.S.C. 827(a), registrants must make an initial and biennial inventory and maintain, on a current basis, a complete and accurate record of each controlled substance manufactured, received, sold, delivered, or otherwise disposed of. The DEA notes, however, that the option to become a collector is voluntary and no entity is required to establish or operate a disposal program as a collector. While the authorization to collect is a new activity, the DEA has estimated the level of participation. The estimated 54,457 respondents are estimated to have an annualized hour burden of 89,406 with an estimated annualized cost of $1,670,064. The DEA will continue to monitor and analyze the potential burden of the new requirements imposed by this rule.

The DEA is authorizing reverse distributors to acquire controlled substances from law enforcement and authorized collectors that have acquired controlled substances from ultimate users and other non-registrants. The DEA is also authorizing distributors to acquire controlled substances from authorized collectors that collect controlled substances from ultimate users. The DEA is requiring these reverse distributors and distributors to maintain complete and accurate records, in accordance with part 1304, of controlled substances received, delivered, or otherwise

[9] The universe of potential participants includes all registrants that could potentially become collectors. It is likely that this estimate will be adjusted downward once the DEA obtains more information.

transferred for the purpose of destruction.

The DEA estimates that the universe of potential respondents to this information collection will be 889 respondents (Distributors—829, Reverse Distributors—60). The DEA estimates that the frequency of response will vary, because, in accordance with 21 U.S.C. 827(a), registrants must make an initial and biennial inventory and maintain, on a current basis, a complete and accurate record of each controlled substance manufactured, received, sold, delivered, or otherwise disposed of. The authorization for reverse distributors to acquire controlled substances collected by law enforcement and collectors, and the authorization for distributors to acquire controlled substances from collectors, is new. Although the DEA has estimated the level of participation, the DEA is unable to estimate the number of information collection events because destruction of multiple acquisitions of controlled substances can be on a single form. The DEA's initial estimate for the annual hour burden is 472 hours (32 minutes per event), with an estimated annualized cost of $10,037. The DEA will continue to analyze the potential burden of the new requirements imposed by this rule.

Title: Registrant Record of Controlled Substances Destroyed—DEA Form 41

OMB Control Number: 1117-0007

Form Number: DEA Form 41

The records that registrants are required to maintain pursuant to law are a vital component of the DEA's enforcement and control responsibilities—such records alert the DEA to diversion and ensure that the system of controlled substances distribution is open only to legitimate handlers of such substances. The DEA is requiring registrants involved in the destruction of controlled substances to record certain information. The record of destruction must include the signature of the two employees of the registrant that witnessed the destruction,

in addition to other information about the controlled substance disposed of and the method of destruction utilized. The DEA is modifying existing DEA Form 41 to record the destruction of controlled substances that remain in the closed system of distribution and to account for registrant destruction of controlled substances collected from ultimate users and other non-registrants outside the closed system pursuant to the Disposal Act. DEA Form 41 has previously been approved by the OMB and assigned OMB control number 1117-0007. In accordance with the CSA, registrants that destroy controlled substances and utilize DEA Form 41 will be required to keep and make available the information in the specified format, for at least two years, for inspection and copying by officers or employees of the United States authorized by the Attorney General. 21 U.S.C. 827(b).

The DEA estimates that there will be 87,736 respondents (Manufacturers—536, Distributors—829, Reverse Distributors—60, Narcotic Treatment Programs—1,332, Hospitals/Clinics—15,953, Retail Pharmacies—69,026) to this information collection. The number of respondents (87,736) represents the total number of registrants in business activities that are most likely to destroy controlled substances. The DEA estimates that the frequency of response will vary, because in accordance with 21 U.S.C. 827(a), registrants must maintain, on a current basis, a complete and accurate record of each controlled substance manufactured, received, sold, delivered, or otherwise disposed of, and, as a result, will make a record of destruction each time they destroy a controlled substance. The DEA estimates that the average time per response will be 30 minutes and that the total annual burden will be 43,868 hours, with an estimated total annual cost burden of $928,247.

Executive Order 12988

This rule meets the applicable standards set forth in §§ 3(a) and 3(b)(2) of Executive Order 12988 to eliminate ambiguity, minimize litigation, establish clear legal standards, and reduce burden.

Executive Order 13132

This rulemaking does not preempt or modify any provision of State law, impose enforcement responsibilities on any State or diminish the power of any State to enforce its own laws. Accordingly, this rulemaking does not have federalism implications warranting the application of Executive Order 13132.

National Environmental Policy Act (NEPA)

This rule provides options for the collection of controlled substances by registrants and non-registrants consistent with DEA regulations and Federal, State, tribal, and local laws and regulations. Provision of these options is intended to result in increased collection and destruction of unused controlled substances and thereby prevent diversion of such unused substances to illicit uses and result in collection and destruction of larger quantities in economical and environmentally sound manners. This rule establishes legal requirements for the handling of controlled substances. Destruction of controlled substances must be consistent with Federal, State, tribal and local laws and regulations.

The DEA and registrants have disposed of controlled substances since passage of the CSA. By regulation, the U.S. Department of Justice categorically excluded the DEA from further NEPA analysis with respect to regulations relating to the storage and destruction of controlled substances. This rule does not authorize any new methods of storage, transportation, or destruction of controlled substances, but is limited to the procedures and records pertaining to the collection of controlled substances for destruction. Accordingly, this proposed rule does not

significantly affect the quality of the human environment. The DEA has, therefore, determined that this rule does not have significant individual or cumulative effects on the human environment and is excluded from detailed analysis pursuant to 28 CFR part 61, Appendix B.

Unfunded Mandates Reform Act

In accordance with the Unfunded Mandates Reform Act (UMRA) of 1995 (2 U.S.C. 1501 *et seq*.), on the basis of information contained in the "Regulatory Flexibility Act" section above, the DEA has determined and certifies pursuant to the UMRA that this action would not result in any Federal mandate that may result "in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted for inflation) in any one year…" Therefore, neither a Small Government Agency Plan nor any other action is required under provisions of the UMRA of 1995.

Executive Order 13175

This rule does not have tribal implications warranting the application of Executive Order 13175. The rule does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal Government and Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes.

Congressional Review Act

This rule is not a major rule as defined by the Congressional Review Act (5 U.S.C. 804). This rule will not result in an annual effect on the economy of $100,000,000 or more, a major increase in costs or prices, or have significant adverse effects on competition, employment, investment, productivity, innovation, or the ability of United States-based companies to compete with foreign based companies in domestic and export markets.

Rule Text

List of Subjects

21 CFR Part 1300

Chemicals, Drug traffic control.

21 CFR Part 1301

Administrative practice and procedure, Drug traffic control, Security measures.

21 CFR Part 1304

Drug traffic control, Reporting and recordkeeping requirements.

21 CFR Part 1305

Drug traffic control.

21 CFR Part 1307

Drug traffic control.

21 CFR Part 1317

Drug traffic control, Security measures.

For the reasons stated in the preamble, the DEA amends 21 CFR chapter II as follows:

PART 1300—DEFINITIONS

1-2. The authority citation for part 1300 is revised to read as follows:

Authority: 21 U.S.C. 802, 821, 822, 829, 871(b), 951, 958(f).

3. In § 1300.01, amend paragraph (b) as follows:

a. Revise the introductory text;

b. Add a definition of "Collection" in alphabetical order;

c. Revise the last sentence in the definition of "Freight forwarding facility";

d. Add a definition of "Reverse distribute" in alphabetical order; and

e. Revise the definition of "Reverse distributor".

The revisions and additions read as follows:

§ 1300.01 Definitions relating to controlled substances.

* * * * *

(b) As used in parts 1301 through 1308, 1312, and 1317 of this chapter, the following terms shall have the meanings specified:

* * * * *

Collection means to receive a controlled substance for the purpose of destruction from an ultimate user, a person lawfully entitled to dispose of an ultimate user decedent's property, or a long-term care facility on behalf of an ultimate user who resides or has resided at that facility. The term *collector* means a registered manufacturer, distributor, reverse distributor, narcotic treatment program, hospital/clinic with an on-site pharmacy, or retail pharmacy that is authorized under this chapter to so receive a controlled substance for the purpose of destruction.

* * * * *

Freight forwarding facility * * * For purposes of this definition, a distributing registrant is a person who is registered with the Administration as a manufacturer, distributor (excluding reverse distributor), and/or importer.

* * * * *

Reverse distribute means to acquire controlled substances from another registrant or law enforcement for the purpose of:

(1) Return to the registered manufacturer or another registrant authorized by the manufacturer to accept returns on the manufacturer's behalf; or

(2) Destruction.

Reverse distributor is a person registered with the Administration as a reverse distributor.

* * * * *

4. Add § 1300.05 to read as follows:

§ 1300.05 Definitions relating to the disposal of controlled substances.

(a) Any term not defined in this part or elsewhere in this chapter shall have the definition set forth in section 102 of the Act (21 U.S.C. 802).

(b) As used in part 1317 of this chapter, the following terms shall have the meanings specified:

Employee means an employee as defined under the general common law of agency. Some of the factors relevant to the determination of employee status include: the hiring party's right to control the manner and means by which the product is accomplished; the skill required; the source of the instrumentalities and tools; the location of the work; the duration of the relationship between the parties; whether the hiring party has the right to assign additional projects to the hired party; the extent of the hired party's discretion over when and how long to work; the method of payment; the hired party's role in hiring and paying assistants; whether the work is part of the regular business of the hiring party; whether the hiring party is in business; the provision of employee benefits; and the tax treatment of the hired party. Other applicable factors may be considered and no one factor is dispositive. The following criteria will determine whether a person is an *employee* of a registrant for the purpose of disposal: the person is directly paid by the registrant; subject to direct oversight by the registrant; required, as a condition of employment, to follow the registrant's procedures and guidelines pertaining to the handling of controlled substances; subject to receive a performance rating or performance evaluation on a regular/routine basis from the registrant; subject to disciplinary action by the registrant; and

required to render services at the registrant's registered location.

Law enforcement officer means a person who is described in paragraph (1), (2) or (3) of this definition:

(1) Meets all of the following criteria:

(i) Employee of either a law enforcement agency, or law enforcement component of a Federal agency;

(ii) Is under the direction and control of a Federal, State, tribal, or local government;

(iii) Acting in the course of his/her official duty; and

(iv) Duly sworn and given the authority by a Federal, State, tribal, or local government to carry firearms, execute and serve warrants, make arrests without warrant, and make seizures of property;

(2) Is a Veterans Health Administration (VHA) police officer authorized by the Department of Veterans Affairs to participate in collection activities conducted by the VHA; or

(3) Is a Department of Defense (DOD) police officer authorized by the DOD to participate in collection activities conducted by the DOD.

Non-retrievable means, for the purpose of destruction, the condition or state to which a controlled substance shall be rendered following a process that permanently alters that controlled substance's physical or chemical condition or state through irreversible means and thereby renders the controlled substance unavailable and unusable for all practical purposes. The process to achieve a non-retrievable condition or state may be unique to a substance's chemical or physical properties. A controlled substance is considered "non-retrievable" when it cannot be transformed to a physical or chemical condition or state as a controlled substance or controlled substance analogue. The purpose of destruction is to render the controlled substance(s) to a non-

retrievable state and thus prevent diversion of any such substance to illicit purposes.

On-site means located on or at the physical premises of the registrant's registered location. A controlled substance is destroyed *on-site* when destruction occurs on the physical premises of the destroying registrant's registered location. A hospital/clinic has an *on-site* pharmacy when it has a pharmacy located on the physical premises of the registrant's registered location.

PART 1301—REGISTRATION OF MANUFACTURERS, DISTRIBUTORS, AND DISPENSERS OF CONTROLLED SUBSTANCES

5. The authority citation for part 1301 is revised to read as follows:

Authority: 21 U.S.C. 821, 822, 823, 824, 831, 871(b), 875, 877, 886a, 951, 952, 953, 956, 957, 958, 965.

6. In § 1301.13, revise paragraphs (e)(1)(i) and (ii) to read as follows:

§ 1301.13 Application for registration; time for application; expiration date; registration for independent activities; application forms, fees, contents and signature; coincident activities.

* * * * *

(e) * * *

(1)

Business Activity	Controlled Substances	DEA Application Forms	Application Fee ($)	Registration Period (years)	Coincident Activities Allowed
(i) Manufacturing	Schedules I–V	New–225 Renewal–225a	3,047	1	Schedules I–V: May distribute that substance or class for which registration

					was issued; may not distribute any substance or class for which not registered. Schedules II–V: May conduct chemical analysis and preclinical research (including quality control analysis) with substances listed in those schedules for which authorization as a mfr. was issued.
(ii) Distributing * * * * * * *	Schedules I–V	New–225 Renewal–225a	1,523	1	May acquire Schedules II–V controlled substances from collectors for the purposes of destruction.

* * * * *

7. In § 1301.25, revise paragraph (i) to read as follows:

§ 1301.25 Registration regarding ocean vessels, aircraft, and other entities.

* * * * *

(i) Controlled substances acquired and possessed in accordance with this section shall be

distributed only to persons under the general supervision of the medical officer employed by the owner or operator of the vessel, aircraft, or other entity, except in accordance with part 1317 of this chapter.

8. Revise § 1301.51 to read as follows:

§ 1301.51 Modification in registration.

(a) Any registrant may apply to modify his/her registration to authorize the handling of additional controlled substances or to change his/her name or address by submitting a written request to the Registration Unit, Drug Enforcement Administration. See the Table of DEA Mailing Addresses in § 1321.01 of this chapter for the current mailing address. Additionally, such a request may be submitted on-line at www.DEAdiversion.usdoj.gov.

(1) The request shall contain:

(i) The registrant's name, address, and registration number as printed on the certificate of registration;

(ii) The substances and/or schedules to be added to the registration or the new name or address; and

(iii) A signature in accordance with § 1301.13(j).

(2) If the registrant is seeking to handle additional controlled substances listed in Schedule I for the purpose of research or instructional activities, the registrant shall attach three copies of a research protocol describing each research project involving the additional substances, or two copies of a statement describing the nature, extent, and duration of such instructional activities, as appropriate.

(b) Any manufacturer, distributor, reverse distributor, narcotic treatment program, hospital/clinic with an on-site pharmacy, or retail pharmacy registered pursuant to this part, may

apply to modify its registration to become authorized as a collector by submitting a written request to the Registration Unit, Drug Enforcement Administration. See the Table of DEA Mailing Addresses in § 1321.01 of this chapter for the current mailing address. Additionally, such request may be submitted on-line at www.DEAdiversion.usdoj.gov.

(1) The request shall contain:

(i) The registrant's name, address, and registration number as printed on the certificate of registration;

(ii) The method(s) of collection the registrant intends to conduct (collection receptacle and/or mail-back program); and

(iii) A signature in accordance with § 1301.13(j).

(2) If a hospital/clinic with an on-site pharmacy or retail pharmacy is applying for a modification in registration to authorize such registrant to be a collector to maintain a collection receptacle at a long-term care facility in accordance with § 1317.80 of this chapter, the request shall also include the name and physical location of each long-term care facility at which the hospital/clinic with an on-site pharmacy, or the retail pharmacy, intends to operate a collection receptacle.

(c) No fee shall be required for modification. The request for modification shall be handled in the same manner as an application for registration. If the modification of registration is approved, the Administrator shall issue a new certificate of registration (DEA Form 223) to the registrant, who shall maintain it with the old certificate of registration until expiration.

9. In § 1301.52, revise the last sentence of paragraph (c) and add paragraph (f) to read as follows:

§ 1301.52 Termination of registration; transfer of registration; distribution upon

discontinuance of business.

* * * * *

(c) * * * Any controlled substances in his/her possession may be disposed of in accordance with part 1317 of this chapter.

* * * * *

(f) Any registrant that has been authorized as a collector and desires to discontinue its collection of controlled substances from ultimate users shall notify the Administration of its intent by submitting a written notification to the Registration Unit, Drug Enforcement Administration. See the Table of DEA Mailing Addresses in § 1321.01 of this chapter for the current mailing address. Additionally, such notice may be submitted on-line at www.DEAdiversion.usdoj.gov. When ceasing collection activities of an authorized mail-back program, the registrant shall provide the Administration with the name, registered address, and registration number of the collector that will receive the remaining mail-back packages in accordance with § 1317.70(e)(3) of this chapter.

10. In § 1301.71, add paragraph (f) to read as follows:

§ 1301.71 Security requirements generally.

* * * * *

(f) A collector shall not employ, as an agent or employee who has access to or influence over controlled substances acquired by collection, any person who has been convicted of any felony offense relating to controlled substances or who, at any time, had an application for registration with DEA denied, had a DEA registration revoked or suspended, or has surrendered a DEA registration for cause. For purposes of this subsection, "for cause" means in lieu of, or as a consequence of, any Federal or State administrative, civil, or criminal action resulting from an

investigation of the individual's handling of controlled substances.

11. In § 1301.72, revise paragraph (a) introductory text to read as follows:

§ 1301.72 Physical security controls for non-practitioners; narcotic treatment programs, and compounders for narcotic treatment programs; storage areas.

(a) *Schedules I and II.* Raw material, bulk materials awaiting further processing, finished products which are controlled substances listed in Schedule I or II (except GHB that is manufactured or distributed in accordance with an exemption under section 505(i) of the Federal Food Drug and Cosmetic Act which shall be subject to the requirements of paragraph (b) of this section), and sealed mail-back packages and inner liners acquired in accordance with part 1317 of this chapter, shall be stored in one of the following secured areas:

* * * * *

12. In § 1301.74, add paragraph (m) to read as follows:

§ 1301.74 Other security controls for non-practitioners; narcotic treatment programs and compounders for narcotic treatment programs.

* * * * *

(m) A reverse distributor shall not employ, as an agent or employee who has access to or influence over controlled substances, any person who has been convicted of any felony offense relating to controlled substances or who, at any time, had an application for registration with the DEA denied, had a DEA registration revoked or suspended, or has surrendered a DEA registration for cause. For purposes of this subsection, "for cause" means in lieu of, or as a consequence of, any Federal or State administrative, civil, or criminal action resulting from an investigation of the individual's handling of controlled substances.

13. In § 1301.75, redesignate paragraphs (c) and (d) as paragraphs (d) and (e) and add a new

paragraph (c) to read as follows:

§ 1301.75 Physical security controls for practitioners.

* * * * *

(c) Sealed mail-back packages and inner liners collected in accordance with part 1317 of this chapter shall only be stored at the registered location in a securely locked, substantially constructed cabinet or a securely locked room with controlled access, except as authorized by § 1317.80(d).

* * * * *

14. In § 1301.76, revise paragraph (c) to read as follows:

§ 1301.76 Other security controls for practitioners.

* * * * *

(c) Whenever the registrant distributes a controlled substance (without being registered as a distributor as permitted in §§ 1301.13(e)(1), 1307.11, 1317.05, and/or 1317.10 of this chapter), he/she shall comply with the requirements imposed on non-practitioners in § 1301.74(a), (b), and (e).

* * * * *

PART 1304—RECORDS AND REPORTS OF REGISTRANTS

15. The authority citation for part 1304 is revised to read as follows:

Authority: 21 U.S.C. 821, 827, 831, 871(b), 958(e)–(g), and 965, unless otherwise noted.

16. Amend § 1304.03 by revising the first and second sentences of paragraph (a) to read as follows:

§ 1304.03 Persons required to keep records and file reports.

(a) Every registrant, including collectors, shall maintain the records and inventories and

shall file the reports required by this part, except as exempted by this section. Any registrant that is authorized to conduct other activities without being registered to conduct those activities, pursuant to §§ 1301.22(b), 1307.11, 1307.13, or part 1317 of this chapter, shall maintain the records and inventories and shall file the reports required by this part for persons registered or authorized to conduct such activities. * * *

* * * * *

17. In § 1304.04, add paragraph (a)(3) to read as follows:

§ 1304.04 Maintenance of records and inventories.

(a) * * *

(3) A collector that is authorized to maintain a collection receptacle at a long-term care facility shall keep all records required by this part relating to those collection receptacles at the registered location, or other approved central location.

* * * * *

18. In § 1304.11, revise paragraphs (e) introductory text and (e)(2) and (3) and add paragraphs (e)(6) and (7) to read as follows:

§ 1304.11 Inventory requirements.

* * * * *

(e) *Inventories of manufacturers, distributors, registrants that reverse distribute, importers, exporters, chemical analysts, dispensers, researchers, and collectors.* Each person registered or authorized (by §§ 1301.13, 1307.11, 1307.13, or part 1317 of this chapter) to manufacture, distribute, reverse distribute, dispense, import, export, conduct research or chemical analysis with controlled substances, or collect controlled substances from ultimate users, and required to keep records pursuant to § 1304.03 shall include in the inventory the

information listed below.

* * * * *

(2) *Inventories of distributors.* Each person registered or authorized to distribute controlled substances shall include in the inventory the same information required of manufacturers pursuant to paragraphs (e)(1)(iii) and (iv) of this section.

(3) *Inventories of registrants that reverse distribute*. Each person registered or authorized to reverse distribute controlled substances shall include in the inventory, the following information:

(i) The name of the substance, and

(ii) The total quantity of the substance:

(A) For controlled substances in bulk form, to the nearest metric unit weight consistent with unit size;

(B) For each controlled substance in finished form: each finished form of the substance (e.g., 10-milligram tablet or 10-milligram concentration per fluid ounce or milliliter); the number of units or volume of each finished form in each commercial container (e.g., 100-tablet bottle or 3-milliliter vial); and the number of commercial containers of each such finished form (e.g., four 100-tablet bottles or six 3-milliliter vials); and

(C) For controlled substances in a commercial container, carton, crate, drum, or other receptacle that has been opened: if the substance is listed in Schedule I or II, make an exact count or measure of the contents; or if the substance is listed in Schedule III, IV, or V, make an estimated count or measure of the contents, unless the container holds more than 1,000 tablets or capsules in which case an exact count of the contents shall be made; or

(iii) For controlled substances acquired from collectors and law enforcement: the

number and size (e.g., five 10-gallon liners, etc.) of sealed inner liners on hand, or

(iv) For controlled substances acquired from law enforcement: the number of sealed mail-back packages on hand.

* * * * *

(6) *Inventories of dispensers and researchers*. Each person registered or authorized to dispense or conduct research with controlled substances shall include in the inventory the same information required of manufacturers pursuant to paragraphs (e)(1)(iii) and (iv) of this section. In determining the number of units of each finished form of a controlled substance in a commercial container that has been opened, the dispenser or researcher shall do as follows:

(i) If the substance is listed in Schedules I or II, make an exact count or measure of the contents; or

(ii) If the substance is listed in Schedule III, IV, or V, make an estimated count or measure of the contents, unless the container holds more than 1,000 tablets or capsules in which case he/she must make an exact count of the contents.

(7) *Inventories of collectors*. Each registrant authorized to collect controlled substances from ultimate users shall include in the inventory the following information:

(i) For registrants authorized to collect through a mail-back program, the record shall include the following information about each unused mail-back package and each returned mail-back package on hand awaiting destruction:

(A) The date of the inventory;

(B) The number of mail-back packages; and

(C) The unique identification number of each package on hand, whether unused or awaiting destruction.

(ii) For registrants authorized to collect through a collection receptacle, the record shall include the following information about each unused inner liner on hand and each sealed inner liner on hand awaiting destruction:

(A) The date of the inventory;

(B) The number and size of inner liners (e.g., five 10-gallon liners, etc.);

(C) The unique identification number of each inner liner.

19. In § 1304.21, revise paragraphs (a), (c), and (d) and add paragraph (e) to read as follows:

§ 1304.21 General requirements for continuing records.

(a) Every registrant required to keep records pursuant to § 1304.03 shall maintain, on a current basis, a complete and accurate record of each substance manufactured, imported, received, sold, delivered, exported, or otherwise disposed of by him/her, and each inner liner, sealed inner liner, and unused and returned mail-back package, except that no registrant shall be required to maintain a perpetual inventory.

* * * * *

(c) Separate records shall be maintained by a registrant for each independent activity and collection activity for which he/she is registered or authorized, except as provided in § 1304.22(d).

(d) In recording dates of receipt, importation, distribution, exportation, other transfers, or destruction, the date on which the controlled substances are actually received, imported, distributed, exported, otherwise transferred, or destroyed shall be used as the date of receipt, importation, distribution, exportation, transfer, or destruction (e.g., invoices, packing slips, or DEA Form 41).

(e) *Record of destruction*. In addition to any other recordkeeping requirements, any

registered person that destroys a controlled substance pursuant to § 1317.95(d), or causes the destruction of a controlled substance pursuant to § 1317.95(c), shall maintain a record of destruction on a DEA Form 41. The records shall be complete and accurate, and include the name and signature of the two employees who witnessed the destruction. Except, destruction of a controlled substance dispensed by a practitioner for immediate administration at the practitioner's registered location, when the substance is not fully exhausted (e.g., some of the substance remains in a vial, tube, or syringe after administration but cannot or may not be further utilized), shall be properly recorded in accordance with § 1304.22(c), and such record need not be maintained on a DEA Form 41.

20. In § 1304.22, revise the section heading, introductory text, and paragraph (e) and add paragraph (f) to read as follows:

§ 1304.22 Records for manufacturers, distributors, dispensers, researchers, importers, exporters, registrants that reverse distribute, and collectors.

Each person registered or authorized (by §§ 1301.13(e), 1307.11, 1307.13, or part 1317 of this chapter) to manufacture, distribute, dispense, import, export, reverse distribute, destroy, conduct research with controlled substances, or collect controlled substances from ultimate users, shall maintain records with the information listed in paragraphs (a) through (f) of this section.

* * * * *

(e) *Records for registrants that reverse distribute.* Each person registered or authorized to reverse distribute controlled substances shall maintain records with the following information for each controlled substance:

(1) For controlled substances acquired for the purpose of return or recall to the manufacturer or another registrant authorized by the manufacturer to accept returns on the

manufacturer's behalf pursuant to part 1317 of this chapter:

(i) The date of receipt; the name and quantity of each controlled substance received; the name, address, and registration number of the person from whom the substance was received; and the reason for return (e.g., recall or return); and

(ii) The date of return to the manufacturer or other registrant authorized by the manufacturer to accept returns on the manufacturer's behalf; the name and quantity of each controlled substance returned; the name, address, and registration number of the person from whom the substance was received; the name, address, and registration number of the registrant to whom the substance was returned; and the method of return (e.g., common or contract carrier).

(2) For controlled substances acquired from registrant inventory for destruction pursuant to § 1317.05(a)(2), (b)(2), and (b)(4) of this chapter:

(i) The date of receipt; the name and quantity of each controlled substance received; and the name, address, and registration number of the person from whom the substance was received; and

(ii) The date, place, and method of destruction; the name and quantity of each controlled substance destroyed; the name, address, and registration number of the person from whom the substance was received; and the name and signatures of the two employees of the registrant that witnessed the destruction.

(3) The total quantity of each controlled substance shall be recorded in accordance with the following:

(i) For controlled substances in bulk form: to the nearest metric unit weight or volume consistent with unit size;

(ii) For controlled substances in finished form: each finished form (e.g., 10-milligram

tablet or 10-milligram concentration per fluid ounce or milliliter); the number of units or volume of finished form in each commercial container (e.g., 100-tablet bottle or 3-milliliter vial); and the number of commercial containers of each such finished form (e.g., four 100-tablet bottles or six 3-milliliter vials); and

(iii) For controlled substances in a commercial container, carton, crate, drum, or other receptacle that has been opened: if the substance is listed in Schedule I or II make an exact count or measure of the contents; or if the substance is listed in Schedule III, IV, or V, make an estimated count or measure of the contents, unless the container holds more than 1,000 tablets or capsules in which case an exact count of the contents shall be made.

(4) For each sealed inner liner acquired from collectors or law enforcement and each sealed mail-back package acquired from law enforcement pursuant to § 1317.55 of this chapter:

(i) The number of sealed inner liners acquired from other persons, including the date of acquisition, the number and, for sealed inner liners the size (e.g., five 10-gallon liners, etc.), of all sealed inner liners and mail-back packages acquired to inventory, the unique identification number of each sealed inner liner and mail-back package, and the name, address, and, for registrants, the registration number of the person from whom the sealed inner liners and mail-back packages were received, and

(ii) The date, place, and method of destruction; the number of sealed inner liners and mail-back packages destroyed; the name, address, and, for registrants, the registration number of the person from whom the sealed inner liners and mail-back packages were received; the number and, for sealed inner liners the size (e.g., five 10-gallon liners, etc.), of all sealed inner liners and mail-back packages destroyed; the unique identification number of each sealed inner liner and sealed mail-back package destroyed; and the name and signatures of the two employees of the

registrant that witnessed the destruction.

(5) For all records, the record of receipt shall be maintained together with the corresponding record of return or destruction (DEA Form 41).

(f) *Records for collectors.* Each person registered or authorized to collect controlled substances from ultimate users shall maintain the following records:

(1) Mail-Back Packages:

(i) For unused packages that the collector makes available to ultimate users and other authorized non-registrants at the collector's registered address: the date made available, the number of packages, and the unique identification number of each package;

(ii) For unused packages provided to a third party to make available to ultimate users and other authorized non-registrants: the name of the third party and physical address of the location receiving the unused packages, date sent, and the number of unused packages sent with the corresponding unique identification numbers;

(iii) For sealed mail-back packages received by the collector: date of receipt and the unique identification number on the individual package; and

(iv) For sealed mail-back packages destroyed on-site by the collector: number of sealed mail-back packages destroyed, the date and method of destruction, the unique identification number of each mail-back package destroyed, and the names and signatures of the two employees of the registrant who witnessed the destruction.

(2) Collection receptacle inner liners:

(i) Date each unused inner liner acquired, unique identification number and size (e.g., 5-gallon, 10-gallon, etc.) of each unused inner liner acquired;

(ii) Date each inner liner is installed, the address of the location where each inner liner is

installed, the unique identification number and size (e.g., 5-gallon, 10-gallon, etc.) of each installed inner liner, the registration number of the collector, and the names and signatures of the two employees that witnessed each installation;

(iii) Date each inner liner is removed and sealed, the address of the location from which each inner liner is removed, the unique identification number and size (e.g., 5-gallon, 10-gallon, etc.) of each inner liner removed, the registration number of the collector, and the names and signatures of the two employees that witnessed each removal;

(iv) Date each sealed inner liner is transferred to storage, the unique identification number and size (e.g., 5-gallon, 10-gallon, etc.) of each sealed inner liner stored, and the names and signatures of the two employees that transferred each sealed inner liner to storage;

(v) Date each sealed inner liner is transferred for destruction, the address and registration number of the reverse distributor or distributor to whom each sealed inner liner was transferred, the unique identification number and the size (e.g., 5-gallon, 10-gallon, etc.) of each sealed inner liner transferred, and the names and signatures of the two employees that transferred each sealed inner liner to the reverse distributor or distributor; and

(vi) For sealed inner liners destroyed on-site by the collector: the same information required of reverse distributors in paragraph (e)(4)(ii) of this section.

21. In § 1304.25, revise the section heading and paragraphs (a)(9) and (b)(9) to read as follows:

§ 1304.25 Records for treatment programs that compound narcotics for treatment programs and other locations.

* * * * *

(a) * * *

(9) The quantity disposed of by destruction, including the reason, date, and manner of

destruction.

(b) * * *

(9) The number of units of finished forms and/or commercial containers destroyed in any manner by the registrant, including the reason, date, and manner of destruction.

22. Amend § 1304.33 by revising the section heading and paragraph (f) and adding paragraph (g) to read as follows:

§ 1304.33 Reports to Automation of Reports and Consolidated Orders System (ARCOS).

* * * * *

(f) *Exceptions.* (1) A registered institutional practitioner that repackages or relabels exclusively for distribution or that distributes exclusively to (for dispensing by) agents, employees, or affiliated institutional practitioners of the registrant may be exempted from filing reports under this section by applying to the ARCOS Unit of the Administration.

(2) Registrants that acquire recalled controlled substances from ultimate users pursuant to § 1317.85 of this chapter may report as a single transaction all recalled controlled substances of the same name and finished form (e.g., all 10-milligram tablets or all 5-milligram concentration per fluid ounce or milliliter) received from ultimate users for the purpose of reporting acquisition transactions.

(g) *Exemptions.* (1) Collectors that acquire controlled substances from ultimate users are exempt from the ARCOS reporting requirements only with respect to controlled substances collected through mail-back programs and collection receptacles for the purpose of disposal.

(2) Reverse distributors and distributors that acquire controlled substances pursuant to § 1317.55(a) or (b) of this chapter are exempt from the ARCOS reporting requirements in this section with regard to any controlled substances acquired pursuant to § 1317.55(a) or (b) of this

chapter.

* * * * *

PART 1305—ORDERS FOR SCHEDULE I AND II CONTROLLED SUBSTANCES

23. The authority citation for part 1305 continues to read as follows:

Authority: 21 U.S.C. 821, 828, 871(b), unless otherwise noted.

24. In § 1305.03, add paragraphs (e), (f), and (g) to read as follows:

§ 1305.03 Distributions requiring a Form 222 or a digitally signed electronic order.

* * * * *

(e) Deliveries to an authorized DEA registrant by an ultimate user, a long-term care facility on behalf of an ultimate user who resides or has resided at that facility, or a person authorized to dispose of the ultimate user decedent's property.

(f) Distributions to reverse distributors and distributors by collectors and law enforcement pursuant to § 1317.55 of this chapter.

(g) Deliveries of controlled substances from ultimate users for the purpose of recalls pursuant to § 1317.85 of this chapter.

PART 1307—MISCELLANEOUS

25. The authority citation for part 1307 continues to read as follows:

Authority: 21 U.S.C. 821, 822(d), 871(b), unless otherwise noted.

26. In § 1307.11, revise section heading and remove and reserve paragraph (a)(2).

The revision reads as follows:

§ 1307.11 Distribution by dispenser to another practitioner.

* * * * *

§ 1307.12 [Removed]

27. Remove § 1307.12.

28. Revise § 1307.13 to read as follows:

§ 1307.13 Incidental manufacture of controlled substances.

Any registered manufacturer who, incidentally but necessarily, manufactures a controlled substance as a result of the manufacture of a controlled substance or basic class of controlled substance for which he is registered and has been issued an individual manufacturing quota pursuant to part 1303 of this chapter (if such substance or class is listed in Schedule I or II) shall be exempt from the requirement of registration pursuant to part 1301 of this chapter and, if such incidentally manufactured substance is listed in Schedule I or II, shall be exempt from the requirement of an individual manufacturing quota pursuant to part 1303 of this chapter, if such substances are disposed of in accordance with part 1317 of this chapter.

§ 1307.21 [Removed]

29. Remove § 1307.21.

30. In § 1307.22, revise the section heading and the first sentence to read as follows:

§ 1307.22 Delivery of surrendered and forfeited controlled substances.

Any controlled substance surrendered by delivery to the Administration under part 1317 of this chapter or forfeited pursuant to section 511 of the Act (21 U.S.C. 881) may be delivered to any department, bureau, or other agency of the United States or of any State upon proper application addressed to the Office of Diversion Control, Drug Enforcement Administration.

* * *

31. Add part 1317 to read as follows:

PART 1317—DISPOSAL

Sec.

1317.01 Scope.

SUBPART A—DISPOSAL OF CONTROLLED SUBSTANCES BY REGISTRANTS

1317.05 Registrant disposal.
1317.10 Registrant return or recall.
1317.15 Reverse distributor registration requirements and authorized activities.

SUBPART B—DISPOSAL OF CONTROLLED SUBSTANCES COLLECTED FROM ULTIMATE USERS AND OTHER NON-REGISTRANTS

1317.30 Authorization to collect from non-registrants.
1317.35 Collection by law enforcement.
1317.40 Registrants authorized to collect and authorized collection activities.
1317.55 Reverse distributor and distributor acquisition of controlled substances from collectors or law enforcement.
1317.60 Inner liner requirements.
1317.65 Take-back events.
1317.70 Mail-back programs.
1317.75 Collection receptacles.
1317.80 Collection receptacles at long-term care facilities.
1317.85 Ultimate user delivery for the purpose of recall or investigational use of drugs.

SUBPART C—DESTRUCTION OF CONTROLLED SUBSTANCES

1317.90 Methods of destruction.
1317.95 Destruction procedures.

Authority: 21 U.S.C. 821, 822, 823, 827, 828, 871(b), and 958.

§ 1317.01 Scope.

This part sets forth the rules for the delivery, collection, and destruction of damaged, expired, returned, recalled, unused, or otherwise unwanted controlled substances that are lawfully possessed by registrants (subpart A) and non-registrants (subpart B). The purpose of such rules is to provide prompt, safe, and effective disposal methods while providing effective controls against the diversion of controlled substances.

SUBPART A—DISPOSAL OF CONTROLLED SUBSTANCES BY REGISTRANTS

§ 1317.05 Registrant disposal.

(a) *Practitioner inventory.* Any registered practitioner in lawful possession of a controlled substance in its inventory that desires to dispose of that substance shall do so in one of the following ways:

(1) Promptly destroy that controlled substance in accordance with subpart C of this part using an on-site method of destruction;

(2) Promptly deliver that controlled substance to a reverse distributor's registered location by common or contract carrier pick-up or by reverse distributor pick-up at the registrant's registered location;

(3) For the purpose of return or recall, promptly deliver that controlled substance by common or contract carrier pick-up or pick-up by other registrants at the registrant's registered location to: the registered person from whom it was obtained, the registered manufacturer of the substance, or another registrant authorized by the manufacturer to accept returns or recalls on the manufacturer's behalf; or

(4) Request assistance from the Special Agent in Charge of the Administration in the area in which the practitioner is located.

(i) The request shall be made by submitting one copy of the DEA Form 41 to the Special Agent in Charge in the practitioner's area. The DEA Form 41 shall list the controlled substance or substances which the registrant desires to dispose.

(ii) The Special Agent in Charge shall instruct the registrant to dispose of the controlled substance in one of the following manners:

(A) By transfer to a registrant authorized to transport or destroy the substance;

(B) By delivery to an agent of the Administration or to the nearest office of the Administration; or

(C) By destruction in the presence of an agent of the Administration or other authorized person.

(5) In the event that a practitioner is required regularly to dispose of controlled substances, the Special Agent in Charge may authorize the practitioner to dispose of such substances, in accordance with subparagraph (a)(4) of this section, without prior application in each instance, on the condition that the practitioner keep records of such disposals and file periodic reports with the Special Agent in Charge summarizing the disposals. The Special Agent in Charge may place such conditions as he/she deems proper on practitioner procedures regarding the disposal of controlled substances.

(b) *Non-practitioner inventory.* Any registrant that is a non-practitioner in lawful possession of a controlled substance in its inventory that desires to dispose of that substance shall do so in one of the following ways:

(1) Promptly destroy that controlled substance in accordance with subpart C of this part using an on-site method of destruction;

(2) Promptly deliver that controlled substance to a reverse distributor's registered location by common or contract carrier or by reverse distributor pick-up at the registrant's registered location;

(3) For the purpose of return or recall, promptly deliver that controlled substance by common or contract carrier or pick-up at the registrant's registered location to: the registered person from whom it was obtained, the registered manufacturer of the substance, or another

registrant authorized by the manufacturer to accept returns or recalls on the manufacturer's behalf; or

(4) Promptly transport that controlled substance by its own means to the registered location of a reverse distributor, the location of destruction, or the registered location of any person authorized to receive that controlled substance for the purpose of return or recall as described in paragraph (b)(3) of this section.

(i) If a non-practitioner transports controlled substances by its own means to an unregistered location for destruction, the non-practitioner shall do so in accordance with the procedures set forth at § 1317.95(c).

(ii) If a non-practitioner transports controlled substances by its own means to a registered location for any authorized purpose, transportation shall be directly to the authorized registered location and two employees of the transporting non-practitioner shall accompany the controlled substances to the registered destination location. Directly transported means the substances shall be constantly moving towards their final location and unnecessary or unrelated stops and stops of an extended duration shall not occur.

(c) *Collected controlled substances.* Any collector in lawful possession of a controlled substance acquired by collection from an ultimate user or other authorized non-registrant person shall dispose of that substance in the following ways:

(1) *Mail-back program*. Upon receipt of a sealed mail-back package, the collector shall promptly:

(i) Destroy the package in accordance with subpart C of this part using an on-site method of destruction; or

(ii) Securely store the package and its contents at the collector's registered location in a manner consistent with § 1301.75(c) of this chapter (for practitioners), or in a manner consistent with the security requirements for Schedule II controlled substances (for non-practitioners) until prompt on-site destruction can occur.

(2) *Collection receptacles*. Upon removal from the permanent outer container, the collector shall seal it and promptly:

(i) Destroy the sealed inner liner and its contents;

(ii) Securely store the sealed inner liner and its contents at the collector's registered location in a manner consistent with § 1301.75(c) of this chapter (for practitioners), or in a manner consistent with § 1301.72(a) of this chapter (for non-practitioners) until prompt destruction can occur; or

(iii) Securely store the sealed inner liner and its contents at a long-term care facility in accordance with § 1317.80(d).

(iv) *Practitioner methods of destruction*. Collectors that are practitioners (i.e., retail pharmacies and hospitals/clinics) shall dispose of sealed inner liners and their contents by utilizing any method in paragraph (a)(1), (a)(2), or (a)(4) of this section, or by delivering sealed inner liners and their contents to a distributor's registered location by common or contract carrier pick-up or by distributor pick-up at the collector's authorized collection location.

(v) *Non-practitioner methods of destruction*. Collectors that are non-practitioners (i.e., manufacturers, distributors, narcotic treatment programs, and reverse distributors) shall dispose of sealed inner liners and their contents by utilizing any method in paragraph (b)(1), (b)(2), or (b)(4) of this section, or by delivering sealed inner liners and their contents to a distributor's registered location by common or contract carrier or by distributor pick-up at the collector's

authorized collection location for destruction. Freight forwarding facilities may not be utilized to transfer sealed inner liners and their contents.

§ 1317.10 Registrant return or recall.

(a) Each registrant shall maintain a record of each return or recall transaction in accordance with the information required of manufacturers in § 1304.22(a)(2)(iv) of this chapter.

(b) Each registrant that delivers a controlled substance in Schedule I or II for the purpose of return or recall shall use an order form in the manner described in part 1305 of this chapter.

(c) Deliveries for the purpose of return or recall may be made through a freight forwarding facility operated by the person to whom the controlled substance is being returned provided that advance notice of the return is provided and delivery is directly to an agent or employee of the person to whom the controlled substance is being returned.

§ 1317.15 Reverse distributor registration requirements and authorized activities.

(a) Any person that reverse distributes a controlled substance shall be registered with the Administration as a reverse distributor, unless exempted by law or otherwise authorized pursuant to this chapter.

(b) A reverse distributor shall acquire controlled substances from a registrant pursuant to §§ 1317.05 and 1317.55(a) and (c) in the following manner:

(1) Pick-up controlled substances from a registrant at the registrant's registered location or authorized collection site; or

(2) Receive controlled substances delivered by common or contract carrier or delivered directly by a non-practitioner registrant.

(i) Delivery to the reverse distributor by an authorized registrant directly or by common or contract carrier may only be made to the reverse distributor at the reverse distributor's

registered location. Once en route, such deliveries may not be re-routed to any other location or person, regardless of registration status.

(ii) All controlled substance deliveries to a reverse distributor shall be personally received by an employee of the reverse distributor at the registered location.

(c) Upon acquisition of a controlled substance by delivery or pick-up, a reverse distributor shall:

(1) Immediately store the controlled substance, in accordance with the security controls in parts 1301 and 1317 of this chapter, at the reverse distributor's registered location or immediately transfer the controlled substance to the reverse distributor's registered location for secure storage, in accordance with the security controls in parts 1301 and 1317 of this chapter, until timely destruction or prompt return of the controlled substance to the registered manufacturer or other registrant authorized by the manufacturer to accept returns or recalls on the manufacturer's behalf;

(2) Promptly deliver the controlled substance to the manufacturer or another registrant authorized by the manufacturer to accept returns or recalls on the manufacturer's behalf; or

(3) Timely destroy the controlled substance in a manner authorized in subpart C of this part.

(d) A reverse distributor shall destroy or cause the destruction of any controlled substance received for the purpose of destruction no later than 30 calendar days after receipt.

SUBPART B—DISPOSAL OF CONTROLLED SUBSTANCES COLLECTED FROM ULTIMATE USERS AND OTHER NON-REGISTRANTS

§ 1317.30 Authorization to collect from non-registrants.

(a) The following persons are authorized to collect controlled substances from ultimate

users and other non-registrants for destruction in compliance with this chapter:

(1) Any registrant authorized by the Administration to be a collector pursuant to § 1317.40; and

(2) Federal, State, tribal, or local law enforcement when in the course of official duties and pursuant to § 1317.35.

(b) The following non-registrant persons in lawful possession of a controlled substance in Schedules II, III, IV, or V may transfer that substance to the authorized persons listed in paragraph (a) of this section, and in a manner authorized by this part, for the purpose of disposal:

(1) An ultimate user in lawful possession of a controlled substance;

(2) Any person lawfully entitled to dispose of a decedent's property if that decedent was an ultimate user who died while in lawful possession of a controlled substance; and

(3) A long-term care facility on behalf of an ultimate user who resides or resided at such long-term care facility and is/was in lawful possession of a controlled substance, in accordance with § 1317.80 only.

§ 1317.35 Collection by law enforcement.

(a) Federal, State, tribal, or local law enforcement may collect controlled substances from ultimate users and persons lawfully entitled to dispose of an ultimate user decedent's property using the following collection methods:

(1) Take-back events in accordance with § 1317.65;

(2) Mail-back programs in accordance with § 1317.70; or

(3) Collection receptacles located inside law enforcement's physical address.

(b) Law enforcement that conducts a take-back event or a mail-back program or maintains a collection receptacle should maintain any records of removal, storage, or destruction

of the controlled substances collected in a manner that is consistent with that agency's recordkeeping requirements for illicit controlled substances evidence.

(c) Any controlled substances collected by law enforcement through a take-back event, mail-back program, or collection receptacle should be stored in a manner that prevents the diversion of controlled substances and is consistent with that agency's standard procedures for storing illicit controlled substances.

(d) Any controlled substances collected by law enforcement through a take-back event, mail-back program, or collection receptacle should be transferred to a destruction location in a manner that prevents the diversion of controlled substances and is consistent with that agency's standard procedures for transferring illicit controlled substances.

(e) Law enforcement that transfers controlled substances collected from ultimate users pursuant to this part to a reverse distributor for destruction should maintain a record that contains the following information: if a sealed inner liner as described in § 1317.60 is used, the unique identification number of the sealed inner liner transferred, and the size of the sealed inner liner transferred (e.g., 5-gallon, 10-gallon, etc.); if a mail-back package as described in § 1317.70 is used, the unique identification number of each package; the date of the transfer; and the name, address, and registration number of the reverse distributor to whom the controlled substances were transferred.

§ 1317.40 Registrants authorized to collect and authorized collection activities.

(a) Manufacturers, distributors, reverse distributors, narcotic treatment programs, hospitals/clinics with an on-site pharmacy, and retail pharmacies that desire to be collectors shall modify their registration to obtain authorization to be a collector in accordance with § 1301.51 of this chapter. Authorization to be a collector is subject to renewal. If a registrant that is

authorized to collect ceases activities as a collector, such registrant shall notify the Administration in accordance with § 1301.52(f) of this chapter.

(b) Collection by registrants shall occur only at the following locations:

(1) Those registered locations of manufacturers, distributors, reverse distributors, narcotic treatment programs, hospitals/clinics with an on-site pharmacy, and retail pharmacies that are authorized for collection; and

(2) Long-term care facilities at which registered hospitals/clinics or retail pharmacies are authorized to maintain collection receptacles.

(c) Collectors may conduct the following activities:

(1) Receive and destroy mail-back packages pursuant to § 1317.70 at an authorized registered location that has an on-site method of destruction;

(2) Install, manage, and maintain collection receptacles located at their authorized collection location(s) pursuant to §§ 1317.75 and 1317.80; and

(3) Promptly dispose of sealed inner liners and their contents as provided for in § 1317.05(c)(2).

§ 1317.55 Reverse distributor and distributor acquisition of controlled substances from collectors or law enforcement.

(a) A reverse distributor is authorized to acquire controlled substances from law enforcement that collected the substances from ultimate users. A reverse distributor is authorized to acquire controlled substances collected through a collection receptacle in accordance with §§ 1317.75 and 1317.80.

(b) A distributor is authorized to acquire controlled substances collected through a collection receptacle in accordance with §§ 1317.75 and 1317.80.

(c) A reverse distributor or a distributor that acquires controlled substances in accordance with paragraph (a) or (b) of this section shall:

(1) Acquire the controlled substances in the manner authorized for reverse distributors in § 1317.15(b)(1) and (2);

(2) Dispose of the controlled substances in the manner authorized for reverse distributors § 1317.15(c) and (d); and

(3) Securely store the controlled substances in a manner consistent with the security requirements for Schedule II controlled substances until timely destruction can occur.

§ 1317.60 Inner liner requirements.

(a) An inner liner shall meet the following requirements:

(1) The inner liner shall be waterproof, tamper-evident, and tear-resistant;

(2) The inner liner shall be removable and sealable immediately upon removal without emptying or touching the contents;

(3) The contents of the inner liner shall not be viewable from the outside when sealed;

(4) The size of the inner liner shall be clearly marked on the outside of the liner (e.g., 5-gallon, 10-gallon, etc.); and

(5) The inner liner shall bear a permanent, unique identification number that enables the inner liner to be tracked.

(b) Access to the inner liner shall be restricted to employees of the collector.

(c) The inner liner shall be sealed by two employees immediately upon removal from the permanent outer container and the sealed inner liner shall not be opened, x-rayed, analyzed, or otherwise penetrated.

§ 1317.65 Take-back events.

(a) Federal, State, tribal, or local law enforcement may conduct a take-back event and collect controlled substances from ultimate users and persons lawfully entitled to dispose of an ultimate user decedent's property in accordance with this section. Any person may partner with law enforcement to hold a collection take-back event in accordance with this section.

(b) Law enforcement shall appoint a law enforcement officer employed by the agency to oversee the collection. Law enforcement officers employed and authorized by the law enforcement agency or law enforcement component of a Federal agency conducting a take-back event shall maintain control and custody of the collected substances from the time the substances are collected from the ultimate user or person authorized to dispose of the ultimate user decedent's property until secure transfer, storage, or destruction of the controlled substances has occurred.

(c) Each take-back event should have at least one receptacle for the collection of controlled substances. The collection receptacle should be a securely locked, substantially constructed container with an outer container and a removable inner liner as specified in § 1317.60 of this chapter. The outer container should include a small opening that allows contents to be added to the inner liner, but that does not allow removal of the inner liner's contents.

(d) Only those controlled substances listed in Schedule II, III, IV, or V that are lawfully possessed by an ultimate user or person entitled to dispose of an ultimate user decedent's property may be collected. Controlled and non-controlled substances may be collected together and be comingled, although comingling is not required.

(e) Only ultimate users and persons entitled to dispose of an ultimate user decedent's property in lawful possession of a controlled substance in Schedule II, III, IV, or V may transfer

such substances to law enforcement during the take-back event. No other person may handle the controlled substances at any time.

§ 1317.70 Mail-back programs.

(a) A mail-back program may be conducted by Federal, State, tribal, or local law enforcement or any collector. A collector conducting a mail-back program shall have and utilize at their registered location a method of destruction consistent with § 1317.90 of this chapter.

(b) Only those controlled substances listed in Schedule II, III, IV, or V that are lawfully possessed by an ultimate user or person lawfully entitled to dispose of an ultimate user decedent's property may be collected. Controlled and non-controlled substances may be collected together and be comingled, although comingling is not required.

(c) Collectors or law enforcement that conduct a mail-back program shall make packages available (for sale or for free) as specified in this paragraph to ultimate users and persons lawfully entitled to dispose of an ultimate user decedent's property, for the collection of controlled substances by common or contract carrier. Any person may partner with a collector or law enforcement to make such packages available in accordance with this section. The packages made available shall meet the following specifications:

(1) The package shall be nondescript and shall not include any markings or other information that might indicate that the package contains controlled substances;

(2) The package shall be water- and spill-proof; tamper-evident; tear-resistant; and sealable;

(3) The package shall be preaddressed with and delivered to the collector's registered address or the participating law enforcement's physical address;

(4) The cost of shipping the package shall be postage paid;

(5) The package shall have a unique identification number that enables the package to be tracked; and

(6) The package shall include instructions for the user that indicate the process for mailing back the package, the substances that can be sent, notice that packages may only be mailed from within the customs territory of the United States (the 50 States, the District of Columbia, and Puerto Rico), and notice that only packages provided by the collector will be accepted for destruction.

(d) Ultimate users and persons lawfully entitled to dispose of an ultimate user decedent's property shall not be required to provide any personally identifiable information when mailing back controlled substances to a collector. The collector or law enforcement may implement a system that allows ultimate users or persons lawfully entitled to dispose of an ultimate user decedent's property to notify the collector or law enforcement that they are sending one of the designated packages by giving the unique identification number on the package.

(e) A collector that conducts a mail-back program pursuant to paragraph (a) shall:

(1) Accept only those controlled substances contained within packages that the collector made available for the collection of controlled substances by mail and packages that are lawfully forwarded to the collector pursuant to paragraph (e)(3) of this section.

(2) Within three business days of receipt, notify the Field Division Office of the Administration in their area of the receipt of a package that likely contains controlled substances that the collector did not make available or did not agree to receive pursuant to subparagraph (e)(3) of this section.

(3) When discontinuing activities as a collector or ceasing an authorized mail-back program:

(i) Make a reasonable effort to notify the public prior to discontinuing such activities or ceasing the authorized mail-back program; and

(ii) Obtain the written agreement of another collector that has and utilizes at its registered location a method of destruction consistent with § 1317.90 of this chapter to receive all remaining mail-back packages that were disseminated but not returned and arrange for the forwarding of only such packages to that location.

(f) Only law enforcement officers employed by the law enforcement agency or law enforcement component of a Federal agency and employees of the collector shall handle packages received through an authorized mail-back program. Upon receipt of a mail-back package by a collector conducting a mail-back program, the package shall not be opened, x-rayed, analyzed, or otherwise penetrated.

§ 1317.75 Collection receptacles.

(a) Collectors or Federal, State, tribal, or local law enforcement may manage and maintain collection receptacles for disposal.

(b) Only those controlled substances listed in Schedule II, III, IV, or V that are lawfully possessed by an ultimate user or other authorized non-registrant person may be collected. Controlled and non-controlled substances may be collected together and be comingled, although comingling is not required.

(c) Collectors shall only allow ultimate users and other authorized non-registrant persons in lawful possession of a controlled substance in Schedule II, III, IV, or V to deposit such substances in a collection receptacle at a registered location. Collectors shall not permit an ultimate user to transfer such substance to any person for any reason. Once a substance has been deposited into a collection receptacle, the substance shall not be counted, sorted, inventoried, or

otherwise individually handled.

(d) Collection receptacles shall be securely placed and maintained:

(1) Inside a collector's registered location, inside law enforcement's physical location, or at an authorized long-term care facility;

(2) At a registered location, be located in the immediate proximity of a designated area where controlled substances are stored and at which an employee is present (e.g., can be seen from the pharmacy counter). Except as follows:

(i) At a hospital/clinic: a collection receptacle shall be located in an area regularly monitored by employees, and shall not be located in the proximity of any area where emergency or urgent care is provided;

(ii) At a narcotic treatment program: a collection receptacle shall be located in a room: that does not contain any other controlled substances and is securely locked with controlled access;

(iii) At a long-term care facility: a collection receptacle shall be located in a secured area regularly monitored by long-term care facility employees.

(e) A controlled substance collection receptacle shall meet the following design specifications:

(1) Be securely fastened to a permanent structure so that it cannot be removed;

(2) Be a securely locked, substantially constructed container with a permanent outer container and a removable inner liner as specified in § 1317.60 of this chapter;

(3) The outer container shall include a small opening that allows contents to be added to the inner liner, but does not allow removal of the inner liner's contents;

(4) The outer container shall prominently display a sign indicating that only Schedule II–

V controlled and non-controlled substances, if a collector chooses to comingle substances, are acceptable substances (Schedule I controlled substances, controlled substances that are not lawfully possessed by the ultimate user, and other illicit or dangerous substances are not permitted); and

(f) Except at a narcotic treatment program, the small opening in the outer container of the collection receptacle shall be locked or made otherwise inaccessible to the public when an employee is not present (e.g., when the pharmacy is closed), or when the collection receptacle is not being regularly monitored by long-term care facility employees.

(g) The installation and removal of the inner liner of the collection receptacle shall be performed by or under the supervision of at least two employees of the authorized collector.

§ 1317.80 Collection receptacles at long-term care facilities.

(a) A long-term care facility may dispose of controlled substances in Schedules II, III, IV, and V on behalf of an ultimate user who resides, or has resided, at such long-term care facility by transferring those controlled substances into an authorized collection receptacle located at that long-term care facility. When disposing of such controlled substances by transferring those substances into a collection receptacle, such disposal shall occur immediately, but no longer than three business days after the discontinuation of use by the ultimate user. Discontinuation of use includes a permanent discontinuation of use as directed by the prescriber, as a result of the resident's transfer from the long-term care facility, or as a result of death.

(b) Only authorized retail pharmacies and hospitals/clinics with an on-site pharmacy may install, manage, and maintain collection receptacles at long-term care facilities and remove, seal, transfer, and store, or supervise the removal, sealing, transfer, and storage of sealed inner liners at long-term care facilities. Collectors authorized to install, manage, and maintain collection

receptacles at long-term care facilities shall comply with all requirements of this chapter, including §§ 1317.60, 1317.75, and 1317.80.

(c) The installation, removal, transfer, and storage of inner liners shall be performed either: by or under the supervision of one employee of the authorized collector and one supervisor-level employee of the long-term care facility (e.g., a charge nurse or supervisor) designated by the authorized collector; or, by or under the supervision of two employees of the authorized collector.

(d) Upon removal, sealed inner liners may only be stored at the long-term care facility for up to three business days in a securely locked, substantially constructed cabinet or a securely locked room with controlled access until transfer in accordance with § 1317.05(c)(2)(iv).

(e) Neither a hospital/clinic with an on-site pharmacy nor a retail pharmacy shall operate a collection receptacle at a long-term care facility until its registration has been modified in accordance with § 1301.51 of this chapter.

§ 1317.85 Ultimate user delivery for the purpose of recall or investigational use of drugs.

(a) In the event of a product recall, an ultimate user in lawful possession of a controlled substance listed in Schedule II, III, IV, or V may deliver the recalled substance to the manufacturer of the substance or another registrant authorized by the manufacturer to accept recalled controlled substances on the manufacturer's behalf.

(b) An ultimate user who is participating in an investigational use of drugs pursuant to 21 U.S.C. 355(i) and 360b(j) and wishes to deliver any unused controlled substances received as part of that research to the registered dispenser from which the ultimate user obtained those substances may do so in accordance with regulations promulgated by the Secretary of Health and Human Services pursuant to 21 U.S.C. 355(i) and 360b(j).

SUBPART C—DESTRUCTION OF CONTROLLED SUBSTANCES

§ 1317.90 Methods of destruction.

(a) All controlled substances to be destroyed by a registrant, or caused to be destroyed by a registrant pursuant to § 1317.95(c), shall be destroyed in compliance with applicable Federal, State, tribal, and local laws and regulations and shall be rendered non-retrievable.

(b) Where multiple controlled substances are comingled, the method of destruction shall be sufficient to render all such controlled substances non-retrievable. When the actual substances collected for destruction are unknown but may reasonably include controlled substances, the method of destruction shall be sufficient to render non-retrievable any controlled substance likely to be present.

(c) The method of destruction shall be consistent with the purpose of rendering all controlled substances to a non-retrievable state in order to prevent diversion of any such substance to illicit purposes and to protect the public health and safety.

§ 1317.95 Destruction procedures.

The destruction of any controlled substance shall be in accordance with the following requirements:

(a) *Transfer to a person registered or authorized to accept controlled substances for the purpose of destruction.* If the controlled substances are transferred to a person registered or authorized to accept the controlled substances for the purpose of destruction, two employees of the transferring registrant shall load and unload or observe the loading and unloading of any controlled substances until transfer is complete.

(b) *Transport to a registered location.* If the controlled substances are transported by a registrant to a registered location for subsequent destruction, the following procedures shall be

followed:

(1) Transportation shall be directly to the registered location (the substances shall be constantly moving towards their final location and unnecessary or unrelated stops and stops of an extended duration shall not occur);

(2) Two employees of the transporting registrant shall accompany the controlled substances to the registered location;

(3) Two employees of the transporting registrant shall load and unload or observe the loading and unloading of the controlled substances until transfer is complete;

(c) *Transport to a non-registered location.* If the controlled substances are transported by a registrant to a destruction location that is not a registered location, the following procedures shall be followed:

(1) Transportation shall be directly to the destruction location (the substances shall be constantly moving towards their final destruction location and unnecessary or unrelated stops and stops of an extended duration shall not occur);

(2) Two employees of the transporting registrant shall accompany the controlled substances to the destruction location;

(3) Two employees of the transporting registrant shall load and unload or observe the loading and unloading of the controlled substances;

(4) Two employees of the transporting registrant shall handle or observe the handling of any controlled substance until the substance is rendered non-retrievable; and

(5) Two employees of the transporting registrant shall personally witness the destruction of the controlled substance until it is rendered non-retrievable.

(d) *On-site destruction.* If the controlled substances are destroyed at a registrant's

registered location utilizing an on-site method of destruction, the following procedures shall be followed:

(1) Two employees of the registrant shall handle or observe the handling of any controlled substance until the substance is rendered non-retrievable; and

(2) Two employees of the registrant shall personally witness the destruction of the controlled substance until it is rendered non-retrievable.

Dated: August 25, 2014

Michele M. Leonhart,
Administrator.

[FR Doc. 2014-20926 Filed 09/08/2014 at 8:45 am; Publication Date: 09/09/2014]

Attachment 5

California State Board of Pharmacy
1625 N. Market Blvd., Suite N219, Sacramento, CA 95834
Phone (916) 574-7900
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www.pharmacy.ca.gov

STATE BUSINESS, CONSUMER SERVICES, AND HOUSING AGENCY
DEPARTMENT OF CONSUMER AFFAIRS
EDMUND G. BROWN, JR., GOVERNOR

April 28, 2014

Drug Enforcement Administration
Attn: DEA Federal Register Representative/ODL
8701 Morrissette Drive
Springfield, VA 22152

RE: COMMENTS OF THE CALIFORNIA STATE BOARD OF PHARMACY
Docket No. DEA-389
Rescheduling of Hydrocodone Combination Products from Schedule III to Schedule II

To Whom It May Concern:

I write on behalf of the California State Board of Pharmacy (Board). We are pleased to have this opportunity to submit comments on Docket No. DEA-389, titled "Schedules of Controlled Substances: Rescheduling of Hydrocodone Combination Products From Schedule III to Schedule II." We will be brief. We strongly support and encourage this timely action, as we believe Schedule II is more appropriate for hydrocodone combination products (HCPs). As we will explain below, however, we do urge you to keep in mind, as you schedule the timing of this transition, the innumerable patients (and their practitioners) who rely on HCPs for legitimate treatment, and respectfully suggest that the Drug Enforcement Administration (DEA) provide sufficient notice and a period of transition to enable those patients and practitioners to adjust their prescribing regimens to the additional requirements that must now be met.

Our experience in California with HCPs illustrates the need for their rescheduling. Our state leads the nation in utilization of HCPs, with over 1.4 billion dosage units dispensed from April 2012 to April 2013.[1] And that figure obviously does not capture usage not pursuant to a prescription. We have seen firsthand the strong potential for abuse of these drugs, which have now significantly surpassed other opioid analgesics, including Schedule II drugs of abuse such as oxycodone and morphine, in their legitimate and illegitimate utilization in California. We are also experiencing consistent and increasing trends in diversion and self-use of these drugs.

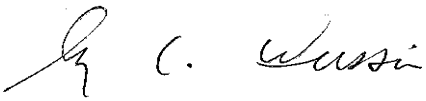
It seems obvious that HCPs belong in Schedule II. We support their rescheduling.

[1] Data from the Controlled Substance Utilization Review and Evaluation System (CURES), California's prescription drug monitoring program (PDMP) to which Schedule II-IV controlled substance prescriptions are reported.

Our only caution would be that you not make this decision suddenly and without some period of time for adjustment and transition. This may occur naturally as a consequence of the rulemaking process, but in the event the rulemaking proceeds relatively quickly, we would ask that you consider building in an adjustment period to allow those patients and practitioners (in long-term care settings, especially) making legitimate use of HCPs for pain management to make changes in their prescribing protocols that will be necessitated by this reclassification, and/or to consider a switch in their treatment plan to another medication or methodology of pain treatment.

Thank you for your attention to these matters, and for your willingness to hear our input. We look forward to continuing to work together to secure the nation's drug supply. Please feel free to contact the Board at any time if we can be of assistance. The best route for contact is via Executive Officer Virginia Herold, at (916) 574-7911, or Virginia.Herold@dca.ca.gov.

Sincerely,



STANLEY C. WEISSER, R.Ph.
President, California State Board of Pharmacy

Census Bureau for statistical purposes. In addition, EEI is used by federal government agencies, such as the Department of State, Immigration and Customs Enforcement, and Customs and Border Protection (CBP) for export control; by other federal government agencies such as the Bureau of Economic Analysis, Bureau of Labor Statistics, and Bureau of Transportation Statistics for statistical purposes; and by other federal agencies as authorized by the Secretary of Commerce or the Census Bureau Director consistent with the agencies' statutory or legal authorities as provided for in paragraph (e) of this section. Absent such authorization, information collected pursuant to this Part shall not be disclosed to anyone by any officer, employee, contractor, agent of the federal government or other parties with access to the EEI other than to the USPPI or the authorized agent of the USPPI. Such disclosure shall be limited to that information provided by each party pursuant to this Part.

(b) *Viewing and using EEI for official purposes.* (1) The EEI may be viewed and used by federal agencies authorized to use export data for official purposes as defined to include, but not limited to:

(i) Improving compliance with U.S. export laws and regulations;

(ii) Detecting and preventing violations of export, census, customs, homeland security, national resource and other laws, regulations and treaties;

(iii) Analysis to assess threats to U.S. and international security such as money laundering, and other potential violations of U.S. and foreign criminal laws;

(iv) Enforcement of U.S. export-related laws and regulations;

(v) Investigation and prosecution of possible violations of U.S. export-related laws and regulations;

(vi) Proof of export for enforcement of laws relating to exemption from or refund, drawback or other return of taxes, duties, fees or other charges;

(vii) Analyzing the impact of proposed and implemented trade agreeements and fulfilling U.S. obligations under such agreements; and

(viii) Preparation of statistics.

(2) The Census Bureau may provide the EEI to the USPPI or authorized agent, for compliance and audit purposes. Such disclosure shall be limited to that information provided to the AES by the USPPI or the authorized agent.

(c) *Supplying EEI for nonofficial purposes.* The official report of the EEI submitted to the U.S. government shall not be disclosed by the USPPI, the authorized agent, or representative of the USPPI for ''nonofficial purposes,'' either in whole or in part, or in any form including but not limited to electronic transmission, paper printout, or certified reproduction. ''Nonofficial purposes'' are defined to include but not limited to providing the official EEI:

(1) In support of claims for exemption from Federal or state taxation, except as related to paragraph (b)(1)(vi) of this section;

(2) To the U.S. Internal Revenue Service for purposes not related to export control or compliance;

(3) To state and local government agencies, and nongovernmental entities or individuals for any purpose; and

(4) To foreign entities or foreign governments for any purpose.

(d) Ocean manifest data can be made public under provision of CBP regulations. For information appearing on the outward manifest, 19 CFR 103.31 allows a shipper (or their authorized employee or official) to submit a certification for confidential treatment of the shipper's name and address.

(e) *Determination by the Secretary of Commerce.* Under 13 U.S.C. 301(g), the EEI collected and accessed by the Census Bureau is exempt from public disclosure unless the Secretary or delegate determines that such exemption would be contrary to the national interest. The Secretary or delegate may make such information available, if he or she determines it is in the national interest, taking such safeguards and precautions to limit dissemination as deemed appropriate under the circumstances. In determining whether it is contrary to the national interest to apply the exemption, the maintenance of confidentiality and national security shall be considered as important elements of national interest. The unauthorized disclosure of confidential EEI granted under a National Interest Determination renders such persons subject to the civil penalties provided for in Subpart H of this part.

(f) *Penalties.* Disclosure of confidential EEI by any officer, employee, contractor, or agent of the federal government, except as provided for in paragraphs (b) and (e) of this section renders such persons subject to the civil penalties.

Dated: August 15, 2014.

John H. Thompson,

Director, Bureau of the Census.

[FR Doc. 2014–19972 Filed 8–21–14; 8:45 am]

BILLING CODE 3510–07–P

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA–389]

Schedules of Controlled Substances: Rescheduling of Hydrocodone Combination Products From Schedule III to Schedule II

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Final rule.

SUMMARY: With the issuance of this final rule, the Administrator of the Drug Enforcement Administration reschedules hydrocodone combination products from schedule III to schedule II of the Controlled Substances Act. This scheduling action is pursuant to the Controlled Substances Act which requires that such actions be made on the record after opportunity for a hearing through formal rulemaking. This action imposes the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule II controlled substances on persons who handle (manufacture, distribute, dispense, import, export, engage in research, conduct instructional activities with, conduct chemical analysis with, or possess) or propose to handle hydrocodone combination products.

DATES: This rule is effective October 6, 2014.

FOR FURTHER INFORMATION CONTACT: Imelda L. Paredes, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152, Telephone: (202) 598–6812.

SUPPLEMENTARY INFORMATION:

Outline

I. Legal Authority
II. Background
III. Determination To Transfer Hydrocodone Combination Products (HCPs) to Schedule II
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2. Requirements Applicable to Prescriptions
3. Patient Access to Medicine
4. Impacts on Unique Populations
5. Impacts on Long-Term Care Facilities (LTCFs)
6. Abuse Prevention
7. Diversion Prevention

8. Responsibilities of Pharmacists
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I. Legal Authority

The DEA implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. Titles II and III are referred to as the ''Controlled Substances Act'' and the ''Controlled Substances Import and Export Act,'' respectively, and are collectively referred to as the ''Controlled Substances Act'' or the ''CSA'' for the purpose of this action. 21 U.S.C. 801–971. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), parts 1300 to 1321. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while providing for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, every controlled substance is classified into one of five schedules based upon its potential for abuse, currently accepted medical use in treatment in the United States, and the degree of dependence the drug or other substance may cause. 21 U.S.C. 812. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and the current list of all scheduled substances is published at 21 CFR part 1308. 21 U.S.C. 812(a).

Pursuant to 21 U.S.C. 811(a)(1), the Attorney General may, by rule, ''add to such a schedule or transfer between such schedules any drug or other substance if he (A) finds that such drug or other substance has a potential for abuse, and (B) makes with respect to such drug or other substance the findings prescribed by [21 U.S.C. 812(b)] for the schedule in which such drug is to be placed * * *.'' The Attorney General has delegated this scheduling authority to the Administrator of the DEA. 28 CFR 0.100(b).

The Administrator may initiate the scheduling of any drug or other substance (1) on her own motion; (2) at the request of the Secretary of the Department of Health and Human Services (HHS); or (3) on the petition of any interested party. 21 U.S.C. 811(a). This action was initiated by a petition to reschedule hydrocodone combination products (HCPs) [1] from schedule III to schedule II of the CSA, and is supported by, *inter alia,* a recommendation from the Assistant Secretary for Health of the HHS [2] and an evaluation of all relevant data by the DEA. This final action imposes the regulatory controls and administrative, civil, and criminal sanctions of schedule II controlled substances on any person who handles, or proposes to handle, HCPs.

II. Background

Hydrocodone was listed in schedule II of the CSA upon the enactment of the CSA in 1971. Public Law 91–513, 84 Stat. 1236, sec. 202(c), schedule II, paragraph (a), clause (1) (codified at 21 U.S.C. 812(c)); initially codified in DEA regulations at 21 CFR 308.12(b)(1)(x) (36 FR 7776, April 24, 1971) (currently codified at 21 CFR 1308.12(b)(1)(vi)). At that time, hydrocodone was listed in schedule III of the CSA when formulated with specified amounts of an isoquinoline alkaloid of opium or one or more therapeutically active nonnarcotic ingredients. Pub. L. 91–513, 84 Stat. 1236, sec. 202(c), schedule III, paragraph (d), clauses (3) and (4) (codified at 21 U.S.C. 812(c)); initially codified at 21 CFR 308.13(e) (3) and (4) (36 FR 7776, April 24, 1971) (currently codified at 21 CFR 1308.13(e)(1) (iii) and (iv)).[3] Any other hydrocodone single-entity products or combinations of hydrocodone with other substances outside the range of specified doses are listed in schedule II of the CSA.[4]

III. Determination To Transfer Hydrocodone Combination Products (HCPs) to Schedule II

Pursuant to 21 U.S.C. 811(a), proceedings to add a drug or substance to those controlled under the CSA, or to transfer a drug between schedules, may be initiated on the petition of any interested party. The DEA received a petition requesting that HCPs be controlled in schedule II of the CSA. In response, in 2004, the DEA submitted a request to the HHS to provide the DEA with a scientific and medical evaluation of available information and a scheduling recommendation for HCPs, pursuant to 21 U.S.C. 811 (b) and (c). In 2008, the HHS provided to the DEA its recommendation that HCPs remain controlled in schedule III of the CSA. In response, in 2009, the DEA requested that the HHS re-evaluate their data and provide another scientific and medical evaluation and scheduling recommendation based on additional data and analysis.

On July 9, 2012, President Obama signed the Food and Drug Administration Safety and Innovation Act (Pub. L. 112–144, 126 Stat. 993) (FDASIA). Section 1139 of the FDASIA directed the Food and Drug Administration (FDA) to hold a public meeting to ''solicit advice and recommendations'' pertaining to the scientific and medical evaluation in connection with its scheduling recommendation to the DEA regarding drug products containing hydrocodone, combined with other analgesics or as an antitussive. Additionally, the Secretary was required to solicit stakeholder input ''regarding the health benefits and risks, including the potential for abuse'' of HCPs ''and the impact of up-scheduling these products.'' Accordingly, on January 24 and 25, 2013, the FDA held a public Drug Safety and Risk Management Advisory Committee (DSaRM) meeting, at which the DEA made a presentation.[5] The DSaRM Committee included members with scientific and medical expertise in the subject of opioid abuse, and a patient representative. Members included

[1] Hydrocodone combination products (HCPs) are pharmaceuticals containing specified doses of hydrocodone in combination with other drugs in specified amounts. These products are approved for marketing for the treatment of pain and for cough suppression.

[2] As discussed in a memorandum of understanding entered into by the Food and Drug Administration (FDA), and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the HHS in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518, Mar. 8, 1985. The Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.

[3] Specifically: (iii) ''Not more than 300 milligrams of dihydrocodeinone (hydrocodone) per 100 milliliters or not more than 15 milligrams per dosage unit, with a fourfold or greater quantity of an isoquinoline alkaloid of opium;'' (iv) ''Not more than 300 milligrams of dihydrocodeinone (hydrocodone) per 100 milliliters or not more than 15 milligrams per dosage unit, with one or more active nonnarcotic ingredients in recognized therapeutic amounts''

[4] In the United States there are currently no approved, marketed, products containing hydrocodone in combination with other active ingredients that fall outside schedule III of the CSA. Further, until recently, there were no approved hydrocodone single-entity schedule II products. In October 2013 the FDA approved Zohydro™ ER, a single-entity, extended release schedule II product. Zohydro™ ER was launched on March 3, 2014. Accordingly, all of the historical data regarding hydrocodone from different national and regional databases that support this rule should refer to HCPs only, regardless of whether the database utilizes the term ''hydrocodone'' or ''hydrocodone combination products.''

[5] The DEA presentation is available at *http://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/drugs/drugsafetyandriskmanagmentadvisorycommittee/ucm346941.pdf.*

representatives from the National Institute on Drug Abuse (NIDA) and the Centers for Disease Control (CDC). There was also an opportunity for the public to provide comment. The DSaRM voted 19 to 10 in favor of recommending that HCPs be placed into schedule II. According to the FDA, 768 comments were submitted to the FDA by patients, patient groups, advocacy groups, and professional societies.

Upon evaluating the scientific and medical evidence, along with the above considerations mandated by the FDASIA, the HHS on December 16, 2013, submitted to the Administrator of the DEA its scientific and medical evaluation entitled, ''Basis for the Recommendation to Place Hydrocodone Combination Products in Schedule II of the Controlled Substances Act.'' Pursuant to 21 U.S.C. 811(b), this document contained an eight-factor analysis of the abuse potential of HCPs, along with the HHS's recommendation to control HCPs in schedule II of the CSA.

The HHS stated that the comments received during the open public hearing and submitted to the docket, and the discussion of the DSaRM members of the FDA DSaRM meeting provided support for its conclusion that: (1) Individuals are taking HCPs in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community; (2) there is significant diversion of HCPs; and (3) individuals are taking HCPs on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs. The HHS stated that it gave careful consideration to the fact that the members of the DSaRM voted 19 to 10 in favor of rescheduling HCPs from schedule III to schedule II under the CSA. The HHS considered the increasing trends, the public comments, the recommendation of the DSaRM, the health benefits and risks, and the information available about the impact of rescheduling, and concluded that HCPs have high potential for abuse.

After a review of the available data, including the scientific and medical evaluation and the scheduling recommendation from the HHS, the Administrator of the DEA published in the **Federal Register** a notice of proposed rulemaking (NPRM) entitled ''Schedules of Controlled Substances: Rescheduling of Hydrocodone Combination Products from Schedule III to Schedule II'' which proposed to reschedule HCPs from schedule III to schedule II of the CSA. 79 FR 11037, Feb. 27, 2014. Both the DEA and HHS eight-factor analyses, as well as the DEA's Economic Impact Analysis (EIA), were made available in their entirety in the public docket for this rule (Docket No. DEA–389) and are available at *http://www.regulations.gov/#!docketDetail;D=DEA-2014-0005* under ''Supporting and Related Material.'' The proposed rule provided an opportunity for interested persons to file a request for hearing in accordance with DEA regulations by March 31, 2014. No requests for such a hearing were received by the DEA. The NPRM also provided an opportunity for interested persons to submit written comments on the proposal on or before April 28, 2014. The DEA specifically solicited comments on the economic impacts of rescheduling with a request that commenters describe the specific nature of any impact on small entities and provide empirical data to illustrate the extent of such impact.

IV. Comments Received

The DEA received 573 comments on the proposed rule to reschedule HCPs. Fifty-two percent (52%) (298 comments) supported, or supported with qualification, controlling HCPs in schedule II of the CSA. Forty-one percent (41%) (235 comments) opposed rescheduling HCPs into schedule II. Seven percent (7%) (40 comments) did not take a definitive position regarding rescheduling of HCPs.

Comments were submitted by a variety of individuals, including among others: Federal and State Government officials, manufacturers, distributors, pharmacies, surgeons, emergency physicians, dentists, physician assistants, nurse practitioners, pharmacists and pharmacy students, ultimate users of HCPs, and members of the general public.[6] [7] The DEA also received comments from a number of national and regional trade associations with memberships comprised of manufacturers and distributors, pharmacists, pharmacies, physicians, pain specialists, doctors of optometry, physician assistants, nurse practitioners, and long term care facilities (LTCFs). In addition, the DEA received comments from patient advocacy groups. The 5 commenter categories with the most submissions were physicians (13%; 73 comments); mid-level practitioners [8] (5%; 31 comments); pharmacists and pharmacy students (21%; 122 comments); the general public (44%; 250 comments); and ultimate users (6%; 35 comments).

As discussed above, 52% of all commenters (298 of 573 comments) supported, or supported with qualification, controlling HCPs in schedule II of the CSA. The majority of those supporting the rule were members of the general public and physicians. Comments submitted by the general public comprised 62% of the total 298 comments that supported, or supported with qualification, the rescheduling. Seventy-four percent (74%) (184 of 250 comments) of all comments submitted by the general public were in support, or supported with qualification, the rescheduling. Comments by physicians comprised 14% of the total 298 comments that supported or supported with qualification rescheduling. Fifty-six percent (56%) (41 of 73 comments) of all comments submitted by physicians were in support, or supported with qualification, rescheduling.

Forty-one percent (41%) of commenters (235 of 573 comments) opposed the proposal to reschedule HCPs from schedule III to schedule II of the CSA. The majority of those opposed to rescheduling HCPs were pharmacists, pharmacy students, and ultimate users. Pharmacists and pharmacy students comprised 31% of the total 235 comments submitted in opposition to the rule. Sixty percent (60%) (122 comments) of all comments submitted by pharmacists and pharmacy students were in opposition to the rule. Comments from ultimate users comprised 14% of the total 235 comments in opposition to the rule. Ninety-one percent (91%) (32 of 35 comments) of all comments submitted by ultimate users were in opposition to rescheduling.

Further discussions of these comments are included below.

A. Support of the Proposed Rule

Two hundred ninety-eight commenters (52%) supported, or supported with qualification, controlling HCPs in schedule II of the CSA. Forty-one percent (41%) of commenters opposed controlling HCPs in schedule II, and 7% of commenters

[6] The term ''ultimate user'' means a person who has lawfully obtained, and who possesses, a controlled substance for his own use or for the use of a member of his household or for an animal owned by him or by a member of his household. 21 U.S.C. 802(27).

[7] Comments from the ''general public'' are distinguished from those submitted by ''ultimate users'' when the commenter did not specifically indicate in their comment that they personally use HCPs.

[8] The term ''mid-level practitioner'' means an individual practitioner, other than a physician, dentist, veterinarian, or podiatrist, who is licensed, registered, or otherwise permitted by the United States or the jurisdiction in which he/she practices, to dispense a controlled substance in the course of professional practice. 21 CFR 1300.01(b).

did not have a clearly defined position either in support or in opposition to the rescheduling. The majority of those supporting the rule were members of the general public (62%) and physicians (14%), with 74% of comments from the general public supporting, or supporting with qualification, and 56% of comments from physicians supporting, or supporting with qualification, making HCPs schedule II controlled substances. Manufacturers, pharmacists, mid-level practitioners, pharmacy students, and trade associations also expressed support for the rule. Of all comments submitted, in support and opposition, 40% of pharmacists, 9% of ultimate users, and 78% of the general public were in support.

The State Attorney General and a U.S. Senator from the State with last year's highest per capita rate of prescription drug overdose in the nation wrote in strong support of rescheduling HCPs. The State Attorney General wrote that, ''This reclassification is not only justified given the high abuse and addiction potential of hydrocodone prescription painkillers * * *, it is necessary to combat the drug abuse epidemic that is destroying so many [ ] communities. I urge you to proceed with your rulemaking without delay. The abuse of hydrocodone is an urgent problem that necessitates urgent action.'' The U.S. Senator wrote that, ''rescheduling hydrocodone combination drugs would be a tremendous step forward in the fight to curb the prescription drug abuse epidemic that has ravaged * * * our country. It will help prevent these highly addictive drugs from getting into the wrong hands and devastating families and communities * * *. I urge the DEA to move quickly in finalizing its regulations so that we are able to save hundreds of thousands of lives.''

Two U.S. Senators from two other States, wrote a joint comment in support of rescheduling, stating that: ''As members of the Judiciary Committee and senators from states hit particularly hard by the opioid epidemic, we are well aware of the alarming rates of diversion and prescription drug abuse,'' and ''we fully support DEA's efforts to combat this nationwide public health crisis.'' All three Senators expressed their desire that patients maintain access to legitimate care.

A major component of the rescheduling of HCPs was to evaluate their abuse potential as required under 21 U.S.C. 812(b)(2). Many commenters indicated support for controlling HCPs in schedule II based on the scientific evidence demonstrating the high abuse potential of HCPs, evidence that HCPs may lead to severe psychological or physical dependence, history and current pattern of abuse, significance of abuse, and risk to the public health and safety. Of the total 47 commenters who referenced the scientific, medical, and epidemiological data that was used to support the statutory requirement under 21 U.S.C. 812(b)(2) for control of HCPs in schedule II of the CSA, 29 agreed with the data used to support control of HCPs in schedule II. Nineteen commenters specifically discussed the eight-factor analysis that was conducted in support of rescheduling HCPs into schedule II. Ten of those 19 commenters were in agreement with the DEA's analysis. Nine of the commenters who cited the DEA's eight-factor analysis indicated that the presented evidence was congruent with the requirements for placing a drug or other substance into schedule II of the CSA. (One commenter, while in agreement with the conclusion of the eight-factor analysis, did not favor rescheduling HCPs.)

Commenters generally agreed that there is psychological and physical dependence associated with HCPs that support placement into schedule II. For example, one commenter stated that rescheduling HCPs from schedule III to schedule II ''would be in the best interest of the general public'' because he has personally witnessed the increase in abuse of prescription pain medication over the course of his 45-year career as a pharmacist. Additional supportive comments included that the mechanism of action of hydrocodone is identical to oxycodone and morphine, both in schedule II as combination and single-entity products. Some commenters indicated that lower doses of hydrocodone in HCPs do not lower abuse and therefore agreed with the transfer to schedule II. Other commenters mentioned that HCPs are metabolized to hydromorphone, a schedule II opioid, and also have similar mechanisms of action to other schedule II opioids including oxycodone, morphine, and fentanyl, suggesting that abuse potential would be comparable. Some of the commenters indicated that HCPs are more likely to be abused due to their greater availability.

Many of the commenters cited one of their primary reasons for supporting the rule was that it would lead to tighter regulation of HCP prescriptions. For example, one commenter stated: ''Hydrocodone combination products should not be available with multiple refills on a single prescription and need to be prescribed more cautiously.'' Similarly, another commenter stated: ''Rescheduling HPCs [*sic*] would directly address the problem of 'leftover' pills in parents [*sic*] medicine cabinets, and would keep kids safe. Furthermore, lowering the quantity a doctor can prescribe will decrease the number of drugs that are sold on the street, which will in turn decrease crime and decrease HCP abuse overtime [*sic*].''

Many of the commenters wrote of their personal experiences with loved ones who suffer or had suffered with abuse and addiction, including many youths and young adults who have tragically died as a result of HCPs or other prescription opioids. The commenters wrote that the path to abuse and addiction was varied—sometimes beginning with a practitioner prescribing HCPs, and other times by recreational use of pills that were available for them to access as a result of practitioner overprescribing. Many of these commenters believe that controlling HCPs as a schedule II controlled substance will impose controls necessary to prevent the abuse and diversion of HCPs.

DEA Response: The DEA appreciates the comments in support of this rulemaking.

B. Request for Extended Comment Period

The DEA received two comments requesting that the DEA reopen the period for public comment. One of the commenters specifically requested that the comment period be reopened for a minimum of 180 days. The stated justification of one of the commenters was that ''[t]he current period is utterly inadequate to large segments of the population who have had no meaningful notice, have extremely limited internet access in small time periods through use of computers at public libraries and are particularly at risk from harm if this rule is adopted.'' Both requests for extended comment periods were accompanied by meaningful comment along with the request for extension.

DEA response: The Administrative Procedure Act does not set a minimum length of time for public comment. 21 U.S.C. 553; *Phillips Petroleum Co.* v. *U.S. E.P.A.,* 803 F.2d 545, 558–59 (10th Cir. 1986) (upholding the EPA's refusal to extend the 45-day comment period on an NPRM, noting that courts have uniformly upheld comment periods of 45 days or less) (internal citations omitted). However, both Executive Orders 12866 and 13563 provide that agencies should afford the public a comment period of at least 60 days. The DEA published in the **Federal Register** the NPRM proposing to reschedule HCPs into schedule II of the CSA on February 27, 2014. 79 FR 11037. The

DEA provided 60 days for interested persons to submit written comments (either online or through the mail) on the proposal. The comment period closed April 28, 2014. Seven hundred twenty-four submissions on the associated docket at *http://www.regulations.gov* were submitted by the close of the comment period. Several paper submissions duplicating electronic submissions were received via the mail as well. (The 724 number differs from the finalized number of 573 comments received because, as alluded to above, many commenters submitted multiple, duplicate submissions. Multiple submissions of exactly identical comments submitted by the same person or entity are considered by the DEA as only a single, submitted comment.) Based on the following considerations, the DEA declines to reopen the period for additional public comment.

The **Federal Register** is published daily, Monday through Friday, except official holidays, by the Office of the Federal Register, National Archives and Records Administration, under the **Federal Register** Act (44 U.S.C. chapter 15). Section 7 of the **Federal Register** Act (44 U.S.C. 307) provides that publication in the **Federal Register** constitutes constructive notice to persons subject thereto or affected thereby. The **Federal Register** is published in paper and on microfiche. It is also available online at no charge at *http://www.gpo.gov/fdsys/.*

The NPRM was also available on *http://www.regulations.gov* to enable the public to conveniently access the proposal and the supporting materials. Of additional consideration, on the same day as publication in the **Federal Register**, the DEA issued a press release stating that the Administration had published in the **Federal Register** an NPRM to move HCPs from schedule III to schedule II (available at *http://www.justice.gov/dea/divisions/hq/2014/hq022714.shtml*). The press release advised individuals where a complete copy of the NPRM could be obtained as well as how they could submit comments in response to the proposal. The DEA accepted written comments submitted either through Regulations.gov or through the mail.

In accordance with the Administrative Procedure Act, the DEA's published NPRM included ''the terms or substance of the proposed rule'' and ''a description of the subject and issues involved.'' 5 U.S.C. 553(b)(3). The quality and quantity of the responses received in response to the published NPRM, as well as the variety of respondents, including those advocating on behalf of persons residing in LTCFs and other populations that may potentially feel distributional regulatory impacts, demonstrate to the DEA that there has been an adequate opportunity for meaningful public participation by interested persons in accordance with the Administrative Procedure Act. 5 U.S.C. 553(c); *Idaho Farm Bureau Fed'n* v. *Babbitt,* 58 F.3d 1392, 1404 (9th Cir. 1995) (holding that comments discussing the proposed action and supporting data were evidence that the public had obtained and reviewed the information and thus adequate opportunity for public comment had been given).

The DEA notes that the submission by a nurse located in Australia shows that the published NPRM was widely read and reviewed. In addition, those commenters requesting additional time for comment accompanied their request for an extension with substantial comment on the rule. This demonstrates to the DEA that adequate notice and opportunity for meaningful comment was provided by the DEA on this rulemaking.

C. Clarification of Affected Drugs and Substances

The DEA received some comments, though limited in number, indicating it would be helpful to provide detailed discussion of what products are affected by this rule. One commenter specifically requested clarification as to whether the action would apply to cough syrups that contain hydrocodone. The second commenter requested the DEA not change the schedule of Zohydro™ ER. The third commenter requested that Zogenix, the manufacturer of Zohydro™ ER, be ''allow[ed] to bring their new drug to market.''

DEA response: This rulemaking action affects hydrocodone combination products, which are those substances described in 21 CFR 1308.13(e)(1) (iii) and (iv). All other products containing hydrocodone are already controlled in schedule II of the CSA and are not impacted by this action. Zohydro™ ER does not meet the definition of either 21 CFR 1308.13(e)(1) (iii) or (iv); it is currently a schedule II controlled substance under 21 CFR 1308.12(b)(1)(vi) and is not affected by this action.

Other than Zohydro™ ER, all pharmaceuticals containing hydrocodone currently on the market in the United States are HCPs and are subject to this rulemaking. Hydrocodone is the most frequently prescribed opioid in the United States with nearly 137 million prescriptions for HCPs dispensed in 2013. IMS Health, National Sales Perspective™ (NSP). There are several hundred brand name and generic hydrocodone products marketed with the most frequently prescribed combination being hydrocodone and acetaminophen (e.g., Vicodin®, Lortab®). Currently marketed HCPs approved as cough suppressants include Hycodan®, Mycodone®, Tussionex®, Pennkinetic®, Tussigon®, and several generics.

D. Opposition to the Proposed Rule

Two hundred thirty-five commenters (41% of all commenters) opposed the proposal to reschedule HCPs from schedule III to schedule II of the CSA. Many comments submitted in opposition came from pharmacists, including pharmacy school students/interns (31%); the general public (23%); and ultimate users (14%). Of all comments submitted, in support and in opposition, 60% of pharmacists were opposed; 22% of the general public were opposed; and 91% of ultimate users were opposed. These commenters opposed the rescheduling HCPs for a variety of reasons. The comments in opposition can be grouped in the following general categories: (1) Concerns over the DEA's authority to reschedule HCPs; (2) concerns over prescribing practices; (3) concerns regarding patient access to medicine; (4) concerns regarding impacts at LTCFs; (5) concerns that rescheduling HCPs will not prevent abuse or diversion; (6) concerns that rescheduling HCPs will increase provider and pharmacist workload; (7) concerns regarding economic impacts to manufacturers, distributors, pharmacies, physicians, and ultimate users; (8) concerns that alternatives to rescheduling had not been explored and/or implemented first; and (9) concerns about the amount of time to comply with the rule. Each of these general categories is addressed below.

1. Authority To Control Drugs or Substances

a. DEA's Authority To Schedule Substances

One commenter questioned the DEA's general authority to schedule drugs.

DEA response: Recognizing the need for a high level of scrutiny over controlled substances due to their potential for abuse and danger to the public health and safety, Congress established a closed system of distribution for all controlled substances with the passage of the Comprehensive Drug Abuse Prevention and Control Act of 1970. *See* H.R. Rep. No. 91–1444, 1970 U.S.C.C.A.N. at 4566. The DEA

implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. 28 CFR 0.100. Pursuant to 21 U.S.C. 811(a)(1), the Attorney General may, by rule, ''add to such a schedule or transfer between such schedules any drug or other substance if he (A) finds that such drug or other substance has a potential for abuse, and (B) makes with respect to such drug or other substance the findings prescribed by [21 U.S.C. 812(b)] for the schedule in which such drug is to be placed * * *.'' Pursuant to 28 CFR 0.100(b), the Attorney General has delegated this scheduling authority to the Administrator of the DEA. The DEA's authority to implement and enforce the CSA, including adding to the schedules, has been repeatedly recognized and upheld in the Courts. *E.g., U.S.* v. *Alexander,* C.A.9 (Cal.) 1982, 673 F.2d 287 (1982), *cert. denied,* 459 U.S. 876 (Congress' delegation to Attorney General of authority to reclassify controlled substances is constitutional); *U.S.* v. *Roya,* C.A.7 (Ill.) 1978, 574 F.2d 386, *cert. denied,* 439 U.S. 857 (finding no merit to the claim that the addition and reclassification of amobarbital and phenmetrazine as schedule II controlled substances by the Attorney General was an unconstitutional delegation of authority under separation of powers doctrine); *U.S.* v. *Kinder,* C.A.5 (Tex.) 1991, 946 F.2d 362, *cert. denied,* 503 U.S. 987, *cert. denied,* 504 U.S. 946, *rehearing denied,* 505 U.S. 1238 (Attorney General followed proper procedures in reclassifying methamphetamine as schedule II controlled substance, pursuant to the CSA; Attorney General properly delegated his authority to the Director of the Bureau of Narcotics and Dangerous Drugs (BNDD) who then reclassified methamphetamine).

b. Conflict With Other Federal Law

One commenter questioned whether the rescheduling action would have illegal discriminatory effects, and ''violate laws against disability and age discrimination.'' This same commenter also asserted without premise that the rescheduling action could potentially conflict with parts of the Affordable Care Act and ''deprivation of rights under color of authority.''

DEA response: Executive Order 12866 of September 30, 1993, ''Regulatory Planning and Review,'' and Executive Order 13563 of January 18, 2011, ''Improving Regulation and Regulatory Review,'' direct Federal agencies to assess costs and benefits of available regulatory alternatives and, if the regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety effects, distributive impacts, and equity). Paragraph (b)(1) of section 1 of Executive Order 12866 specifically directs Federal agencies to ''avoid regulations that are inconsistent, incompatible, or duplicative with its other regulations or those of other Federal agencies.'' The DEA has reviewed the impacts of this scheduling action against the principles edified by Executive Orders 12866 and 13563 and finds no basis that it would have illegal discriminatory effects, or ''violate laws against disability and age discrimination.''

c. Factors Determinative of Control

Twenty-six commenters opposed rescheduling HCPs as schedule II controlled substances based on concerns regarding the eight-factor analyses. Twenty-four commenters believed that the eight-factor analyses did not support rescheduling into schedule II and that HCPs should remain in schedule III. Two commenters believed that HCPs should be rescheduled into a lower schedule than schedule III. (One commenter stated that HCPs should be down-scheduled into schedule V and made over-the-counter for those 21 years and older.)

i. Evaluation of Abuse Potential of HCPs and Data Used To Support Placement of HCPs into Schedule II of the CSA

Eighteen commenters expressed disagreement about the data that was used to support the statutory requirement under 21 U.S.C. 811(c) and 812(b)(2) for placement into schedule II of the CSA. Some of these commenters stated that the available data are limited and do not support rescheduling HCPs into schedule II. Some commenters indicated that there was no scientific consensus in support of moving HCPs from schedule III to schedule II.

Many of the comments in opposition to the proposed scheduling action were statements by ultimate users of HCPs that HCPs are not abused by patients with legitimate prescriptions. Some of the commenters stated that the small amounts of hydrocodone in HCPs have never contributed to addiction and acetaminophen in HCPs would actually decrease abuse rates. Commenters suggested that abuse potential of HCPs is lowered or negated by the fact that it is often used with other substances such as alcohol. Some commenters supported their assertions with statements that deaths are extremely rare with HCPs.

DEA response: The DEA conducted a comprehensive evaluation of epidemiological, diversion, pharmacological, and pharmacokinetic data to conclude that HCPs have a high abuse potential. All of the data was reviewed collectively, and the data supports the finding that HCPs have a high abuse potential similar to other schedule II controlled substances, such as oxycodone products. The DEA's decision to reschedule HCPs from schedule III to schedule II is also supported by the HHS review and the FDA's DSaRM recommendation.

The DEA disagrees that there is a lack of scientific consensus among scientific experts. Some commenters, in support of their dissenting opinions, cited some selective information presented in the briefing document for the FDA's DSaRM meeting in January 2013. It should be noted that the DSaRM members received the selected information cited by the commenters, and, upon deliberating extensively on all the available data voted 19 to 10 in favor of rescheduling HCPs from schedule III to schedule II. The DEA's determination of the appropriate schedule under the CSA in which to place HCPs is based on a comprehensive review of all available data, rather than selected portions of available data, and the DEA did in fact review and consider the selected information presented by the commenters. The DEA also considered the HHS scientific and medical evaluation and scheduling recommendations.

The DEA finds that the scientific, medical, and epidemiological data are robust and support rescheduling HCPs into schedule II of the CSA. Various drug abuse indicators for HCPs indicate that HCPs are widely diverted and abused at rates largely similar to that of oxycodone products (schedule II). The data indicate that HCPs have an abuse potential similar to schedule II opioid analgesics such as oxycodone and their abuse is associated with severe psychological or physical dependence. Abuse of HCPs is also associated with large numbers of individuals being admitted to addiction treatment centers. Individuals are taking these drugs in sufficient quantities to create a hazard to their health, and abuse of HCPs is associated with large numbers of deaths. Further, data from several different drug abuse monitoring databases support the conclusion that HCPs have a high potential for abuse similar to other schedule II opioid analgesics.

Contrary to the views expressed by some commenters, the review by the DEA and HHS of all the relevant data found that HCPs are abused at high rates and have high dependence potential as indicated by the data reported by the National Survey on Drug Use and

Health (NSDUH), Monitoring the Future (MTF), National Poison Data System (NPDS), Drug Abuse Warning Network (DAWN), and Treatment Episode Data Set (TEDS). There have been large numbers of deaths and emergency department visits associated with abuse of HCPs. In addition, the data indicate that HCPs and oxycodone products have similar abuse potential. Based on these considerations, the DEA believes that the high abuse and dependence potential and harm associated with HCPs support rescheduling into schedule II of the CSA.

Contrary to statements made by some ultimate users, even low doses of HCPs have the potential for adverse impacts on the public health and safety. According to the CDC, while an estimated 80% of patients who are prescribed opioids are prescribed low doses (<100 mg morphine equivalent dose per day) by a single practitioner, these patients account for an estimated 20% of all prescription drug overdoses.[9] (An estimated 10% of patients who are prescribed opioids are prescribed high doses (≥100 mg morphine equivalent dose per day) by single prescribers. These patients account for an estimated 40% of all prescription opioid overdoses. An estimated 10% of patients are patients who seek care from multiple doctors and are prescribed high daily doses of opioids. They account for another 40% of all opioid overdoses.) *Id.*

After careful consideration of relevant data, the DEA finds that HCPs have abuse potential supporting placement into schedule II.

ii. Criteria for Abuse

One commenter wanted the DEA to draw distinctions among abuse, addiction, and dependence. A second commenter objected to the DEA's consideration of ''individuals taking the drug or other substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs'' as a criterion of abuse.

DEA response: As noted by researchers, ''[t]here is no agreement between researchers for terms such as drug abuse, psychological dependence, drug dependence and drug addiction,'' and that, ''[o]ften these terms are used interchangeably.'' [10] The DEA is aware that the most recent version of the Diagnostic and Statistical Manual, the DSM–V, released in 2013, removed the distinction between abuse and dependence for diagnostic purposes, and replaced them with a combined single disorder called ''substance use disorder.'' However, the DEA derives authority from the CSA, and when acting under its authority must speak under the terms and conditions imposed by it. The CSA does not define ''abuse'' in terms of the DSM; in fact it does not define the term at all. The CSA uses terms such as ''potential for abuse,'' ''pattern of abuse,'' and ''significance of abuse.'' *E.g.,* 21 U.S.C. 811 and 812.

One looks first to the face of a law to understand its meaning, and ''[i]f the statute's meaning is plain and unambiguous, there is no need for further inquiry.'' *United States* v. *Fisher,* 289 F.3d 1329, 1337–38 (11th Cir.2002) (internal quotation marks and citation omitted). However, if the language is ambiguous, the relevant legislative history may be used to aid in understanding meaning. *United States* v. *Dodge,* 597 F.3d 1347, 1352 (11th Cir. 2010). The legislative history of the CSA suggests four factors that may be considered in determining whether a particular drug or substance has a ''potential for abuse,'' including whether individuals are taking the drug or drugs containing such a substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs in the course of his professional practice.[11] Accordingly, the DEA uses this as one factor in determining a substance's potential for abuse.

''Addict'' is defined by the CSA as a person who ''habitually uses any narcotic so as to endanger the public morals, health, safety, or welfare, or who is so far addicted to the use of narcotic drugs as to have lost the power of self-control with reference to his addiction.'' 21 U.S.C. 802(1). The DEA uses this definition for the terms ''addict'' and ''addiction.''

iii. Appropriate Drug Comparator

One commenter asserted that HCPs were not compared to appropriate reference drugs and have lower abuse ratios and abuse potential than schedule II oxycodone combination products. Another commenter expressed the opinion that HCPs are substantially cheaper than oxycodone products which would affect drug selection as opposed to the notion that HCPs have more addiction potential. The commenters did not provide any appropriate alternative comparison drug for HCPs.

DEA response: HCPs were compared to oxycodone products, currently schedule II controlled substances, to evaluate abuse potential. The DEA, in agreement with the HHS review, considers the comparison of HCPs to oxycodone products appropriate due to similarities between their pharmacological properties, therapeutic uses and patterns, as well as market history. In their eight-factor analysis, the FDA noted that it is not always possible to identify an ''appropriate opioid comparator in Schedule III.'' The FDA went on to state that: ''While FDA considered codeine as a potential comparator, it was deemed inappropriate for several reasons * * *. Given the absence of an appropriate Schedule III comparator, FDA focused its analyses on comparing the abuse liability of hydrocodone combination products (Schedule III) with oxycodone products (Schedule II).''

With regard to the comment about the lower costs of HCPs contributing to its high abuse potential, it is important to note that abuse potential of a given drug is also influenced by various other factors (e.g., pharmacological properties, ease of availability, etc.). Additionally, actual abuse data comparing HCPs and oxycodone combination drugs indicate that the abuse potential between the two drugs is similar. Contrary to the views expressed by some commenters, the review by the DEA of all the relevant data found that HCPs are abused at high rates and have high dependence potential as indicated by the data

[9] Centers for Disease Control, *CDC Grand Rounds: Prescription Drug Overdoses—a U.S. Epidemic,* 61(01) Morbidity and Mortality Weekly Report (MMWR) 10 (2012) (internal citations omitted) available at *http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6101a3.htm.*

[10] Laxmaiah Manchikanti, MD *et al., National All Schedules Prescription Electronic Reporting Act (NASPER): Balancing Substance Abuse and Medical Necessity,* 5 Pain Physician 294, 299, n.3 (2002).

[11] As provided in the CSA's legislative history:

* * * [A] substance has a potential for abuse because of its depressant or stimulant effect on the central nervous system or its hallucinogenic effect if: (1) There is evidence that individuals are taking the drug or drugs containing such a substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or of the community; or (2) There is a significant diversion of the drug or drugs containing such a substance from legitimate drug channels; or (3) Individuals are taking the drug or drugs containing such a substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs in the course of his professional practice; or (4) The drug or drugs containing such a substance are new drugs so related in their action to a drug or drugs already listed as having a potential for abuse to make it likely that the drug will have the same potentiality for abuse as such drugs, thus making it reasonable to assume that there may be significant diversions from legitimate channels, significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community.

Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No 91–1444, 91st Cong., Sess.1 (1970) reprinted in U.S.C.C.A.N. 4566, 4603.

reported by the NSDUH, MTF, NPDS, DAWN, and TEDS. There have been large numbers of deaths and emergency department visits associated with abuse of HCPs. Based on these considerations, the DEA believes that the high abuse and dependence potential and harm associated with HCPs support rescheduling into schedule II of the CSA.

iv. Balanced Presentation of the Eight-Factor Analysis

Nine commenters disagreed with the conclusions in the DEA's eight-factor analysis. These commenters asserted that the DEA's eight-factor analysis was not a balanced presentation and did not include the therapeutic benefits or the negative impact on patients with a legitimate medical use for HCPs. In addition, some of the commenters stated that the DEA's eight-factor analysis used flawed analytical methods and failed to show that HCPs were more dangerous or more abused than oxycodone. Several of these commenters requested that DEA include both sides of the clinical argument and peer-reviewed clinical research.

DEA response: The DEA reviewed the required eight factors in accordance with the provisions stated in 21 U.S.C. 811(c), specifically exploring the abuse potential and potential harms of HCPs. The DEA's analysis also acknowledges that there is a currently accepted medical use, and accordingly therapeutic benefit, of HCPs. Consistent with the CSA, an evaluation of abuse and dependence potential, risk to the public health and safety, and other factors are included in the analysis. 21 U.S.C. 811(c). The CSA does not require that HCPs be *more* dangerous or abused than oxycodone in order to be placed in schedule II. Rather, relative abuse potential must be established. The DEA's analysis shows that HCPs have a high potential for abuse, and the abuse potential of HCPs is *comparable* to the schedule II controlled substance oxycodone. Thus, HCPs are appropriately placed in schedule II, along with oxycodone. Further, the analytical methods that were presented in the DEA's eight-factor analysis were consistent with the HHS's eight-factor analysis that was finalized in December 2013. The DEA used the best available methods based on current science to complete the eight-factor analysis.

2. Requirements Applicable to Prescriptions

a. Authority To Prescribe HCPs as Schedule II Controlled Substances

Nineteen commenters opposed rescheduling HCPs as schedule II controlled substances based on concerns related to the restricted authority of mid-level practitioners to prescribe medications that are schedule II controlled substances.

DEA response: The DEA recognizes that some States do not allow all providers to prescribe schedule II controlled substances. However, it is outside of the DEA's scope of authority under the CSA to determine what categories of practitioners may prescribe controlled substances. Under the CSA, it is up to each State to decide who has the authority to prescribe controlled substances within that State. This is reflected in 21 U.S.C. 823(f), which requires DEA to register a practitioner who is authorized under the laws of the State in which he practices unless the practitioner's registration would be inconsistent with the public interest. 21 U.S.C. 823, 824. This is also echoed in 21 CFR 1306.03, which states that a practitioner can issue a prescription for controlled substances so long as the practitioner is authorized to prescribe controlled substances by the jurisdiction where he is licensed to practice his profession and is registered or exempted from registration pursuant to 21 CFR 1301.22(c) and 21 CFR 1301.23. Each State has this authority, so long as it does not conflict with federal law.

b. Transmittal Method of HCPs as Schedule II Controlled Substances

i. Oral and Facsimile Prescriptions

Multiple commenters opposed rescheduling HCPs as schedule II controlled substances based on concerns related to the transmittal methods available for schedule II as compared to schedule III controlled substances, specifically the circumstances required in order to provide oral prescriptions and to transmit prescriptions via facsimile. Both ultimate users and providers expressed concern that HCPs as schedule II controlled substances will not be available on nights and weekends. They were especially concerned about dental emergencies that might occur over the weekend. Four commenters stated that patients needing night or weekend prescriptions for HCPs will overburden Emergency Departments (EDs).

DEA response: The requirements for issuing an emergency oral prescription for a schedule II controlled substance do not hinder legitimate access to HCPs. The procedural requirements relating to transmission of a legitimate prescription do not hinder legitimate access either.

Contrary to concerns of commenters, practitioners will still be allowed to call-in prescriptions for HCPs in the event of an emergency. In the event of an emergency, as defined by 21 CFR 290.10, a pharmacist may dispense a schedule II controlled substance upon receiving oral authorization of a prescribing individual practitioner in accordance with 21 CFR 1306.11(d).

ii. Triplicate Prescriptions

Five commenters opposed rescheduling HCPs as schedule II controlled substances based on concerns regarding ''triplicate prescriptions.'' One commenter stated that emergency physicians do not have triplicate prescription forms, and as a result, they will be required to prescribe drugs that are less effective for pain management. Two commenters stated that emergency physicians do not want to carry a triplicate prescription pad.

DEA response: Neither the CSA nor DEA regulations require prescriptions to be prepared in triplicate. The DEA recognizes that some States, such as Texas and California, require the use of triplicate prescription forms for some or all controlled substances. As stated in the November 19, 2007, final rule, ''Issuance of Multiple Prescriptions for Schedule II Controlled Substances,'' the ''DEA supports the efforts of States to take the specific action they deem necessary to prevent the diversion of controlled substances within their jurisdictions.'' 72 FR 64921, 64923.

> Under the CSA, Congress envisioned that the Federal and State Governments would work in tandem to regulate activities relating to controlled substances. This is reflected in 21 U.S.C. 903, which indicates that Congress did not intend to preempt state controlled substance laws, so long as such state laws do not conflict with federal law. Thus, each state may enact controlled substance laws that go beyond the requirements of the CSA, provided such laws do not conflict with the CSA. Given this aspect of the CSA, it would not be appropriate for DEA to seek to preempt or supersede state laws relating to the prescribing of controlled substances, provided such laws do not conflict with the CSA or DEA regulations.

Id. at 64927.

c. Quantity and Frequency of Fills and Refills for HCPs as Schedule II Controlled Substances

Pharmacists, prescribers, and ultimate users expressed concern about the quantity and frequency of fills and refills for HCPs as schedule II controlled substances that would be allowed if HCPs were placed into schedule II.

Several commenters, mostly ultimate users, asserted that up-scheduling would result in patients being limited to a 30-day supply of medication and would correspondingly need to begin seeing their doctors monthly. Other commenters, primarily pharmacists and physicians, expressed their belief that rescheduling HCPs will result in larger quantities of pills being authorized on each prescription to prevent patients from running out of medication and being in pain. Most of these commenters had corresponding concerns that these larger prescriptions would lead to more unused medication in the home that would be available for diversion. Examples include the following: One commenter mentioned his concern that since larger prescriptions would be authorized, he would be unable to monitor whether the patient is taking the medication or taking too much of it. An emergency physician opined that removing the ability to get refills on HCPs may result in prescriptions for more potent medications being issued. One ultimate user was concerned that the elimination of refills on HCPs would result in patients getting insufficient quantities to treat the acute illness for which it was prescribed.

DEA response: While courts have recognized that prescribing an ''inordinately large quantity of controlled substances'' can be evidence of a violation of the CSA,[12] generally neither the CSA nor DEA regulations impose a specific quantitative minimum or maximum limit on the amount of medication that may be prescribed on a single prescription, or the duration of treatment intended with the prescribed controlled substance. The quantity prescribed and dispensed is limited in an emergency situation as defined by 21 CFR 290.10 when dispensing a schedule II controlled substance upon oral authorization in accordance with 21 CFR 1306.11(d). The CSA and implementing regulations require all controlled substance prescriptions to be ''valid.'' A prescription is not ''valid'' unless it is issued for a legitimate medical purpose and within the usual course of professional practice. 21 CFR 1306.04(a). A pharmacist who fills a prescription has a corresponding responsibility, and the person who fills an illegitimate prescription is subject to penalty. *Id.*

While the CSA and DEA regulations generally contain no specific limit on the quantity that may be prescribed on a single prescription, or the duration of treatment intended for a single prescription, some States do impose specific limits on prescribing schedule II controlled substances. Likewise, some limitations on the quantity or frequency of schedule II controlled substances may be limited by individual prescription benefit providers. Any limitations imposed by State law apply, in addition to the corresponding requirements under Federal law, so long as the State requirements do not conflict with or contravene the Federal requirements. 21 U.S.C. 903; 21 CFR 1306.12(b)(1)(v); ''Clarification of Existing Requirements Under the Controlled Substances Act for Prescribing Schedule II Controlled Substances,'' 70 FR 50408, Aug. 26, 2005.

Although the CSA prohibits refills of prescriptions for schedule II controlled substances, a practitioner may issue multiple schedule II prescriptions in order to provide up to a 90-day supply of medication in accordance with 21 CFR 1306.12. Furthermore, DEA regulations do not require patients to be seen monthly by their provider. Rather, practitioners must determine on their own, based on sound medical judgment, and in accordance with established medical standards how often to see their patients when prescribing controlled substances.

Note, however, that DEA regulations should not be ''construed as mandating or encouraging individual practitioners to issue multiple prescriptions or to see their patients only once every 90 days when prescribing Schedule II controlled substances. Rather, individual practitioners must determine on their own, based on sound medical judgment, and in accordance with established medical standards, whether it is appropriate to issue multiple prescriptions and how often to see their patients when doing so.'' 21 CFR 1306.12(b)(2). The DEA does not regulate the general practice of medicine and the agency lacks the authority to issue guidelines (or make policy statements) that constitute advice on the general practice of medicine.

3. Patient Access to Medicine

The DEA received numerous comments, predominantly from ultimate users, who voiced concerns about the possible effects rescheduling would have on patients' access to appropriate treatment for pain. Commenters were concerned about the possible need for increased provider visits, and associated increased time and cost to receive medical care. Commenters were concerned about access to health care providers, such as possibly needing to change health care providers and in some cases having to drive longer distances to get to practitioners' offices because of limitations on types of practitioners who can prescribe schedule II controlled substances. Commenters were also concerned that rescheduling could result in doctors changing prescriptions to alternative medications which might be less effective for treating some kinds of pain and/or cause adverse health effects.

a. Impact on Prescribing Practices

Several commenters were concerned that because of the rescheduling, practitioners will be less likely to prescribe HCPs. One commenter suggested that since a practitioner can no longer call in or fax a prescription to the pharmacy, the practitioner will be reluctant to prescribe HCPs. Other commenters stated the scheduling action will impose additional burdens on practitioners and therefore they will stop prescribing for HCPs and prescribe less effective drugs. One commenter stated that many EDs do not typically prescribe schedule II narcotics. Likewise, two commenters suggested that cumbersome and slow ordering processes for schedule II substances will cause local shortages of HCPs, and thus practitioners will turn to prescribing other drugs.

DEA Response: The processes and procedures associated with dispensing a controlled substance are not relevant factors to the determination of whether a substance should be controlled or under what schedule a substance should be placed if it is controlled. *See* 21 U.S.C. 811 and 812. Nonetheless, controlling HCPs as a schedule II controlled substance should not hinder legitimate access to the medicine. As recognized and noted by commenters, scheduling a medication does not make it impossible to prescribe, dispense, or administer the medication. However, it does alert prescribing-practitioners, pharmacists medical support professionals and perhaps even some patients and non-professional caregivers that the medication has potential dangers for addiction and misuse, and careful monitoring and evaluation of use of such drugs is necessary for appropriate patient care. ''The placing of a drug into [a particular schedule of the CSA] will alert a physician that the drug does cause physical and psychological dependence. This is valuable information for a physician to possess before prescribing any drug.'' 50 FR 8104, 8107, Feb. 28, 1985 (''Schedules of Controlled Substances; Rescheduling of Buprenorphine From Schedule II to Schedule V of the Controlled Substances Act'').

[12] *United States* v. *Rosen,* 582 F.2d 1032, 1036 (5th Cir. 1978).

The DEA does not intend for legitimate patients to go without adequate care. A prescription for a controlled substance to be effective must be issued for a legitimate medical purpose by an individual practitioner acting in the usual course of his professional practice. 21 CFR 1306.04(a). When a practitioner prescribes a medication that is a controlled substance for a patient, it must be because he/she has made a professional medical determination that it would be medically appropriate for the patient's medical condition to treat with that specific controlled substance.

The DEA recognizes that rescheduling a legitimately marketed pharmaceutical controlled substance may have some effect on the decision of a practitioner to prescribe that particular controlled substance. There may be some practitioners who are reluctant to prescribe a schedule II controlled substance although authorized by State law to do so. However, the DEA notes that other schedule II controlled substances are widely prescribed. Given that classification has not deterred practitioners from prescribing those drugs, the DEA believes that when a practitioner makes a medical determination that a particular controlled substance is appropriate to treat a patient's medical condition, the practitioner will prescribe the appropriate controlled substance, regardless of the substance's schedule. The DEA notes that a doctor from New York, one of the States that has already scheduled HCPs as schedule II controlled substances under State law, asserted in his comment that up-scheduling ''has reduced unconscious (or conscience-less) prescribing without impacting patients' access to medications.''

b. Impact of Criminal Action

Some commenters expressed concern that transferring HCPs to schedule II would deter prescribers from properly treating pain for fear of facing criminal action. According to one commenter, many providers limit the number of pills for schedule II medications ''because they feel they are being watched by monitoring programs and are afraid the DEA 'will investigate' them for too many CII scripts.''

DEA response: One of the most important principles underlying the CSA is that every prescription for a controlled substance must be issued for a legitimate medical purpose by an individual practitioner acting in the usual course of his professional practice. 21 CFR 1306.04(a); *U.S.* v. *Moore,* 423 U.S. 122 (1975) (holding registered physicians may be prosecuted for violation of the CSA when their activities fall outside the usual course of professional practice). The DEA policy statement entitled ''Dispensing Controlled Substances for the Treatment of Pain,'' 71 FR 52715, Sept. 6, 2006, makes clear that this longstanding requirement should in no way interfere with the legitimate practice of medicine or cause any practitioner to be reluctant to provide legitimate pain treatment. Practitioners (as well as ultimate users) become subject to administrative, civil, and/or criminal action when their activity involving controlled substances is not authorized by, or is in violation of, the CSA, regardless of whether the activity involves a schedule II controlled substance or a schedule III controlled substance.

c. Impact on Drug Availability

Two commenters suggested this rule will result in limited drug availability because wholesalers are limiting distributions to community pharmacies. These commenters assert that if a pharmacy goes over a pre-determined amount, they cannot obtain the needed pharmaceuticals until the following month. The commenter asserted that this practice may have particularly adverse impacts in rural areas where a pharmacy may only be serviced by one distributor. Another commenter suggested there will be local shortages of HCPs because of the cumbersome and slow schedule II ordering process. Two commenters were concerned that limited availability may result from delays associated with manufacturer production due to annual production requirements for schedule II controlled substances.

DEA response: DEA registered distributors are required to provide effective controls against diversion of controlled substances. However, the DEA does not limit the quantity of controlled substances that may be legitimately distributed to pharmacies. Any arbitrary limits placed on community pharmacies by distributors are the result of a business decision of that distributor.

The DEA does impose requirements for distributors to operate a system to disclose suspicious orders of controlled substances. 21 CFR 1301.74(b). Suspicious orders include orders of unusual size, orders deviating substantially from a normal pattern, and orders of unusual frequency. *Id.* Part of the due diligence associated with that requirement, as well as the general requirement under 21 CFR 1301.71(a) for registrants to ''provide effective controls and procedures to guard against theft and diversion of controlled substances,'' is to ''know your customer.'' While order volume may be one indicator of a suspicious order, the totality of circumstances must be used in making a determination. Generally, no single indicator is independently a suggestion that a given order is suspicious. Order volume should be examined not only on an industry-wide comparison level, but also on a local level. For example, a pharmacy located near an oncology clinic may be more likely to regularly order higher volumes of certain controlled pharmaceuticals than one that is not.

The DEA does not find evidence to support the claim that the ordering process for schedule II controlled substances will result in limited availability of HCPs. A DEA Form 222, or its electronic equivalent—the Controlled Substance Ordering System (CSOS), is required for all distributions of schedule I or II controlled substances, with specific exceptions, 21 U.S.C. 828(a); 21 CFR 1305.03, which enables the DEA to monitor the flow of these controlled substances from their point of manufacture through commercial distribution. It takes approximately an hour to complete each order using the paper DEA Form 222. It takes approximately three minutes to complete an order using CSOS. (The DEA Form 222 permits ten line items per form; electronic orders are not subject to the same requirement and may contain an unlimited number of transactions (line items)). While CSOS transactions are faster, the paper DEA Form 222 orders are also able to be processed quickly through the system. In 2013, 109,632 registrants ordered schedule I or II controlled substances. About 4.8 million orders were processed on Form 222s and 924,257 were processed electronically via CSOS (approximately 16% of all orders). The paper orders represented roughly 27.7 million transactions (or about 6 per order); the electronic orders represented roughly 21.2 million transactions or slightly more than 23 per order.

There should be no impact on availability due to schedule II annual production requirements (i.e., manufacturing quota). Registrants that manufacture hydrocodone are already required to obtain an annual quota in order to manufacture hydrocodone because it is a schedule II controlled substance unless and until it is formulated into dosage form HCPs.

Manufacturing quotas are issued to bulk manufacturers who manufacture either from synthetic routes (e.g., hydrocodone from codeine), or extraction from narcotic raw material.

Bulk manufacturing quota will not be impacted by the movement of HCPs from schedule III into schedule II.

Procurement quotas are typically issued to dosage form manufacturers and repackagers or relablers for manufacturing activities. As related to HCPs, a procurement quota is required to: (1) Receive bulk Active Pharmaceutical Ingredients to be manufactured into dosage units; and (2) for a company to receive bulk finished dosage units for relabeling or repackaging.

d. Providers Authorized To Prescribe Schedule II Controlled Substances

Nine commenters expressed concern about the ability to access health care providers who can prescribe schedule II controlled substances. Specifically, commenters stated that mid-level health care providers such as physician assistants and nurse practitioners, who provide primary health care, cannot prescribe schedule II controlled substances in many States. As a result, these patients will not have access to the medicine they need to treat their pain. In addition, one commenter stated this will have a negative impact on patients who visit rural practices where mid-level practitioners often prescribe pain medication. Moreover, one commenter stated the scheduling action would make it mandatory for a patient to see a physician for pain. Another commenter stated that because of this scheduling they would now have to find new doctors, which would increase travel time and the amount of money spent on gas.

DEA response: State authorization to handle controlled substances is both a necessary precondition for Federal authorization to handle controlled substances and a qualifying determinate as to the extent of the practitioner's scope of authority in regard to such substances. *U.S.* v. *Moore,* 423 U.S. 122, 141 (1975) (''The federal registration, which follows automatically, extends no further [than the scope of authority granted by the State to practice medicine and to dispense drugs in connection with their professional practice].''). A DEA registered practitioner may only engage in those activities involving controlled substances that are authorized by the laws of the State on which the practitioner's Federal registration is based. If an individual practitioner, or a class of practitioners, has not been granted authorization to prescribe certain controlled substances that is the rightful determination of the State under its authority to regulate the practice of medicine.

e. Treatment for Pain

Concerns were raised that changes in the scheduling for HCPs could drive the use of alternative treatments. One class of commenters who were particularly concerned about this was emergency physicians who work in States that require triplicate prescriptions and/or facilities whose policy is not to handle schedule II controlled substances in their emergency departments. Some emergency providers in triplicate-prescription States said that they did not carry triplicate prescriptions due to concerns about them being stolen. Some emergency physicians who work in States that require triplicate prescription forms (but who are able to write schedule II controlled substance prescriptions while working in their emergency departments) stated that if ''forced to get a triplicate,'' then he will start writing for more schedule II controlled substances, such as Percocet, because it is a ''better pain med[icine] than HCPs.'' Other commenters were concerned that some prescribers might switch to prescribing ''stronger drugs with significant abuse potential,'' or alternatively switch to medications such as non-steroidal anti-inflammatory drugs (NSAIDs) which are less effective for treating some kinds of pain and may cause other adverse effects, leaving people in untreated pain. One commenter was concerned that tramadol would be prescribed in place of HCPs, which worried them because of issues with tramadol specific to renal patients.

DEA response: The DEA does not regulate the general practice of medicine and the agency lacks authority to issue guidelines (or make policy statements) that constitute advice on the general practice of medicine. A prescription for a controlled substance must be issued for a legitimate medical purpose by an individual practitioner acting in the usual course of his professional practice. 21 CFR 1306.04(a); *U.S.* v. *Moore,* 423 U.S. 122 (1975). A practitioner must use sound medical judgment to determine which controlled substance they will prescribe to appropriately treat his or her patient's medical condition, rather than make a determination based upon whether a triplicate prescription form is required by the State or by their employer's policy to not prescribe schedule II controlled substances.

f. Shift to the Black Market

Several commenters stated that making HCPs schedule II controlled substances would limit access to HCPs, causing people to buy drugs on the street, including HCPs and heroin.

DEA response: As discussed above, schedule II controlled substances are readily available for legitimate medical use.

g. Monitoring Access

A national advocacy group for cancer patients requested that the DEA ''require monitoring plans and an annual report to Congress, in the event that HCPs are upscheduled, that assess the impact on access by patients with legitimate needs, as emphasized and urged by HHS'' and to ''adjust policy accordingly if it finds that access is impeded for patients who legitimately need HCPs for pain management.''

DEA response: Once upscheduled the DEA will continue to monitor the diversion of HCPs. However, it is outside the scope of the DEA's authority under the CSA to require monitoring plans or reports not authorized under the Act.

4. Impacts on Unique Populations

The DEA received several comments regarding the impact on patients who suffer from chronic pain, cancer, rare diseases, chronic and end-stage renal disease, as well as dental and surgical post-op patients, and rural residents. Many commenters also voiced concerns about possible effects of rescheduling on the elderly and disabled. Several commenters who are affected by chronic pain voiced a concern that the scheduling action will be a burden and make it harder for them to obtain their medicine. As a result, these commenters stated they will suffer solely because of the people that abuse HCPs. Another commenter stated that because of this burden, patients might start self-medicating. One commenter said that practitioners will start prescribing drugs that are not as effective as HCPs, which could have a negative impact on patients mentally. One commenter stated that many cancer patients are in chronic pain, and because of this action, these patients will suffer as they cannot get their required medication. Others suggested post-op patients will have to suffer in pain after their surgeries because they will not be able to get the required medications from doctors on weekends. Several commenters stated that patients in rural areas who are currently seen by mid-level practitioners will need to drive an hour or more to be treated by a physician because their mid-level provider is not authorized to issue prescriptions for schedule II controlled substances. In addition, another commenter stated that many rural physicians are already

overbooked, which will cause rural patients to suffer in pain until they can get an appointment. Another commenter stated that rural patients have a tough time physically picking up handwritten prescriptions. Several commenters noted that the nearest doctor is more than an hour away and that having to drive that distance once a month to obtain HCPs is inconvenient.

DEA response: Scheduling determinations are based on scientific determinations regarding the substance's potential for abuse, its potential for psychological and physical dependence, and whether the substance has a currently accepted medical use in treatment in the United States. 21 U.S.C. 812(b). The DEA may not reschedule, or refuse to reschedule, a drug or other substance based merely on the population it is intended or approved to treat.

5. Impact on Long-Term Care Facilities (LTCFs)

a. Treatment for Pain

Many commenters, including two U.S. Senators, requested that the DEA closely examine possible impacts of rescheduling HCPs in the long-term care facility (LTCF) setting. Many commenters had concerns that placing HCPs into schedule II will impact a substantial number of LTCF residents and may result in untreated pain due to the lack of ready-access to other appropriate medications. For example, according to one commenter, ''HCPs are the current, albeit less preferred alternative because of its combination with acetaminophen, which has to be restricted in older adults due to toxicity risk. However, long-term care providers have been forced to use HCPs as a substitute for Schedule II drugs'' because they are more readily available for administration due to less restrictive handling requirements for controlled substances in lower schedules than schedule II. According to this same commenter, ''the remaining pain care options still in schedule II are not as clinically effective in treating pain for the elderly as HCPs.''

Two commenters stated that LTCF residents, especially post-surgical patients, need medications immediately and that obtaining prescriptions is not quick because most LTCFs do not operate with in-house doctors on site.

DEA response: As previously discussed, scheduling determinations are based on scientific determinations regarding the substance's potential for abuse, its potential for psychological and physical dependence, and whether the substance has a currently accepted medical use in treatment in the United States. 21 U.S.C. 812(b). Nonetheless, the DEA has promulgated many regulations to accommodate the unique circumstances of LTCF residents. For example, in accordance with 21 CFR 1306.11(f), a prescription for a schedule II controlled substance for a resident of an LTCF may be transmitted by the practitioner or practitioner's agent to the dispensing pharmacy by facsimile. In accordance with 21 CFR 1306.13(b), a prescription for a schedule II controlled substance written for a patient in an LTCF may be filled by the pharmacy in partial quantities to include individual dosage units.

b. Request for Exemption for LTCFs

Several commenters requested that the DEA waive/exempt LTCFs from the more restrictive schedule II handling requirements with respect to HCPs. Some commenters asserted that such a waiver/exemption would be justified based on their assertion that there is a lower risk of misuse, abuse, and diversion of HCPs in an LTCF setting as compared to other settings. One nationwide professional association stated that:

> [T]he long-term care setting has special and unique protections against diversion that are required by federal regulations and makes abuse and diversion very difficult and therefore, less likely to occur. * * * The regulatory standards and mandatory procedural checks in most cases make it difficult or impossible for any suspected abuse or diversion to occur over a sustained period of time. This makes diversion by staff difficult * * *. Other than anecdotal case here and there, there is no evidence that diversion is a systemic or frequent problem in SNF [skilled nursing facility] setting nor that the current proposed rule will correct [it].

This same commenter asserted that the ''nursing home population is unlikely to be drug abusers'' because ''[t]heir health conditions often make them bed-bound or otherwise dependent on nurses for the administration of their medications.''

DEA response. Nursing home residents take, on average, eight to ten medications per day.[13] At least 17% of those medications are unused.[14] Controlled substance medications are often stored and administered in LTCF settings as monthly punch cards (a.k.a. ''bingo cards''), and liquid controlled substances are often dispensed in large-volume packaging.[15] [16] In addition, a 2011 report by the HHS Office of Inspector General found that almost all sampled nursing facilities employed one or more individuals with at least one criminal conviction, and nearly half of sampled nursing facilities employed five or more individuals with at least one conviction. Further, 44% of employees with convictions were convicted of crimes against property (e.g., burglary, shoplifting, writing bad checks).[17] LTCFs are unique potential sources of diversion because the care provided to residents results in the accumulation of large amounts of controlled substances in a single, un-registered, relatively unsecure environment, where the disabled and elderly cannot defend themselves or adequately report what has happened.

While focusing on the limited mobility of many residents in LTCFs as justification for why LTCFs should be able to adhere to less restrictive handling requirements for HCPs, commenters gave little consideration to potential diversion by employees, contractors, outside professionals, or visitors who may have access to their facilities. Direct access to controlled substances around a vulnerable population provides many opportunities for diversion of controlled substances, to the detriment of the LTCF residents as well as the general public. For example, the Oregon Aging and People with Disabilities Division, alone, investigated 29 instances of drug theft at 17 different LTCFs in three counties, between 2009 and 2013.[18] The average was 15.8 cases of medication theft per 1,000 beds/units, with the most often stolen products being narcotic

[13] The Lewin Group. CMS Review of Current Standards of Practice for Long-Term Care Pharmacy Services: Long-Term Care Pharmacy Primer. Prepared for: Centers for Medicare and Medicaid Services. December 30, 2004.

[14] Gary Bazalo, MS, MBA, and Richard C. Weiss, MS, Managed Solutions, LLC. Measurement of Unused Prescription Drugs in Medicare Part D Nursing Stays. Jan. 12, 2011 at p. 6 (reporting survey results of consulting pharmacists conducted by the American Society of Consultant Pharmacists).

[15] Marti A. Burton and Linda J. May Ludwig, *Fundamentals of Nursing Care: Concepts, Connections & Skills* 857 (2011); Norman V. Carroll, Ph.D., Michael T. Rupp, Ph.D., and David A. Holdford, Ph.D., *Analysis of Costs to Dispense Prescriptions in Independently Owned, Closed-Door Long-Term Care Pharmacies,* 20(3) JMCP 291 (2014) (76% of independently owned, closed-door pharmacies dispense 76% of doses to LTCFs in 28–31 day cycles).

[16] Comment of American Society of Consultant Pharmacists on Docket No. DEA–316, ''Disposal of Controlled Substances,'' Feb. 19, 2013 available at *http://www.regulations.gov/#!documentDetail;D=DEA-2012-0008-0144.*

[17] U.S. Department of Health and Human Services, Office of Inspector General, OEI–07–09–00110, Nursing Facilities' Employment of Individuals with Criminal Convictions (2011), *available at http://oig.hhs.gov/oei/reports/oei-07-09-00110.pdf.*

[18] Mac McLean, *Drug Theft Affects Care,* The Bulletin, Sept. 8, 2013, available at *http://www.bendbulletin.com/news/1340250-153/drug-theft-affects-care.*

painkillers—such as HCPs.[19] These medication thefts occurred in both large nursing homes and small adult foster homes.[20]

Although not addressing LTCFs directly, the Mayo Clinic has reported on the diversion of drugs from within health care facilities and the threat to public health and safety such actions cause.[21] Those risks included risk to patients receiving adulterated or contaminated drugs in place of the diverted drug as well as the risk of receiving substandard care from addicted employees.[22] The Oregon investigations also included reports of having a patient's medication replaced with blood pressure medication—thus causing the combined risk of not receiving proper medication with the risk of overdose of another medication.

The most cursory of searches readily reveals multiple allegations reported in the news of thefts of controlled substances in nursing homes. For example, in 2012 six nursing home employees in Oklahoma were charged with operating a drug ring out of the facility for whom they were employed. *Charges Filed in Nursing Home Drug Theft,* KWGS News, July 5, 2012, available at *http://publicradiotulsa.org/post/charges-filed-nursing-home-drug-theft.* The Oklahoma Bureau of Narcotics (OBN) reported that 9,000 dosage units of controlled substances had been diverted from the facility by the nursing home employees, 8,400 of which involved hydrocodone. Press Release, Oklahoma Bureau of Narcotics and Dangerous Drugs Control (July 5, 2012) (on file with the Oklahoma Bureau of Narcotics); *Oklahoma Nursing Home Employees Accused of Running Drug Ring: State* v. *Alexander,* 15 No. 1 Westlaw Journal Nursing Home 4 (2012). The spokesman for OBN stated that employees would call in fraudulent prescriptions of hydrocodone for residents: ''These residents had not been prescribed the Hydrocodone by doctors. There is no evidence that any resident was deprived of their legitimate medications. Evidence suggests some of the employees would personally use small amount of the diverted medication, but the majority of the fraudulent drugs were sold on the streets * * *.'' *Id.*

Criminal acts at LTCFs ''often go undocumented, are seldom reported to law enforcement, and are rarely prosecuted.''[23] Even so, theft and diversion at LTCFs likely occurs on a local level, and when reported, are investigated and prosecuted at the local level. The diversion of controlled substances at LTCFs, whether widespread or discrete events, are a threat to the public health and safety, especially considering that such activity poses a real and direct threat to a vulnerable population. Public health and safety threats to disadvantaged, underrepresented, and historically vulnerable populations, including the elderly and mentally, physically, and emotionally/behaviorally disabled, disordered, or challenged, must be taken that much more seriously by those public bodies charged with protecting the public health and welfare. The DEA further notes that the misuse, abuse, and diversion of controlled substances, including pharmaceutical controlled substances, are not limited to any particular age group or functional level.

c. Transmission Method for Prescriptions

One commenter requested two changes to the transmittal methods for prescriptions: (1) Allow a prescribing practitioner to call in to the pharmacy an order for a limited supply, up to a 72 hour quantity, of a schedule II medication for an LTCF patient in an emergency situation, under existing regulations for schedule III–V controlled substances; and (2) Allow a practitioner's agent, acting on behalf of a prescribing practitioner, to call in the prescribing practitioner's verbal order for a small (72 hour) supply of a schedule II medication for an LTCF patient in an emergency situation, under existing regulations for schedule III–V controlled substances.

DEA response: The CSA requires that prescriptions for schedule II controlled substances be written, except in emergency situations as defined by the HHS. 21 U.S.C. 829(a). Pursuant to 21 CFR 1306.11(d), in the case of an emergency situation, a pharmacist may dispense a schedule II controlled substance upon receiving oral authorization from a prescribing individual practitioner provided that the quantity prescribed and dispensed is limited to the amount adequate to treat the patient during the emergency period (dispensing beyond the emergency period must be pursuant to a written prescription signed by the prescribing individual practitioner).

The DEA recognizes the unique challenges and issues pertaining to handling and using controlled substances at LTCFs and has previously addressed these issues within the limits of the CSA.[24] For example, a prescription for a schedule II controlled substance for an LTCF resident may be transmitted by the practitioner or the practitioner's agent to the dispensing pharmacy by facsimile. 21 CFR 1306.11(f). In addition, a prescription for a schedule II controlled substance for an LTCF resident may be filled in partial quantities to include individual dosage units. 21 CFR 1306.13(b).

It is emphasized that a DEA registered practitioner may not delegate to a nurse, a pharmacist, or anyone else, his or her authority to make a medical determination whether to prescribe a particular controlled substance. Note that the practitioner remains responsible for ensuring that the prescription conforms in all essential respects to the law and regulations, 21 CFR 1306.05(f). 75 FR 61613, 61614, Oct. 6, 2010. This requires the practitioner alone to determine on a prescription by prescription basis whether the prescription is supported by a legitimate medical purpose and that all the essential elements of the prescriptions are met.

d. E-Prescribing

One commenter requested that the DEA ''promote the adoption of e-prescribing by requiring facilities and their respective pharmacy suppliers to allow physicians to electronically prescribe controlled substances consistent with the law and appropriate safeguards.''

DEA response: This request is outside the scope of this rulemaking.

e. Emergency Kits

One commenter requested that the DEA ''promote adoption of consistent and effective laws and policies across all states for the content and use of emergency kits (E-Kits) in the PA/LTC setting.''

DEA response: This request is outside the scope of this rulemaking.

6. Abuse Prevention

Commenters raised concerns that, despite the scheduling of drugs, individuals will always find substances to abuse. These commenters argued that the proposed schedule II controls for

[19] *Id.*

[20] *Id.*

[21] Keith H. Berge, *et. al., Diversion of Drugs Within Health Care Facilities, a Multiple-Victim Crime: Patterns of Diversion, Scope, Consequences, Detection, and Prevention,* 87(7) Mayo Clin. Proc. 674 (2012).

[22] *Id.*

[23] Wes Bledsoe, *Criminal Offenders Residing in Long-Term Care Facilities,* 2(3) J Forensic Nurs. 142 (2006).

[24] *E.g.,* ''Preventing the Accumulation of Surplus Controlled Substances at Long Term Care Facilities,'' 66 FR 20833, Apr. 25, 2001; ''Role of Authorized Agents in Communicating Controlled Substance Prescriptions to Pharmacies,'' 75 FR 61613, Oct. 6, 2010.

HCPs will not address or stop the abuse of HCPs because other schedule II controlled substances such as oxycodone products are highly abused and diverted.

DEA response: The cycle of abuse between licit and illicit opioids, abuse of licit and illicit non-narcotic prescription drugs, and continued abuse of schedule I controlled substances such as LSD demonstrates that what individuals and communities are facing is not a problem specific to HCPs. Rather, it is an addiction problem. Heroin use and prescription drug abuse are both addictions that begin with use and are sustained and promoted through increased trafficking. This serious public health problem can be addressed by education, appropriate screening and treatment, recovery, support, and enforcement. These initiatives can be effective regardless of whether the problem is fed by heroin or prescription drugs, including HCPs, and the DEA supports all of these initiatives to address both prescription drug misuse and abuse and heroin use.

The problem of prescription drug abuse is fueled due to a combination of excessive prescribing, drug availability through friends and family, rogue pain clinics, practitioners who prescribe pharmaceutical controlled substances without legitimate medical purpose or outside the usual course of professional practice, pharmacies that dispense illegitimate prescriptions, and supply chain wholesalers and manufacturers that fail to provide effective controls and procedures to guard against diversion—all of which fuel illicit access at the expense of the public health and safety.

A balanced drug control strategy, one that includes strong enforcement, education, prevention, and treatment components, can make significant progress in protecting our nation from the dangers of drug abuse.

The DEA's enforcement responsibility as it pertains to drugs and other substances is clearly delineated in Federal law. Pursuant to 21 U.S.C. 811(a), the CSA authorizes the DEA, under authority delegated by the Attorney General, to add to a schedule any drug or other substance if it is found that the drug or other substance has a potential for abuse, and makes with respect to such drug or other substance the findings prescribed by 21 U.S.C. 812(b). As such, the legal system established by Congress specifically accounts for new substances to be added to the list of controlled substances without regard to the number of substances already controlled. *See also* 21 U.S.C. 812(a) (''Such schedules shall *initially* consist of * * *'' (*emphasis added*)).

The dynamic structure constructed in the establishment of the schedules of controlled substances takes into consideration that the conclusions reached under each of the eight-factors specified under 21 U.S.C. 811(c) may change over time. Scientific knowledge about a drug or substance grows, pharmacological knowledge increases, history and current patterns of abuse change, etc. The CSA scheduling protocols also take into account that new drug applications for drugs with abuse potential are submitted to and approved by the FDA as well as that clandestine chemists attempt to manipulate the molecular structures of controlled substances to create synthetic drugs that would have the same pharmacologic properties of a controlled drug, but not expose the chemist or distributor to criminal violations. The CSA, however does not only account for one-time scheduling determinations regarding the control of drugs and other substances. In addition to the initial control of drugs and other substances to schedules, the CSA likewise takes into account and provides for the transfer of a drug or other substance between schedules, or for a drug or other substance to be removed entirely from the schedules. 21 U.S.C. 811(a) and (b).

Nevertheless, the DEA disagrees that control of HCPs in schedule II will not decrease abuse of HCPs. Control of HCPs in schedule II will result in increased monitoring of these drugs as well as increased safeguards for legitimate prescriptions.

7. Diversion Prevention

Commenters also questioned whether moving HCPs to schedule II would reduce diversion of HCPs. These commenters argued that the proposed schedule II controls for HCPs will not address or stop the diversion of HCPs because other schedule II controlled substances such as oxycodone products are still diverted despite their schedule II status.

DEA response: The DEA disagrees that control of HCPs as schedule II controlled substances will not decrease their diversion. Control of HCPs into schedule II will result in increased monitoring of these drugs as well as increased safeguards for legitimate prescriptions.

8. Responsibilities of Pharmacists

The DEA received many comments, from pharmacists, physicians, ultimate users, and the general public, who were concerned that the increased administrative burden on pharmacists that might occur as a result of moving HCPs into schedule II would cause pharmacists to devote time to the administrative burdens rather than on patient counseling and safety. Commenters stated that the administrative burden would be greatly increased in the pharmacy setting because: separate prescriptions would have to be entered for every HCP; pharmacists would have to count the prescriptions, as technicians are not legally allowed to do so in some States; inventories would be required of all HCPs; and increased workload associated with recordkeeping requirements (i.e., DEA Form 222).

DEA response: The processes and procedures associated with dispensing a controlled substance are not relevant factors to the determination of whether a substance should be controlled or under what schedule a substance should be placed if it is controlled. *See* 21 U.S.C. 811 and 812.

9. Requirements Applicable to Manufacturers and Distributors

a. Effective Date

Several of the comments submitted by members of industry (manufacturers, wholesale distributors, veterinary distributors, retail pharmacies), and/or trade associations representing them, focused on the timeframe for implementation of various handling requirements. A national trade association comprised of manufacturers and distributors of generic pharmaceutical products requested that the DEA ''allow sufficient time for all parts of the supply chain to integrate the new requirements into their business operations.'' Similar requests were also posed by an individual manufacturer of HCPs, a wholesale distributor, and a retail pharmacy/mail pharmacy service provider, each who proposed a blanket six month delay before a final rule would go into effect. A national trade association comprised of distributors requested that the DEA allow at least 12 to 24 months, with opportunity for additional extension for individual registrants on an as needed basis, from the effective date of the final rule to allow for changes to facilities, policies and procedures. The national trade association requested that during the interim period registrants be allowed to continue to hold HCPs in cages rather than to be immediately required to place these items in vaults. Specifically, the association proposed that the DEA ''[r]ecognize a registrant's compliance with the physical security requirements if the registrant has, by the implementation date of the storage

requirements resulting from a rescheduling decision, submitted to the agency plans, blueprints, sketches, or other materials, including but not limited to signed contracts with contractors to implement any proposed physical security changes to the registrant's premises, and has otherwise been and continues to be in compliance with physical security requirements pursuant to [21 CFR 1301.72] for HCPs subject to this rescheduling decision as of the date prior to the effective date of a rescheduling decision.'' The national trade association additionally requested that the DEA provide specifics regarding the ''process for submission of the materials demonstrating the vault construction plans'' and how they might be able to ''demonstrate compliance in lieu of vault construction completion.''

DEA Response: In accordance with the Administrative Procedure Act, generally, DEA scheduling actions are effective 30 days from the date of publication of the final rule in the **Federal Register**. 5 U.S.C. 553(d). In order to ensure the continued availability of HCPs for legitimate medical use, while also ensuring they are not subject to misuse, abuse, and diversion, the DEA is establishing an effective date 45 days from the date of publication of this final rule. This 45-day period is a reasonable amount of time for registrants to comply with the handling requirements for a schedule II controlled substance and was established upon a full consideration of the totality of circumstances specific to HCPs.

The DEA understands that 45 days to implement all schedule II handling requirements may be perceived as short by some distributors. While the DEA acknowledges that the supply chain will need to plan and coordinate efforts, and may even need to temporarily modify existing ordering and inventory management practices, the DEA is required to consider the risk of diversion and risk to public health and safety of U.S. residents.

As summarized in the NPRM and the DEA presentation at the January 24, 2013, public DSaRM meeting, available at *http://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/drugs/drugsafetyandriskmanagmentadvisorycommittee/ucm346941.pdf,* and discussed in detail in the supporting eight-factor analyses, HCPs are being abused with adverse effects both individually and to the public health and safety, accordingly, it should be placed into schedule II as soon as practicable. Prescription drug abuse refers to the intentional misuse of a medication by using more than medically indicated in order to feel the drug's psychoactive effects and/or using the drug in a manner that is not medically indicated. Prescription drug abuse has increased exponentially in the last 15 years and is the Nation's fastest growing drug problem. Factors including excessive prescriptions, drug availability through friends and family, Internet trafficking, rogue pain clinics, pharmacies that dispense illegitimate prescriptions, and failed safeguards by wholesalers and manufacturers to guard against diversion have all contributed to the prescription drug abuse problem.

The increase in prescription drug abuse has also been attributed to ease of obtaining the drug and the misconception that abusing prescription drugs is much safer than using and abusing street drugs. According to the 2012 Partnership Attitude Tracking Study (PATS), 43% of teenagers believe that prescription medications are ''easier to obtain'' than illegal drugs. In addition, the 2012 PATS also reported that 27% of teens believe that misusing or abusing prescription drugs is ''safer'' than using street drugs. Some of the increased demand for prescription opioid painkillers is from people who use them non-medically (using drugs without a prescription or just for the high they cause), sell them, or get them from multiple prescribers at the same time (CDC Vital Signs, July 2014, Opioid Painkiller Prescribing, Where You Live Makes a Difference).

According to the 2012 National Survey on Drug Use and Health (NSDUH), approximately 2.6% or 6.8 million people ages 12 and older are nonmedical users of prescription drugs. Abuse of opioid drugs, including HCPs, can lead to addiction, respiratory depression, and death. There were more than 16,000 deaths due to abuse of opioid drugs including HCPs in 2010. That is more than 1,333 people dying each month. According to the CDC, 38,329 people died from a drug overdose in the United States in 2010. Of these deaths, 22,134 people or 60% involved prescription drugs. Seventy-five percent of the prescription drug overdose deaths (16,651 people) were due to opioid drugs primarily containing oxycodone, hydrocodone, or methadone.

Abuse of prescription drugs is particularly alarming since data are strongly indicating that prescription opioid drug abuse can lead to heroin abuse.[25] Specifically, the data show that the population with the highest rate of heroin initiation was that population with prior nonmedical pain reliever use. The rate of heroin initiation among prior nonmedical pain reliever users was approximately 19 times greater than those who did not have such prior use. The rate of heroin initiation increased with increases in the frequency of past year nonmedical pain reliever use. *Id.*

The DEA has long held that increased heroin use is driven primarily by an increase in the misuse and abuse of prescription opioid drugs, particularly HCPs. The DEA's investigations indicate that the cost of prescription opioid drugs on the street may be as high as $80.00 per tablet and makes it difficult for teens and young adults to purchase drugs in support of their addiction. Therefore, abusers of prescription opioid drugs may resort to using heroin, a much cheaper alternative that produces similar euphoric effects, to keep the drug seeker/abuser from experiencing painful withdrawal symptoms. According to the most recent NSDUH, there were 335,000 heroin users in 2012, which is more than double the number in 2007 (161,000). In the decade from 2002 to 2011, the annual number of drug poisoning deaths involving heroin doubled, from 2,089 deaths in 2002 to 4,397 deaths in 2011.[26]

HCPs are the most prescribed drug in the United States. Production of HCPs has increased from 15,359 kilograms in 1998 to 63,338 kilograms in 2012 (IMS, 2014). Increased production of HCPs is directly due to the increased prescription of these drugs to treat and alleviate pain. Even though there is legitimate use of HCPs, data indicate that a considerable population misuse HCPs. The National Poison Data System (NPDS) reported during the period of 2006–2012, that 45.4% of the total exposures to HCPs were considered intentional exposures, a surrogate to usage for abuse or misuse. The high percentage of HCPs for misuse supports that HCPs are contributing to prescription opioid drug abuse and may consequently lead to heroin abuse and death.

In order to prevent continued misuse, abuse and diversion, it is necessary to set an effective date for this scheduling action, including security and labeling requirements, with all reasonable haste.

[25] SAMHSA, Center for Behavioral Health Statistics and Quality, Data Review, Associations of Nonmedical Pain Reliever Use and Initiation of Heroin Use in the United States. August 2013 available at *http://www.samhsa.gov/data/2k13/DataReview/DR006/nonmedical-pain-reliever-use-2013.htm.*

[26] Hedegaard H, Chen L–H, and Warner M. Quick Stats: Rates of Drug Poisoning Deaths Involving Heroin, * by Selected Age and Racial/Ethnic Groups—United States, 2002 and 2011, MMWR 2014; 63:595.

After careful consideration of the risk to the U.S. public health and safety related to the diversion and abuse of HCPs, the DEA believes the 45-day effective date is reasonable.

From the 2007 Economic Census, the DEA estimates that the inventory turnover ratio for the industry [27] is approximately 11.3.[28] The inventory turnover ratio represents the number of times the inventory sells (turns) in a year. The 11.3 inventory turnover ratio equates to an average of 32 days to sell inventory. The 11.3 turnover ratio is consistent with that of large distributors where financial information was publicly available and reviewed. The inventory turnover ratio is a reasonable estimate for the entire industry and all products under the circumstances. Publicly reviewed data show that about 85% of all revenues (an indirect indicator of dosage units moved) from drug distribution in the United States come from three public wholesalers, each with annual revenue in the billions. The DEA additionally notes that many regional and specialist pharmaceutical wholesalers have been acquired by the largest three distribution companies. Because the 32 days to sell inventory is an average based on industry-wide Census data, it is possible for an individual company and/or product line to experience a shorter or longer time to sell.

Since HCPs are the most prescribed opioid drugs in the United States, with over 137 million prescriptions dispensed in 2013,[29] the DEA expects distributors to continue to receive and distribute HCPs at high volume and with regularity; thus, anticipating shorter than average days to sell HCPs than the overall industry average ratio. In other words, the very high volume of sales indicates that HCPs are moving very quickly through the supply chain to meet demand, indicating high turnover and low inventory. However, to accommodate those manufacturers and distributors that have lower than average industry turnover ratio, the DEA is establishing an effective date of this final rule, including labeling and packaging requirements, 45 days from the date of publication. Based on the available information, and the lack of specific information regarding manufacturer and distributor inventory practices with respect to HCPs, the DEA believes this will provide a reasonable time for distributors to sell existing stock with pre-control labeling and packaging (C–III) and to stock inventory with post-control labeling and packaging (C–II).

The DEA anticipates manufacturers to begin developing inventory of HCPs with schedule II labels prior to the effective date of the rule to have stock ready to be distributed upon effect of this rule. The DEA estimates that 45 days is a reasonable amount of time for manufacturers and distributors to deplete existing inventory of HCPs. The packaging and labeling requirements for manufacturers and distributors do not apply to dispensers. Dispensers with HCPs in commercial containers labeled as schedule III may continue to dispense these HCPs after the implementation of this rule.

The DEA believes that HCPs labeled as C–III can be exchanged with HCPs containing new labels at nominal cost. The rule allows this exchange in a similar manner to the return of expired controlled substances authorized under existing regulations. Since manufacturers are expected to have ready-inventory of HCPs with new labels, exchanges are expected to occur without delay. In this rule, the DEA is allowing transfers of HCPs labeled as schedule III to be returned in exchange for HCPs labeled as schedule II without the requirement for procurement quota. Therefore, the DEA believes HCP manufacturers and distributors can reasonably make the necessary labeling changes and have inventory to meet the demands of customers.

The DEA acknowledges distributors may need to make some modifications to their inventory management system and operating procedures. However, these changes are expected to be procedural changes with only nominal impact on the burden created by the activities. For example, a distributor will need to receive, unpack, record the product in inventory, store, accept orders, and ship out to customers. These are all activities that occur regardless of the control status of HCPs. The anticipated changes may be a modification to the inventory management system and possible expansion of storage space (vaults).

The DEA has carefully considered the security requirements for compliance with this rule. As confirmed by the national trade association comprised of distributors, current distributors of HCPs are DEA registrants with existing controlled substance storage facilities that comply with DEA regulations. The DEA believes the DEA regulations provide flexibility that enables the supply chain to quickly implement the new rule without delay or significant cost.

Modifications necessary for physical security compliance will be a one-time modification primarily to provide for appropriate storage. The DEA understands that handlers of HCPs may also need to make modifications to their current security procedures for compliance. To a lesser extent, there may be necessary modifications to operating procedures, staff training, and amendments to suspicious order monitoring systems. However, due to the high diversion and abuse profile of HCPs, it is reasonably likely that most, if not all, manufacturers and distributors already provide controls and procedures to guard against theft and diversion of HCPs. That is, due to the high diversion potential of HCPs, most, if not all, manufacturers and distributors likely already have operating procedures (e.g., suspicious order monitoring systems, staff training) to guard against theft and diversion of HCPs, thereby necessitating minimal (if any) changes to these non-physical security controls. The DEA believes that a 45-day period will provide handlers of HCPs a reasonable amount of time to implement any one-time modifications to comply with the DEA regulations. Registrants are familiar with the applicable security regulations, and already have systems in place with respect to other schedule II controlled substances. Accordingly, it is reasonable to revise operating procedures, amend monitoring systems, and train staff with respect to HCPs as schedule II controlled substances within the 45-day compliance timeframe.

The DEA has specifically chosen not to stagger implementation dates of handling requirements for the reasons stated herein. Also, different implementation dates leads to confusion and inconsistent application of the law, particularly with respect to rescheduling a drug from schedule III to schedule II. Schedule II and III substances are subject to different recordkeeping and reporting requirements, for example, and registrants would have difficulty keeping and maintaining records and inventories. Also, if one registrant category were to handle HCPs as schedule III controlled substances while another registrant category were to handle HCPs as schedule II controlled substances, it would be confusing (for the registrants and for enforcement authorities), particularly with respect to the relevant transaction records.

[27] NAICS 424210—Drugs and druggists' sundries merchant wholesalers; Merchant wholesalers, except manufacturers' sales branches and offices.

[28] The inventory turnover ratio of 11.3 was calculated by dividing the 2007 ''cost of goods sold'' for the industry of $280,481,051,000 by the average end-of-year 2006 and 2007 total inventories of $24,782,835,000.

[29] IMS Health, National Sales Perspective ™ (NSP).

The DEA strongly advises registrants to work closely with their local DEA office regarding submission of materials, storage containers, all applicable security requirements, and any necessary modifications due to compliance with this rule. 21 CFR 1301.71(d); *see also* 21 CFR 1307.03. After 45 days from the date of publication, HCPs will be subject to schedule II security requirements and must be handled and stored pursuant to 21 U.S.C. 821 and 823 and in accordance with 21 CFR 1301.71–1301.93.

b. Distribution of C–III Labeled HCPs Post Implementation

The comments of a manufacturer, wholesale distributor, and national trade association comprised of distributors, each discussed their concerns about how commercial containers of HCPs labeled as ''C–III'' would be handled. The manufacturer requested that the DEA allow at least nine months from the date of issuance of the final rule for distribution of commercial products labeled as ''C–III'' in order to allow time for the supply chain to be restocked. This same company also requested that the DEA clarify the ability of reverse distributors and other registrants to continue to handle HCPs labeled as ''C–III'' for at least three months after the expiration date of the substance, in order to account for handling HCPs for purposes of destruction. The wholesale distributor wrote in favor of immediate implementation of the use of DEA Form 222, while allowing HCPs already labeled as C–III to be continuously distributed until depleted.

DEA response: For the reasons discussed in response to the previous comments, as of the effective date of the final rule, pursuant to 21 U.S.C. 821, 825, and 958(e) and in accordance with 21 CFR 1302.03, manufacturers are required to print upon the labeling of each commercial container of HCPs they distribute the designation of HCPs as ''C–II.'' It shall be unlawful for commercial containers of HCPs to be distributed downstream without bearing the label properly identifying them as schedule II controlled substances in accordance with 21 CFR part 1302. As clearly stated in 21 CFR 1302.05, ''[a]ll labels on commercial containers of, and all labeling of, a controlled substance which either is transferred to another schedule or is added to any schedule shall comply with the requirements of § 1302.03, on or before the effective date established in the final order for the transfer or addition.'' Accordingly, the DEA is requiring that commercial containers of HCPs distributed on or after 45 days from the date of publication of the final rule be labeled as ''C–II'' and be packaged in accordance with 21 CFR part 1302.

A distribution of HCPs on or after the effective date of this final rule, is a distribution of a schedule II controlled substance, and a DEA Form 222 is required to be used to conduct the transfer in accordance with 21 CFR 1305.03. A registrant may transfer commercial containers of HCPs labeled as ''C–III'' upstream on or after the effective date of the final rule, with utilization of a DEA Form 222 as required in accordance with 21 CFR 1305.03. Utilization of the DEA Form 222 ensures that schedule I and II controlled substances are accounted for, and allows for the detection and prevention of diversion.

Additionally, as discussed previously in more detail in the Economic Impact Analysis, the DEA believes that any manufacturer or distributor that requires more than 45 days to sell HCP inventory under normal circumstances can make minor modifications to ordering and stocking procedure for a transitional period to meet the established effective date. Distributors also have the option of returning excess stock of HCPs labeled as ''C–III'' to the manufacturer, or the manufacturer's authorized agent, as authorized by this final rule, or in accordance with 21 CFR 1307.12.

The DEA takes this opportunity to clarify that the regulation pertaining to labeling of commercial containers applies to distributions by manufacturers and distributors. The DEA does not regulate the labeling and packing of commercial containers of controlled substance downstream of distributors.

c. Exemption of Distributors and Manufacturers

A national trade association comprised of distributors and an individual manufacturer of HCPs requested that the DEA provide an exemption from the schedule II controlled substance security requirements for manufacturers and distributors of HCPs. Both commenters based this request on the assertion that manufacturers and distributors are not a documented significant source of diversion.

DEA response: Scheduling determinations are based on scientific determinations regarding the drug or other substance's potential for abuse, its potential for psychological and physical dependence, and whether the drug or other substance has a currently accepted medical use in treatment in the United States. 21 U.S.C. 812(b). The DEA may not reschedule, or refuse to reschedule, a drug or other substance based on purported sources of diversion. One of the primary functions of the DEA Diversion Control Program is to ensure that registrants are in compliance with the safeguards inherent in the CSA. This proactive approach is designed to identify and prevent the large scale diversion of controlled substances and listed chemicals into the illicit market. Manufacturers and distributors pose the greatest potential for large-scale diversion. As discussed in the final rule, ''Controlled Substances and List I Chemical Registration and Reregistration Fees,'' there is great risk and grave consequences associated with the quantity and purity of controlled substances and/or chemicals with each manufacturer at this point in the closed system. 77 FR 15234, 15241, March 15, 2012. Accordingly, non-practitioners such as manufacturers and distributors must adhere to very stringent physical security requirements. The DEA has determined that there is a high potential for abuse of HCPs, and this, *inter alia,* requires that HCPs be controlled in schedule II. The physical security requirements applicable to schedule II controlled substances will provide secure controls to detect and prevent diversion of HCPs. Accordingly, the DEA declines to exempt manufacturers or distributors from the physical security requirements applicable to HCPs upon control in schedule II. However, the DEA encourages manufacturers and distributors to work closely with their local DEA office regarding submission of materials, storage containers, all applicable security requirements, and any necessary modifications due to compliance with this rule. 21 CFR 1301.71(d); *see also* 21 CFR 1307.03.

10. Economic Impact

a. Cost to Ultimate Users

Several commenters stated that the DEA had failed to fully take into account costs and impacts to ultimate users in its economic impact analysis.

DEA response: Scheduling decisions are based on scientific determinations regarding the drug or other substance's potential for abuse, its potential for psychological and physical dependence, and whether the drug or other substance has a currently accepted medical use in treatment in the United States. 21 U.S.C. 812(b). The DEA may not reschedule, or refuse to reschedule, a drug or other substance based on the population it is intended or approved to treat, or potential impacts thereon. However, as

discussed above, scheduling or rescheduling a drug does not hinder legitimate access to needed medication. For the reasons discussed earlier in this document, the DEA does not believe that there will be significant impacts, if any, on ultimate users associated with this rulemaking.

b. Cost of Physical Security

Several commenters suggested that it would cost millions of dollars for distributors and retail pharmacies to obtain new vaults or increase the size of their vaults to accommodate for the influx of HCPs. Another commenter suggested that only a limited number of firms can build vaults that meet the requirements of the DEA and because of this, constructing a vault would be time consuming and costly.

DEA response: Scheduling determinations are based on scientific determinations regarding the drug or other substance's potential for abuse, its potential for psychological and physical dependence, and whether the drug or other substance has a currently accepted medical use in treatment in the United States. 21 U.S.C. 812(b). The DEA may not reschedule, or refuse to reschedule, a drug or other substance based on economic impacts.

Retail pharmacies are not required by the CSA or DEA regulations to place schedule II controlled substances in a vault or safe. In accordance with 21 CFR 1301.75(b), pharmacies may disperse schedule II controlled substances throughout their stock of noncontrolled substances in such a manner as to obstruct the theft or diversion of the controlled substances.

11. Proposed Alternatives

a. Establishment of a National Prescription Drug Monitoring Program (PDMP)

Several commenters requested the implementation of a national prescription drug monitoring program (PDMP) either as an alternative to rescheduling HCPs, or possibly in addition thereto, as a means of curtailing doctor shopping and preventing abuse. For example, one commenter noted that ''Despite broad consensus that prescribers and public health officials need these essential tools modernized to support clinical decision-making and identify state and regional patterns of abuse and diversion, state-based PDMPs continue to have limited financial resources and interoperability * * *.'' Another commenter stated that PDMPs ''can be improved by creating incentives for inter-state connectivity, making data available in a more timely fashion and unifying standard submissions.''

DEA response: One of the best ways to combat the rising tide of prescription drug abuse is the implementation and use of PDMPs. PDMPs help prevent and detect the diversion and abuse of pharmaceutical controlled substances, particularly at the retail level where no other automated information collection system exists. PDMPs are valuable tools for prescribers, pharmacists, and law enforcement agencies to identify, detect, and prevent prescription drug abuse and diversion.

The DEA supports and encourages the development and maintenance of PDMPs at the State level. Currently, 48 States have an operational PDMP (meaning collecting data from dispensers and reporting information from the database to authorized users). One State has enacted legislation enabling the program to come online; Missouri has no state PDMP. As of February, 2014, only 16 States mandate usage of PDMP. Of those 16 States, 6 States mandate its usage in designated circumstances and 10 mandate its use in broader circumstances. Currently, 26 States have adopted the Interconnect platform for data sharing.

The DEA agrees with these commenters that the use of PDMPs is challenging across State lines because interconnectivity is limited. Interconnectivity or a nationwide system would help deter and detect drug traffickers and drug seekers, many of whom willingly travel hundreds of miles to gain easy access to unscrupulous pain clinics and physicians.

The Department has supported the development of PDMPs through the Harold Rogers Prescription Drug Monitoring grant program, distributing a total of over $87 million from FY 2002 to FY 2014, including $7 million in FY 2014. The purpose of this program is to enhance the capacity of regulatory and law enforcement agencies to collect and analyze controlled substance prescription data. It focuses on providing help for States that want to establish a PDMP or expand an existing PDMP. In 2012, the Department provided further policy guidance on data sharing efforts among State PDMPs, a critical aspect of the program.

b. Better Utilization of Currently Established State PDMPs Already in Existence

One commenter suggested that State monitoring systems should be used in a way to specifically identify usage of HCPs in the respective State. The commenter stated that this would allow each State to develop its own methods for handling the abuse of HCPs problem rather than making a nationwide rule rescheduling HCPs to schedule II. Another commenter suggested that practitioners should use State prescription monitoring programs more to prevent unnecessary refills and prescriptions, thereby preventing abuse. Another commenter suggested that States should be mandated to implement a PDMP if they don't already have one in existence.

DEA response: As mentioned above, States are free to implement their own PDMP. Moreover, States may customize their PDMP in a way that is most beneficial to that State. The States can do this so long as the laws governing the program do not conflict with the CSA, DEA regulations, or other federal law.

However, the DEA, as required by the CSA, has an obligation to control drugs or other substances that have a potential for abuse. Once the DEA controls a drug or substance, it must apply the provisions of the CSA to that newly controlled drug or substance. As stated, scheduling determinations are based on scientific determinations regarding the drug or other substance's potential for abuse, its potential for psychological and physical dependence, and whether the drug or other substance has a currently accepted medical use in treatment in the United States. 21 U.S.C. 812(b).

c. Establishment of a List of ''Vetted Patients''

One commenter suggested ''that people who genuinely need the medication * * * be listed in the state monitoring system as patients who have been vetted and should be prescribed the medication without [schedule II] requirements.'' The commenter proposed that such vetting could be done on a six month renewal basis.

DEA response: The CSA does not prevent the States from enacting laws related to controlled substances or prevent States from creating stricter laws. *See* 21 U.S.C. 903. However, States cannot create rules that are more relaxed than the CSA, and its implementing regulations, as this would be a conflict. *See Id.* Creating a list of vetted patients who do not have to comply with schedule II requirements would be in direct conflict with the CSA and schedule II prescription requirements. An individual practitioner must determine if an individual has a legitimate medical purpose to be issued a prescription for a controlled substance each time a prescription is issued. There is no

mechanism to ''vet'' a patient in the CSA.

d. Monitoring and/or Enforcement

One commenter stated that ''I believe more effort should go into the monitoring the narcotics registry and targeting [of] patients or doctors that are suspicious for abuse rather than trying to restrict the narcotics given.'' Another suggested to ''vet the patients by 2 different doctor evaluations, vetting to extend for 6 months. Register the vetted patients in the state drug monitoring programs as 'OK' to obtain 90-day supplies. Patients not vetted get a very limited supply.''

DEA response: The DEA actively pursues administrative action and civil and criminal prosecution of DEA registrants and individuals who divert controlled substances. One of the primary functions of the DEA Diversion Control Program is to ensure that all DEA registrants are in compliance with the safeguards inherent in the CSA. This proactive approach is designed to identify and prevent diversion of controlled substances and listed chemicals into the illicit market. Insofar as the issuance of and the filling of controlled substance prescriptions is concerned, prescribers and pharmacies, have an obligation to ensure that they do not prescribe or dispense controlled substances to individuals with no legitimate medical purpose for the controlled substance.

e. Change of Prescription Requirements While Retaining Schedule III Status

Several commenters suggested that the DEA change prescription requirements for HCPs while keeping them as schedule III controlled substances instead of transferring them to schedule II of the CSA. For example, some commenters suggested that subcategories be created for specific categories of practitioners, such as oncologists or emergency practitioners. Other commenters suggested that the DEA should limit the quantity of HCPs prescribed or number of refills authorized instead of rescheduling HCPs. As an example, one commenter suggested that any HCP prescriptions of 30 tablets and under should remain as a schedule III controlled substance and prescriptions for over 30 tablets of HCPs should be a schedule II controlled substance.

DEA response: The DEA cannot retain schedule III status for HCPs, as the DEA has determined that HCPs satisfy the criteria for control in schedule II of the CSA. 21 U.S.C. 812(b).

The Assistant Secretary of the HHS provided a scientific and medical evaluation and a scheduling recommendation to control HCPs as a schedule II controlled substance. In accordance with 21 U.S.C. 811(c), the DEA conducted its own analysis of the eight factors determinative of control. Besides published literature, various other data as detailed in the supporting documents were considered in making the scheduling determination for HCPs. Thus, the scheduling determination is based on a comprehensive evaluation of all available data as related to the required eight factors. The summary of each factor as analyzed by the HHS and the DEA, and as considered by the DEA in this scheduling action, was provided in the proposed rule. Both the DEA and the HHS analyses have been made available in their entirety under ''Supporting and Related Material'' of the public docket for this rule at *http://www.regulations.gov* under Docket No. DEA–389. Based on the review of the HHS evaluation and scheduling recommendation and all other relevant data, the DEA found that HCPs have an abuse potential and meets the requirements for schedule II controls under the CSA.

f. Education of Prescribing Practitioners

Several commenters suggested that prescribing practitioners should receive education about the problems of HCP abuse, addiction, and prevention of diversion rather than rescheduling HCPs.

DEA response: The DEA fully supports efforts by medical professionals, acting alone and as part of professional organizations, as well as industry associations, to educate members of their profession/industry on the risks associated with prescription opioid use and on ways to prevent misuse, abuse, and diversion of prescription opioid products. These efforts are an important and integral part of tackling the problem of prescription opioid abuse.

However, as recognized by the CDC, the United States is in the midst of a public health crisis regarding prescription painkiller overdose. Individuals, families, and society are suffering the effects of abuse and addiction. People are dying. In their 2011 report, the CDC estimated that 75 opioid-related deaths occur each day. That equates to over 27,000 people each year. As a society, America simply cannot afford to wait for self-initiated educational programs and measures by medical professionals and industry to solve the problem on their own. As acknowledged by commenters advocating solely for an educational approach, opioid consumption in the United States continues to increase despite self-initiated professional educational endeavors such as symposia and scientific articles.

One physician who wrote in support of rescheduling asserted that only a limited number of practitioners have paid attention to the warnings issued regarding the risk of addiction, overdose, and death associated with use of HCPs. It was this physician's belief that: ''The opioid epidemic has mainly resulted from a large volume of misinformed doctors failing to understand the risks and limited benefits of these drugs, especially for chronic noncancer pain, one of the most common reasons why patients seek medical care.'' This concern has been echoed by the HHS. The HHS has noted ''Multiple studies have shown that a small percentage of prescribers are responsible for prescribing the majority of opioids.'' Behavioral Health Coordinating Committee, Prescription Drug Abuse Subcommittee, HHS. *Addressing Prescription Drug Abuse in the United States: Current Activities and Future Opportunities.* 2013. (internal citations omitted). The HHS points out, however, that ''Providers who are not high-volume prescribers may also contribute to opioid abuse and overdose because of a lack of education and awareness about appropriate opioid prescribing * * *.'' The HHS additionally stated, ''Even when sufficient information exists, studies show that some providers do not follow risk mitigation strategies even for patients known to be at high risk for abuse.'' *Id.* The physician-commenter asserted that ''Upscheduling hydrocodone combination products will, at the very least, send a clear message to these providers that hydrocodone is a narcotic in the same class as oxycodone, morphine and heroin, which should be prescribed and refilled with the utmost of selectivity, caution and close patient follow-up.''

The problem must be addressed both nationally and locally by using all available legal and social measures at hand. At the Federal level, this includes following the legal path directed by Congress to address issues of substance abuse and trafficking. As part of a comprehensive approach involving multiple Federal and State actors to address these concerns, Congress has charged the DEA with the responsibility to implement and enforce, to the fullest extent of the law, the requirements of the CSA. This includes ensuring that drugs and other substances are appropriately scheduled concordant with the factors for each schedule under 21 U.S.C. 812(b).

g. Education and Rehabilitation of Ultimate Users

Several commenters suggested that patient education and/or rehabilitation was the proper route to address abuse of HCPs rather than rescheduling.

DEA response: A multi-pronged approach, one that includes education, treatment, monitoring, and law enforcement is needed to combat this epidemic. The DEA supports all efforts to educate patients about the risks associated with use of substances with abuse potential. As discussed above, an analysis of the eight factors determinative of control demonstrates that HCPs warrant control II of the CSA. 21 U.S.C. 812(b).

h. Strict Enforcement/Sanctions

Several commenters voiced an opinion that there should be strict enforcement against those that have diverted and illegally sold prescription HCPs. These commenters stated it would be a good idea to ban these offenders from receiving HCPs or reduce limits on how much HCPs an offender can receive. In addition, several commenters suggested tougher sanctions and enforcement should be applied to providers who are not lawfully practicing their trade rather than punishing those who are obeying the laws.

DEA response: The DEA mission is to implement and enforce the CSA and corresponding regulations to the fullest extent of the law. The DEA actively pursues administrative action and civil and criminal prosecution of DEA registrants and other individuals who divert controlled substances. One of the primary functions of the DEA Diversion Control Program is to ensure that registrants are in compliance with the safeguards inherent in the CSA. The DEA supports State and local law enforcement, and State professional and regulatory boards in their efforts to prevent diversion and enforce the controlled substances laws.

V. Scheduling Conclusion

Based on consideration of all comments, the scientific and medical evaluation and accompanying recommendation of the HHS, and based on the DEA's consideration of its own eight-factor analysis, the DEA finds that these facts and all other relevant data constitute substantial evidence of potential for abuse of HCPs. As such, the DEA is rescheduling HCPs as a schedule II controlled substance under the CSA.

VI. Determination of Appropriate Schedule

The CSA outlines the findings required to transfer a drug or other substance between schedules (I, II, III, IV, or V) of the CSA. 21 U.S.C. 811(a); 21 U.S.C. 812(b). After consideration of the analysis and rescheduling recommendation of the Assistant Secretary for Health of the HHS and review of available data, the Administrator of the DEA, pursuant to 21 U.S.C. 811(a) and 21 U.S.C. 812(b)(2), finds that:

1. HCPs have a high potential for abuse. The abuse potential of HCPs is comparable to the schedule II controlled substance oxycodone;

2. HCPs have a currently accepted medical use in treatment in the United States. Several pharmaceutical products containing hydrocodone in combination with acetaminophen, aspirin, other NSAIDs, and homatropine are approved by the FDA for use as analgesics for pain relief and for the symptomatic relief of cough and upper respiratory symptoms associated with allergies and colds; and

3. Abuse of HCPs may lead to severe psychological or physical dependence.

Based on these findings, the Administrator of the DEA concludes that HCPs warrant control in schedule II of the CSA. 21 U.S.C. 812(b)(2).

VII. Requirements for Handling HCPs

Upon the effective date of this final rule, any person who handles HCPs will be subject to the CSA's schedule II regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, dispensing, importing, exporting, engaging in research, conducting instructional activities, and conducting chemical analysis, of schedule II controlled substances, including the following:

Registration. Any person who handles (manufactures, distributes, dispenses, imports, exports, engages in research, conducts instructional activities with, or conducts chemical analysis with) HCPs, or who desires to handle HCPs, must be registered with the DEA to conduct such activities pursuant to 21 U.S.C. 822, 823, 957, and 958, and in accordance with 21 CFR parts 1301 and 1312 as of October 6, 2014.

Security. HCPs are subject to schedule II security requirements and must be handled and stored pursuant to 21 U.S.C. 821 and 823, and in accordance with 21 CFR 1301.71–1301.93 as of October 6, 2014.

Labeling and Packaging. All labels, labeling, and packaging for commercial containers of HCPs must comply with 21 U.S.C. 825 and 958(e), and be in accordance with 21 CFR part 1302 as of October 6, 2014, except with respect to exchanges for purposes of relabeling/repackaging as provided below under ''Quotas.''

Quotas. A quota assigned pursuant to 21 U.S.C. 826 and in accordance with 21 CFR part 1303 is required in order to manufacture HCPs as of October 6, 2014. Registrants required to obtain an individual manufacturing quota shall not manufacture HCPs on or after October 6, 2014, unless an individual manufacturing quota is granted for such quantities of HCP to be manufactured. Registrants required to obtain a procurement quota shall not procure HCPs on or after October 6, 2014, unless a procurement quota is granted for such quantities of HCP to be procured.

Except, registrants authorized to manufacture schedule II and III controlled substances may relabel/repackage HCPs labeled as ''CIII'' or ''C–III'' without obtaining procurement quota for such activity, under the following conditions:

(1) The manufacturing activity occurs before December 8, 2014;

(2) if the manufacturer is relabeling/repackaging HCPs that were returned to the manufacturer, the manufacturer returns the same quantity and strength of HCPs labeled as ''CII'' or ''C–II'' back to the registrant that returned HCPs labeled as ''CIII'' or ''C–III'' to the manufacturer; and

(3) an invoice or the DEA Form 222 (whichever is applicable) records the transfer and reflects that the transfer occurred pursuant to the authority contained in this final rule.

For example, if before October 6, 2014, distributor A transfers 5 packages of 100-bottle 5/325 HCPs labeled as CIII/C–III to manufacturer B, solely for the purpose of relabeling, the invoice would reflect that the transfer occurred pursuant to the authority in this final rule. If the return occurs after October 6, 2014, the DEA Form 222 would reflect that the transfer occurred pursuant to the authority contained in this final rule. When the manufacturer distributes HCPs labeled as ''CII'' or C–II'' back to the registrant that returned the HCPs labeled as ''CIII'' or ''C–III,'' the manufacturer must return the same quantity and strength that was originally received for relabeling/repackaging. The DEA Form 222 will, again, reflect that the transfer occurred pursuant to the authority contained in this final rule.

In the above example, the manufacturer would not be required to obtain a procurement quota in order to relabel/repackage 5 packages of 100-bottle 5/325 HCPs, so long as

manufacturer B subsequently transfers to distributor A 5 packages of 100-bottle 5/325 HCPs labeled as CII/C–II, unless the relabel/repackage activity occurs after December 8, 2014.

Registrants may continue to return HCPs pursuant to 21 CFR 1307.12.

Inventory. Any person who becomes registered with the DEA on or after the effective date of the final rule must take an initial inventory of all stocks of controlled substances (including HCPs) on hand on the date the registrant first engages in the handling of controlled substances pursuant to 21 U.S.C. 827 and 958, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11(a) and (b) as of October 6, 2014.

After the initial inventory, every DEA registrant must take a new inventory of all stocks of controlled substances (including HCPs) on hand every two years pursuant to 21 U.S.C. 827 and 958, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

Records and Reports. Every DEA registrant must maintain records and submit reports with respect to HCPs pursuant to 21 U.S.C. 827 and 958, and in accordance with 21 CFR parts 1304 and 1312 as of October 6, 2014. Each pharmacy with a modified registration under 21 U.S.C. 823(f) that authorizes the dispensing of controlled substances by means of the Internet must submit reports to the DEA regarding HCPs pursuant to 21 U.S.C. 827 and in accordance with 21 CFR 1304.55 as of October 6, 2014.

Orders for HCPs. Every DEA registrant who distributes HCPs must comply with order form requirements, pursuant to 21 U.S.C. 821, 828, 871 and in accordance with 21 CFR parts 1305 and 1307 as of October 6, 2014.

Prescriptions. All prescriptions for HCPs must comply with 21 U.S.C. 829(a) and must be issued in accordance with 21 CFR part 1306 and subpart C of 21 CFR part 1311 as of October 6, 2014. No prescription for HCPs issued on or after October 6, 2014 shall authorize any refills. Any prescriptions for HCPs that are issued before October 6, 2014, and authorized for refilling, may be dispensed in accordance with 21 CFR 1306.22–1306.23, 1306.25, and 1306.27, if such dispensing occurs before April 8, 2015.

Importation and Exportation. All importation and exportation of HCPs must be in compliance with 21 U.S.C. 952, 953, 957, and 958, and in accordance with 21 CFR part 1312 as of October 6, 2014.

Liability. Any activity involving HCPs not authorized by, or in violation of, the CSA or its implementing regulations, occurring as of October 6, 2014, is unlawful, and may subject the person to administrative, civil, and/or criminal action.

VIII. Regulatory Analyses

Executive Orders 12866 and 13563

In accordance with 21 U.S.C. 811(a), this scheduling action is subject to formal rulemaking procedures performed ''on the record after opportunity for a hearing,'' which are conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth the procedures and criteria for scheduling a drug or other substance. Such actions are exempt from review by the Office of Management and Budget (OMB) pursuant to section 3(d)(1) of Executive Order 12866 and the principles reaffirmed in Executive Order 13563.

Executive Order 12988

This regulation meets the applicable standards set forth in sections 3(a) and 3(b)(2) of Executive Order 12988 Civil Justice Reform to eliminate drafting errors and ambiguity, minimize litigation, provide a clear legal standard for affected conduct, and promote simplification and burden reduction.

Executive Order 13132

This rulemaking does not have federalism implications warranting the application of Executive Order 13132. The rule does not have substantial direct effects on the States, on the relationship between the national government and the States, or the distribution of power and responsibilities among the various levels of government.

Executive Order 13175

This rule does not have tribal implications warranting the application of Executive Order 13175. It does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal Government and Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes.

Regulatory Flexibility Act

The Administrator, in accordance with the Regulatory Flexibility Act (5 U.S.C. 601–612) (RFA), has reviewed this rule, and by approving it, certifies that it will not have a significant economic impact on a substantial number of small entities. The purpose of this rule is to place HCPs into schedule II of the CSA. No less restrictive measures (i.e., non-control or control in a lower schedule) would enable the DEA to meet its statutory obligation under the CSA.

HCPs are widely prescribed drugs for the treatment of pain and cough suppression. Handlers of HCPs primarily include manufacturers, distributors, exporters, pharmacies, practitioners, mid-level practitioners, and hospitals/clinics.[30] It is possible that other registrants, such as importers, researchers, analytical labs, teaching institutions, etc., also handle HCPs. However, based on its understanding of its registrant population, the DEA assumes for purposes of this analysis that for all business activities other than manufacturers, distributors, exporters, pharmacies, practitioners, mid-level practitioners, and hospitals/clinics, that the volume of HCPs handled is nominal, and therefore *de minimis* to the economic impact determination of this rescheduling action.

Because HCPs are so widely prescribed, for the purposes of this analysis, the DEA conservatively assumes all distributors, exporters, pharmacies, practitioners, mid-level practitioners, and hospitals/clinics currently registered with the DEA to handle schedule III controlled substances are also handlers of HCPs. The DEA estimated the number of manufacturers and exporters handling HCPs directly from DEA records. In total, the DEA estimates that nearly 1.5 million controlled substance registrations, representing approximately 376,189 entities, would be affected by this rule.

The DEA does not collect data on company size of its registrants. The DEA used DEA records and multiple subscription-based and public data sources to relate the number of registrations to the number of entities and the number of entities that are small entities. The DEA estimates that of the 376,189 entities that would be affected by this rule, 366,351[31] are ''small entities'' in accordance with the RFA and Small Business Administration size

[30] For purposes of performing regulatory analysis, the DEA uses the definition of a ''practitioner'' as a physician, veterinarian, or other individual licensed, registered, or otherwise permitted, by the United States or the jurisdiction in which he/she practices, to dispense a controlled substance in the course of professional practice, but does not include a pharmacist, pharmacy, or hospital (or other person other than an individual). For the purposes of performing regulatory analysis, ''mid-level practitioner'' means an individual registered with the DEA as a ''mid-level practitioner'' but does not include practitioners as defined above. Examples of mid-level practitioners include, but are not limited to, health care providers such as nurse practitioners, nurse midwives, nurse anesthetists, clinical nurse specialists and physician assistants.

[31] The estimated break-down is as follows: 50 manufacturers; 4 exporters; 683 distributors; 50,774 pharmacies; and 314,840 persons registered as or employing practitioners/mid-level practitioners/hospitals/clinics.

standards. 5 U.S.C. 601(6); 15 U.S.C. 632.

The DEA examined the registration, security (including storage), labeling and packaging, quota, inventory, recordkeeping and reporting, ordering, prescribing, importing, exporting, and disposal requirements for the 366,351 small entities estimated to be affected by the rule. The DEA estimates that only the physical security requirements will have material economic impact and such impacts will be limited to manufacturers, exporters, and distributors. Many manufacturers and exporters are likely to have sufficient space in their existing vaults to accommodate HCPs. However, the DEA understands that some manufacturers, exporters, and distributors will need to build new vaults or expand existing vaults to store HCPs in compliance with schedule II controlled substance physical security requirements. Due to the uniqueness of each business, the DEA made assumptions based on research and institutional knowledge of its registrant community to quantify the costs associated with physical security requirements for manufacturers, exporters and distributors.

The DEA estimates there will be significant economic impact on 1 (2.0%) of the affected 50 small business manufacturers, and 54 (7.9%) of the affected 683 small business distributors. The DEA estimates no significant impact on the remaining affected 4 small business exporters, 50,774 small business pharmacies, or 314,840 small business practitioners/mid-level practitioners/hospitals/clinics.

In summary, 55 of the 366,351 (0.015%) affected small entities are estimated to experience significant impact, (i.e., incur costs greater than 1% of annual revenue) as a result of this rule being finalized. The percentage of small entities with significant economic impact is below the 30% threshold for all registrant business activities. The DEA's assessment of economic impact by size category indicates that the rule to reschedule HCPs as schedule II controlled substances will not have a significant economic impact on a substantial number of small entities.

Unfunded Mandates Reform Act of 1995

On the basis of information contained in the ''Regulatory Flexibility Act'' section above, the DEA has determined and certifies pursuant to the Unfunded Mandates Reform Act (UMRA) of 1995 (2 U.S.C. 1501 *et seq.*), that this action would not result in any Federal mandate that may result ''in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted for inflation) in any one year * * *.'' Therefore, neither a Small Government agency Plan nor any other action is required under provisions of the UMRA of 1995.

Paperwork Reduction Act of 1995

This action does not impose a new collection of information requirement under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3521). This action would not impose recordkeeping or reporting requirements on State or local governments, individuals, businesses, or organizations. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Congressional Review Act

This rule is not a major rule as defined by section 804 of the Small Business Regulatory Enforcement Fairness Act of 1996 (Congressional Review Act (CRA)). This rule will not result in: an annual effect on the economy of $100,000,000 or more; a major increase in costs or prices for consumers, individual industries, Federal, State, or local government agencies, or geographic regions; or significant adverse effects on competition, employment, investment, productivity, innovation, or on the ability of United States-based companies to compete with foreign based companies in domestic and export markets. However, pursuant to the CRA, the DEA has submitted a copy of this final rule to both Houses of Congress and to the Comptroller General.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, 21 CFR part 1308 is amended as follows:

PART 1308—SCHEDULES CONTROLLED SUBSTANCES

■ 1. The authority citation for 21 CFR part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b) unless otherwise noted.

§ 1308.13 [Amended]

■ 2. Amend § 1308.13 by removing paragraphs (e)(1)(iii) and (iv) and redesignating paragraphs (e)(1)(v) through (viii) as (e)(1)(iii) through (vi), respectively.

Dated: August 15, 2014.

Michele M. Leonhart,

Administrator.

[FR Doc. 2014–19922 Filed 8–21–14; 8:45 am]

BILLING CODE 4410–09–P

DEPARTMENT OF THE TREASURY

Internal Revenue Service

26 CFR Part 1

[TD 9676]

RIN 1545–BJ59

Allocation and Apportionment of Interest Expense; Correction

AGENCY: Internal Revenue Service (IRS), Treasury.

ACTION: Correcting amendment.

SUMMARY: This document contains corrections to final regulations (TD 9676) that were published in the **Federal Register** on Wednesday, July 16, 2014 (79 FR 41424) providing guidance concerning the allocation and apportionment of interest expense by corporations owning a 10 percent or greater interest in a partnership, as well as the allocation and apportionment of interest expense using the fair market value method. These regulations also update the interest allocation regulations to conform to the statutory changes made by section 216 of the legislation commonly referred to as the Education Jobs and Medicaid Assistance Act (EJMAA), enacted on August 10, 2010, affecting the affiliation of certain foreign corporations for purposes of section 864(e). These regulations affect taxpayers that allocate and apportion interest expense.

DATES: This correction is effective on August 22, 2014, and is applicable July 16, 2014.

FOR FURTHER INFORMATION CONTACT: Jeffrey L. Parry at (202) 317–6936 (not a toll-free number).

SUPPLEMENTARY INFORMATION:

Background and Explanation of Provisions

The final regulations that are the subject of this document are under section 864(e) of the Internal Revenue Code.

Need for Correction

As published, final regulations (TD 9676) contain errors that may prove to be misleading and are in need of clarification.

Attachment 6

Pharmacy_Subscriberlist@DCA

From: General Board of Pharmacy Subscriber List <PHARM-GENERAL@DCALISTS.CA.GOV> on behalf of Board of Pharmacy <pharmacy.subscriberlist@DCA.CA.GOV>
Sent: Friday, August 15, 2014 5:29 PM
To: PHARM-GENERAL@DCALISTS.CA.GOV
Subject: CA State Board of Pharmacy Subscriber Alert

Please be aware that effective August 18, Tramadol will move to Schedule IV in the Federal Controlled Substances Schedule. A link to the DEA's website where this action is formally listed is http://www.deadiversion.usdoj.gov/fed_regs/rules/2014/fr0702.htm

This classification also makes Tramadol a Schedule IV medication in California.

In California, the prescribing of C-IV drugs is governed by the Health & Safety Code, including section 111164. This means a California security prescription form will now be required to prescribe Tramadol in writing, just like any other Schedule IV medication. Additionally, oral orders for Tramadol, as a Schedule IV medication, are permitted.

California law provides that Schedule IV medications can be refilled according to the parameters specified in Health & Safety Code section 11200.

Also on August 18, the dispensing of Tramadol is required to be reported in CURES.

Patients with a new prescription for Tramadol written on or after August 18 need to be written on security paper or turned into an oral prescription by the pharmacy, which will require a confirming call to the prescriber's office.

An existing prescription for Tramadol with refills on file in a pharmacy can be refilled for up to six months from August 18, unless the refills indicated on the prescription run out sooner, or reach the quantity limits specified in Health & Safety Code section 11200.

To unsubscribe from this email list please click on the link below and follow the instructions on the web page.

https://www.dca.ca.gov/webapps/pharmacy/subscribe.php

(ii) *Indications for use.* For reduction of the incidence of cervical abscesses; treatment of bacterial swine enteritis (salmonellosis or necrotic enteritis caused by *Salmonella choleraesuis* and vibrionic dysentery); prevention of these diseases during times of stress; and maintenance of weight gains in the presence of atrophic rhinitis.

(iii) *Limitations.* Feed as the sole ration. Withdraw 15 days prior to slaughter.

§ 558.145 [Amended]

■ 3. In § 558.145, in paragraph (a)(2), remove ''Nos. 048164 and 054771'' and in its place add ''No. 048164''.

Dated: June 25, 2014.

Bernadette Dunham,

Director, Center for Veterinary Medicine.

[FR Doc. 2014–15274 Filed 6–30–14; 11:15 am]

BILLING CODE 4164–01–P

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA–351]

Schedules of Controlled Substances: Placement of Tramadol Into Schedule IV

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Final rule.

SUMMARY: With the issuance of this final rule, the Deputy Administrator of the Drug Enforcement Administration places the substance 2-[(dimethylamino)methyl]-1-(3-methoxyphenyl)cyclohexanol (tramadol), including its salts, isomers, and salts of isomers, into schedule IV of the Controlled Substances Act. This scheduling action is pursuant to the Controlled Substances Act which requires that such actions be made on the record after opportunity for a hearing through formal rulemaking. This action imposes the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule IV controlled substances on persons who handle (manufacture, distribute, dispense, import, export, engage in research, conduct instructional activities with, or possess) or propose to handle tramadol.

DATES: Effective August 18, 2014.

FOR FURTHER INFORMATION CONTACT: Erika Gehrmann, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598–6812.

SUPPLEMENTARY INFORMATION:

Legal Authority

The Drug Enforcement Administration (DEA) implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. Titles II and III are referred to as the ''Controlled Substances Act'' and the ''Controlled Substances Import and Export Act,'' respectively, but they are collectively referred to as the ''Controlled Substances Act'' or the ''CSA'' for the purposes of this action. 21 U.S.C. 801–971. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), parts 1300 to 1321. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while providing for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, every controlled substance is classified in one of five schedules based upon its potential for abuse, currently accepted medical use, and the degree of dependence the drug or other substance may cause. 21 U.S.C. 812. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c) and the current list of scheduled substances is published at 21 CFR part 1308.

Pursuant to 21 U.S.C. 811(a)(1), the Attorney General may, by rule, ''add to such a schedule or transfer between such schedules any drug or other substance if he (A) finds that such drug or other substance has a potential for abuse, and (B) makes with respect to such drug or other substance the findings prescribed by [21 U.S.C. 812(b)] for the schedule in which such drug is to be placed * * *.'' The Attorney General has delegated scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA, 28 CFR 0.100, who in turn has redelegated that authority to the Deputy Administrator of the DEA, 28 CFR part 0, appendix to subpart R.

The CSA provides that scheduling of any drug or other substance may be initiated by the Attorney General (1) on his own motion, (2) at the request of the Secretary of the Department of Health and Human Services (HHS),[1] or (3) on the petition of any interested party. 21 U.S.C. 811(a). This action was initiated by four petitions to schedule tramadol under the CSA, and is supported by, *inter alia,* a recommendation from the Assistant Secretary of the HHS and an evaluation of all relevant data by the DEA. This action imposes the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule IV controlled substances on persons who handle or propose to handle tramadol.[2]

Background

Tramadol is a centrally acting opioid analgesic that produces its primary opioid-like action through an active metabolite, referred to as the ''M1'' metabolite (O-desmethyltramadol). It was first approved for use in the United States by the U.S. Food and Drug Administration (FDA) in 1995 under the trade name ULTRAM®. Subsequently, the FDA approved for marketing generic, combination, and extended release tramadol products.

Because of its chemical structure, 2-[(dimethylamino)methyl]-1-(3-methoxyphenyl) cyclohexanol can exist as different isomeric forms. Thus, various prefixes can be associated with the name. Some examples of these prefixes include *dextro, levo, d, l, R, S, cis, trans, erythro, threo,* (+), (−), racemic, and may include combinations of these prefixes sometimes with numerical designations. Any such isomer is, in fact, 2-[(dimethylamino)methyl]-1-(3-methoxyphenyl)cyclohexanol. Tramadol is typically formulated as a racemic mixture identified as (±)-*cis*-2-[(dimethylamino)methyl]-1-(3-methoxyphenyl)cyclohexanol hydrochloride.[3]

HHS and DEA Eight-Factor Analyses

On September 16, 2010, the Assistant Secretary of the HHS provided to the DEA a scientific and medical evaluation and scheduling recommendation entitled ''Basis for the Recommendation to Schedule Tramadol in Schedule IV of the Controlled Substances Act.'' After considering the eight factors in 21

[1] As discussed in a memorandum of understanding entered into by the Food and Drug Administration (FDA) and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the HHS in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518, Mar. 8, 1985. The Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.

[2] *See* infra note 3.

[3] For simplicity, from this point forward in the document, ''tramadol'' is used to refer to 2-[(dimethylamino)methyl]-1-(3-methoxyphenyl)cyclohexanol, its salts, isomers, salts of isomers, and all isomeric configurations of possible forms.

U.S.C. 811(c), as well as the substance's abuse potential, legitimate medical use, and dependence liability, the Assistant Secretary of the HHS recommended that tramadol be controlled in schedule IV of the CSA under 21 U.S.C. 812(b). The DEA conducted its own eight-factor analysis of tramadol pursuant to 21 U.S.C. 811(c). Both the DEA and HHS analyses are available in their entirety in the public docket for this rule (Docket No. DEA–351) at *http://www.regulations.gov* under ''Supporting and Related Material.''

Determination To Schedule Tramadol

After a review of the available data, including the scientific and medical evaluation and the scheduling recommendation from the HHS, the Deputy Administrator of the DEA published in the **Federal Register** a notice of proposed rulemaking (NPRM) entitled ''Schedules of Controlled Substances: Placement of Tramadol Into Schedule IV'' which proposed to place tramadol in schedule IV of the CSA. 78 FR 65923, Nov. 4, 2013. The proposed rule provided an opportunity for interested persons to file a request for hearing in accordance with DEA regulations by December 4, 2013. No requests for such a hearing were received by the DEA. The NPRM also provided an opportunity for interested persons to submit written comments on the proposed rule on or before January 3, 2014.

Comments Received

The DEA received 27 comments on the proposed rule to schedule tramadol. Sixteen commenters expressed support for controlling tramadol as a schedule IV controlled substance, nine commenters were opposed to tramadol being placed into schedule IV of the CSA, and two commenters did not take a position.

Support of the Proposed Rule

Sixteen commenters supported controlling tramadol as a schedule IV controlled substance. Among those 16 commenters expressing support were two State Boards of Pharmacy. One veterinary distributor's association stated that it supports the DEA designating tramadol as a schedule IV controlled substance because it will enable distributors to operate with efficiency and consistency across the United States along with requiring an increased level of due diligence and monitoring. A national veterinary medical association, a national healthcare association, and a national pharmacy association were also among those who expressed support for the rule.

Several commenters supporting the rule expressed their concern regarding the abuse potential and resulting threat to public health posed by tramadol. Writing in support of scheduling tramadol, a local multi-agency prescription drug abuse task force described tramadol as a '' 'loop hole' drug which is addictive, abused, and diverted,'' but which is not yet realized as such by many patients and prescribers due to its current non-controlled status. One commenter stated that given the abuse potential of tramadol (which according to the commenter is often abused in combination with other controlled substances), scheduling this drug will ensure that it is subject to the same controls as other similarly addictive controlled substances. Yet another commenter noted that although analgesics are addictive to a very small percentage of people that use them, scheduling this drug would reduce the number of emergency room visits and number of overdose deaths.

A certified pharmacy technician described her experiences of witnessing the abuse of tramadol by patients on a daily basis. She stated the stricter controlled substance laws of the State of Mississippi have seemed to lessen the abuse. A group of pharmacy students noted that tramadol, marketed as ULTRAM®, is currently the only uncontrolled opioid on the market. Another commenter who supported the rule stated: ''In the field of pharmacy, some patients have expressed concern about the reclassification of tramadol, believing that new regulations could complicate or impede new and chronic patients from receiving their prescriptions.'' This commenter noted that this is a common misconception since schedule IV controlled medications are in fact readily available for those with a valid prescription and the appropriate medical condition. In addition, the commenter noted that these types of prescriptions also have the added convenience of being easily transferrable between pharmacies, phoned-in by prescribers, and refilled five times over a six month period.

DEA Response: The DEA appreciates the support for the rule.

Opposition to the Proposed Rule

1. Access to Pain Medication by the Elderly

An association for consulting pharmacists stated that controlling tramadol would limit access to needed pain medications for elderly patients and opposed the proposed scheduling until a workable solution to ensure timely access for patients in long-term care facilities (LTCFs) can be reached. Specifically, the commenter expressed concern that, should tramadol become a controlled substance, LTCF nurses would no longer be able to call-in or fax a chart order directly to the pharmacy. According to the commenter, in LTCFs, prescribers must call, hand deliver, or fax controlled substance prescriptions to pharmacies, and this in turn involves LTCF employees having to track down the (often non-employee) prescriber. This practice, according to the commenter, can severely impede delivery of prescription medications to LTCF patients.

DEA Response: The processes and procedures associated with dispensing a controlled substance are not relevant factors to the determination whether a substance should be controlled or under what schedule a substance should be placed if it is controlled. *See* 21 U.S.C. 811 and 812. Nonetheless, controlling tramadol as a schedule IV controlled substance should not hinder legitimate access to the medicine, whether within the LTCF setting or elsewhere. As summarized by a State Board of Pharmacy who wrote in support of controlling tramadol: ''Scheduling a medication does not make it impossible to prescribe, dispense and administer the medication. However, it does alert practitioners, dispensers and perhaps even some patients that the medication has some potential dangers for addiction and misuse, and frequent monitoring and evaluation by practitioners and dispensers of such drugs is necessary for appropriate patient care.''

Currently, tramadol is a non-controlled medication that the FDA has approved only for prescription use. Tramadol, as a schedule IV controlled substance, will continue to require a prescription, either orally or in writing. 21 U.S.C. 829(b). The CSA allows for the legitimate prescribing and use of controlled substances; therefore, the control of tramadol should not hinder patient access to the medication. The prescription for tramadol, as a controlled substance, may only be issued by an individual practitioner who is either registered with the DEA or exempt from registration. 21 CFR 1306.03. A prescription for a controlled substance must also be issued for a legitimate medical purpose by an individual practitioner acting in the course of his professional practice. 21 CFR 1306.04(a). Upon the effective date of this rule, tramadol prescriptions may be filled up to six months after the date prescribed, and may be refilled up to

five times within six months after the date on which such prescription was issued. 21 U.S.C. 829(b); 21 CFR 1306.22 (a) and (e); *see also* 21 CFR 1306.23 (b) and (c). In addition, there are no dosage unit limitations for prescriptions for schedule III, IV, or V controlled substances unless the controlled substance is prescribed for administration to an ultimate user who is institutionalized. 21 CFR 1306.24(c).

The substantive requirement that a practitioner acting in the usual course of professional practice determine that tramadol is medically necessary to treat the patient does not hinder legitimate access; the procedural requirements relating to transmission of a legitimate prescription do not hinder legitimate access either. Once an individual practitioner makes a medical determination to prescribe a schedule III through V controlled substance, a prescriber's agent may call-in or fax a prescription for it. *See* 21 CFR 1306.03(b), 1306.21(a). The DEA recognizes the unique challenges pertaining to handling and using controlled substances at LTCFs and has previously addressed related concerns.[4] A DEA registered practitioner may not delegate to a nurse, a pharmacist, or anyone else his or her authority to make a medical determination whether to prescribe a particular controlled substance. However, oral prescriptions for controlled substances in schedules III–V may be communicated to a pharmacy by an employee or agent of the prescribing practitioner, 21 CFR 1306.03(b). Note that the prescribing practitioner remains responsible for ensuring that the prescription conforms ''in all essential respects to the law and regulations,'' 21 CFR 1306.05(f). 75 FR 61613, 61614, Oct. 6, 2010. This requires the practitioner alone to determine—on a prescription by prescription basis—whether the prescription is supported by a legitimate medical purpose and that all the essential elements of the prescription are met.

2. Fear of Criminal Action

Some commenters expressed concern that scheduling tramadol would deter prescribers from properly treating pain for fear of facing criminal action.

DEA Response: One of the most important principles underlying the CSA is that every prescription for a controlled substance must be issued for a legitimate medical purpose by an individual practitioner acting in the usual course of his professional practice. 21 CFR 1306.04(a); *U.S.* v. *Moore,* 423 U.S. 122 (1975) (holding registered physicians may be prosecuted for violation of the CSA when their activities fall outside the usual course of professional practice). The DEA Policy Statement entitled ''Dispensing Controlled Substances for the Treatment of Pain,'' 71 FR 52715 (Sept. 6, 2006), makes clear that this longstanding requirement should in no way interfere with the legitimate practice of medicine or cause any practitioner to be reluctant to provide legitimate pain treatment. Providers (as well as ultimate users) become subject to administrative, civil, and/or criminal proceedings when their activity involving controlled substances is not authorized by, or in violation of, the CSA.

3. Shift to the Black-Market

Several commenters stated that scheduling tramadol would limit their access to tramadol, causing them to have to buy tramadol on the street.

DEA Response: As discussed above, schedule IV controlled medications are readily available for legitimate medical use.

4. Scientific Data Not Sufficient

One commenter reviewed selected published literature and submitted a short review document with a conclusion that ''the current available scientific evidence supports the continuation of a non-controlled classification'' of tramadol.

DEA Response: The CSA mandates that both the HHS and DEA conduct a review of the drug or other substance as related to the eight factors enumerated in 21 U.S.C. 811(c): (1) Its actual or relative potential for abuse; (2) scientific evidence of its pharmacological effect, if known; (3) the state of current scientific knowledge regarding the drug or other substance; (4) its history and current pattern of abuse; (5) the scope, duration, and significant of abuse; (6) what, if any, risk there is to the public health; (7) its psychic or physiological dependence liability; and (8) whether the substance is an immediate precursor of a substance already controlled. The Assistant Secretary of the HHS provided a scientific and medical evaluation and a scheduling recommendation to control tramadol as a schedule IV controlled substance. In accordance with 21 U.S.C. 811(c), the DEA conducted its own analysis of the eight factors determinative of control. Besides published literature, various other data as detailed in the supporting documents were considered in making the scheduling determination for tramadol. Thus, the scheduling determination is based on a comprehensive evaluation of all available data as related to the above mentioned eight factors. The summary of each factor as analyzed by the HHS and the DEA, and as considered by the DEA in this scheduling action, was provided in the proposed rule. Both the DEA and the HHS analyses have been made available in their entirety under ''Supporting and Related Material'' of the public docket for this rule at *http://www.regulations.gov* under Docket No. DEA–351.

As discussed in detail in the DEA's eight-factor analysis, collectively, the available information regarding tramadol supports an abuse potential that is less than that of schedule III and similar to that for schedule IV. Preclinical self-administration studies show that tramadol produces limited reinforcing effects, consistent with schedule IV. At supra-therapeutic doses, tramadol can produce subjective reinforcing effects similar to that of morphine (C–II) and approaching that of oxycodone (C–II). At high doses (but not therapeutic doses), tramadol can produce subjective reinforcing effects similar to propoxyphene (C–IV). For both tramadol and propoxyphene, the doses required to produce significant subjective reinforcing effects are in a range causing sufficient adverse effects. These observations indicate that the subjective reinforcing effects, a reflection of abuse potential, of tramadol are less than that of morphine or oxycodone, but similar to that of propoxyphene.

Based on the review of the HHS evaluation and scheduling recommendation and all other relevant data, the DEA has found that tramadol has an abuse potential and meets the requirements for schedule IV controls under the CSA.

5. Disagreement With Tramadol Classification as an Opioid

One commenter who supported the rule stated that tramadol should not be compared to hydrocodone because hydrocodone is an opioid and tramadol is psychotropic in nature and very similar to, if not the same as, a serotonin-norepinephrine reuptake inhibitor (SNRI).

DEA Response: In the NPRM and supporting documents, the DEA compared tramadol mainly to propoxyphene (narcotic schedule IV). Based on both the HHS and the DEA analyses, there is strong scientific evidence that tramadol and propoxyphene are similar regarding

[4] *E.g.,* ''Preventing the Accumulation of Surplus Controlled Substances at Long Term Care Facilities,'' 66 FR 20833, Apr. 25, 2001; ''Role of Authorized Agents in Communicating Controlled Substance Prescriptions to Pharmacies,'' 75 FR 61613, Oct. 6, 2010.

their behavioral pharmacology and abuse potential pattern, thus suggesting that it is appropriate to control tramadol as a schedule IV controlled substance.

In addition, as stated in the supporting scientific documents, both the HHS and the DEA deem tramadol to be an opioid because tramadol shares similar pharmacological activities with opioids that are controlled under the CSA (schedules II–IV). (The labeling for FDA approved tramadol products states that tramadol is a centrally acting opioid analgesic.) An examination of the general pharmacology (including behavioral pharmacology) of tramadol reveals that tramadol produces many pharmacological effects similar to those of other opioids. These pharmacological effects include, but are not limited to, analgesia, respiratory depression, miosis, cough suppression, and inhibition of bowel mobility, and as such, tramadol is considered an opioid. The opioid pharmacology of tramadol primarily resides with its metabolite, O-desmethyltramadol, designated ''M1,'' and to a much lesser extent with tramadol, the parent drug. In addition, tramadol resembles some opioids insofar as it has the additional pharmacological effects of blocking the reuptake of norepinephrine and serotonin.

The CSA defines an ''opiate'' as ''any drug or other substance having an addiction-forming or addiction-sustaining liability similar to morphine or being capable of conversion into a drug having such addiction-forming or addiction-sustaining liability.'' 21 U.S.C. 802(18). Opium, opiates, derivatives of opium and opiates, including their isomers, whether produced directly or indirectly by extraction from substances of vegetable origin, or independently by means of chemical synthesis, are ''narcotic drugs'' as defined by the CSA, 21 U.S.C. 802(17).[5] As discussed in the supporting eight-factor documentation, preclinical studies demonstrate that tramadol, as other opioids in schedules I through IV, exhibits complete generalization to morphine and is able to produce some reinforcing effects. Repeated administration of tramadol in animals caused dependence development, evidenced by a withdrawal syndrome similar in intensity to pentazocine (schedule IV) or propoxyphene (narcotic schedule IV).

Although, generally, the controls imposed by the CSA on drugs and other substances depend on the schedule into which they are placed, there are certain additional requirements and restrictions for narcotic drugs. For example, narcotic drugs in schedule III, IV, or V may not be imported into the United States unless it is found that such importation is needed to provide for the legitimate medical, scientific, or other legitimate purposes under the specified, limited circumstances described in 21 U.S.C. 952(a). Narcotic controlled substances may not be exported unless the conditions imposed by 21 U.S.C. 953(a) are satisfied.

6. Never-Ending Practice of Drug Scheduling

Two commenters raised concerns that, despite the scheduling of drugs such as tramadol, individuals will always find substances to abuse, thus creating ''a never ending story of scheduling drugs.''

DEA Response: Pursuant to 21 U.S.C. 811(a), the CSA authorizes the DEA, under authority delegated by the Attorney General, to add to such a schedule any drug or other substance if it is found that the drug or other substance has a potential for abuse, and makes with respect to such drug or other substance the findings prescribed by 21 U.S.C. 812(b). As such, the scheduling authority established by Congress specifically allows new substances to be added to the list of controlled substances without regard to the number of substances already controlled. *See also* 21 U.S.C. 812(a) (''Such schedules shall *initially* consist of * * *'' (*emphasis added*)).

Requests for Staggered Implementation of Various Portions of the Rule

A national association that represents primary healthcare distributors commented that although they recognized the underlying reasons for scheduling tramadol and agreed with the reasoning and basis for controlling tramadol, the DEA should provide an extended time period before implementation to allow registrants to become compliant with portions of the rule regarding security, labeling and packaging, and reporting.[6] The association requested that the requirement for conducting inventory of tramadol products within wholesale distribution centers take place as of the effective date of the final scheduling decision. The association's concerns (as well as the DEA's responses) are outlined and discussed below.

1. Request for Staggered Effective Dates, Generally

The association requested that the DEA implement handling requirements for tramadol in stages. For example, they requested that the requirement for conducting inventory of tramadol products within wholesale distribution centers take place as of the effective date of the final scheduling decision but delaying the requirements for compliance with the security provisions of 21 CFR 1301.71–1301.93.

DEA Response: Generally, scheduling actions for drugs and other substances currently marketed in the United States are effective 30 days from the date of publication of the final rule in the **Federal Register**. In order to ensure the continued availability of tramadol for legitimate medical use, while also ensuring it is not subject to misuse, abuse, and diversion, the DEA is establishing an effective date of this final rule for all handling requirements 45 days from the date of publication. This 45-day period will provide a reasonable time for registrants to comply with the handling requirements for a schedule IV controlled substance and was established upon a full consideration of the totality of circumstances specific to tramadol.

Although the DEA has in the past, for some scheduling actions, allowed for additional time for compliance with certain handling requirements beyond the general effective date, the DEA has specifically chosen to forgo staggered implementation dates of handling requirements as different implementation dates leads to confusion and inconsistent application of the law.

2. Security

The association recommended a minimum of 120 days from the date of the final rule to allow for compliance in order to provide storage, revise operating procedures, train staff, and amend monitoring systems.

DEA Response: In order to ensure the continued availability of tramadol for legitimate medical use, while also ensuring it is not subject to misuse, abuse, and diversion, the DEA is establishing an effective date of this final rule, including security requirements, 45 days from the date of publication. Upon promulgation, registrants must comply with the applicable security provisions of 21 CFR 1301.71–1301.93. This 45-day period will provide a reasonable time for registrants to comply with the security

[5] Including their isomers, esters, ethers, salts, and salts of isomers, whenever the existence of such isomers, esters, ethers, and salts is possible within the specific chemical designation; however, does not include the isoquinoline alkaloids of opium.

[6] Pursuant to 5 U.S.C. 553(d) and in accordance with 21 CFR 1308.45, a final rule scheduling a substance shall not be effective less than 30 days from the date of its publication in the **Federal Register** unless the Administrator finds that conditions of public health or safety necessitate an earlier effective date.

requirements for a schedule IV controlled substance. As noted by the association, it is believed that distributors of tramadol already have adequate space within their warehouse cages to store the anticipated volume of tramadol and ''thus construction or expansion of cage space is unlikely to result * * *.'' Accordingly, it is reasonably likely that handlers and proposed handlers of tramadol have already instituted or made plans to institute the necessary modifications regarding security, including amendments to their suspicious orders monitoring systems to include tramadol orders. In order to provide handlers of tramadol a reasonable time period to comply with schedule IV handling requirements, including those for security, the DEA is allowing an additional 15 days, as compared to the generally allotted 30 days, from publication in the **Federal Register** before this rule becomes effective. After 45 days from the date of the final rule, tramadol will be subject to schedule III–V security requirements.

The DEA has carefully considered the security requirements for compliance with this rule. As confirmed by the association, current distributors of tramadol are DEA registrants with existing controlled substance storage that complies with DEA regulations. The DEA understands that handlers of tramadol may need to make modifications to their current security procedures for compliance. These modifications necessary for security compliance will be a one-time modification to provide for the appropriate storage, revision of operating procedures, training of staff, and amendments to suspicious order monitoring systems to include customer verifications. The DEA believes that a 45-day period will provide handlers of tramadol adequate time to implement these one-time modifications in compliance with the DEA security regulations. Registrants are familiar with the applicable security regulations, and already have systems in place with respect to other controlled substances. Accordingly, revising operating procedures, amending monitoring systems, and training staff with respect to tramadol should be easily accomplished within the 45-day compliance timeframe. The DEA strongly advises current registrants (and those entities that may seek registration as a result of this action) to work closely with their local DEA office regarding the applicable security requirements and any necessary modifications due to compliance with this rule. 21 CFR 1301.71(d).

3. Distribution of Products With the Pre-Control Label

The association stated that in accordance with 21 CFR 1302.05, the DEA has the authority to set a date on which labeling and packaging requirements will become effective, and requested clarification of when the distribution of products with the pre-scheduling label should cease. The association also requested clarification as to whether the cessation of the manufacture of products for commercial containers with the pre-scheduling labeling will also mean that manufacturers would be required to cease distribution to wholesale distributors of products they might have in stock bearing the pre-scheduling label. The association stated that the ambiguity of the compliance period poses a dilemma for those in the tramadol supply chain, and requested the DEA to act to meet healthcare needs and avoid waste by allowing products bearing the pre-scheduling label to move through the supply chain until the inventory is depleted. Alternatively, the association suggested that the DEA allow distributors to continue to sell pre-scheduling labeled product for at least 180 days after the effective date of the final rule.

DEA Response: As of the effective date of the final rule, pursuant to 21 U.S.C. 821, 825, and 958(e) and in accordance with 21 CFR 1302.03, manufacturers are required to print upon the labeling of each commercial container of tramadol they distribute the designation of tramadol as ''C–IV.'' It shall be unlawful for commercial containers of tramadol to be distributed without bearing the label properly identifying it as a schedule IV controlled substance in accordance with 21 CFR part 1302. As clearly stated in 21 CFR 1302.05, ''[a]ll labels on commercial containers of, and all labeling of, a controlled substance which either is transferred to another schedule or is added to any schedule shall comply with the requirements of § 1302.03, on or before the effective date established in the final order for the transfer or addition.'' Accordingly, the DEA is requiring that commercial containers of tramadol distributed on or after 45 days from the date of publication of the final rule be labeled as ''C–IV'' and be packaged in accordance with 21 CFR part 1302.

From the 2007 Economic Census, the DEA estimates that the inventory turnover ratio for the industry [7] is approximately 11.3.[8] The inventory turnover ratio represents the number of times the inventory sells (turns) in a year. The 11.3 inventory turnover ratio equates to an average of 32 days to sell inventory. The 11.3 turnover ratio is consistent with that of large distributors where financial information was publicly available and reviewed. Publicly reviewed data reports that about 85% of all revenues (an indirect indicator of dosage units moved) from drug distribution in the United States come from three public wholesalers, each with annual revenue in the billions. The DEA additionally notes that many regional and specialist pharmaceutical wholesalers have been acquired by the largest three distribution companies. The inventory turnover ratio is a reasonable estimate for the entire industry and all products under the circumstances. Because the 32 days to sell inventory is an average based on industry-wide census data, it is possible for an individual company and/or product line to have shorter or longer time to sell.

Since tramadol is a widely prescribed drug, with nearly 40 million prescriptions written in 2012,[9] the DEA expects distributors to receive and distribute tramadol at high volume and with regularity; thus, anticipating shorter than average days to sell tramadol than overall industry average inventory. However, to accommodate those distributors that have lower than average industry turnover ratio, the DEA is establishing an effective date of this final rule, including labeling and packaging requirements, 45 days from the date of publication. The DEA believes this will provide a reasonable time for distributors to sell existing stock with pre-control labeling and packaging and to stock inventory with post-control labeling and packaging.

Additionally, the DEA believes that any distributor that requires more than 45 days to sell tramadol inventory under normal circumstances can make minor modifications to ordering and stocking procedure for a transitional period to meet the established effective date at minimal cost. Distributors also have the option of returning excess stock of tramadol product without the ''C–IV''

[7] NAICS 424210—Drugs and druggists' sundries merchant wholesalers; Merchant wholesalers, except manufacturers' sales branches and offices.

[8] The inventory turnover ratio of 11.3 was calculated by dividing the 2007 ''cost of goods sold'' for the industry of $280,481,051,000 by the average end-of-year 2006 total inventories of $24,782,835,000.

[9] IMS Health, National Sales Perspective™ (NSP).

label to the manufacturer, as authorized by 21 CFR 1307.12.

The DEA takes this opportunity to clarify that the regulation pertaining to labeling of commercial containers applies only to distributions by manufacturers and distributors. The DEA does not regulate the labeling and packing of commercial containers of controlled substances downstream of distributors.

As summarized in the NPRM, and discussed in detail in the supporting eight factor analyses, tramadol meets the statutory requirements for control and for placement in schedule IV. Based upon the reasons discussed above, the DEA believes that 45 days is a reasonable amount of time for registrants to modify their operations so that the necessary safeguards are in place to prevent the abuse and diversion of tramadol.

4. Automation of Reports and Consolidated Orders System (''ARCOS'') Reporting

The association stated that only schedule I and II (and some schedule III) products are subject to reporting under the DEA's Automation of Reports and Consolidated Orders System (''ARCOS''), so it would be an error to require distributors to report tramadol (a schedule IV narcotic) to ARCOS.

DEA Response: DEA regulations do not require distributors to file ARCOS reports for schedule IV narcotics.

Scheduling Conclusion

Based on consideration of all comments, the scientific and medical evaluation and accompanying recommendation of the HHS, and based on the DEA's consideration of its own eight-factor analysis, the DEA finds that these facts and all other relevant data constitute substantial evidence of potential for abuse of tramadol. As such, the DEA is scheduling tramadol as a controlled substance under the CSA.

Determination of Appropriate Schedule

The CSA establishes five schedules of controlled substances known as schedules I, II, III, IV, and V. The CSA outlines the findings required for placing a drug or other substance in any particular schedule. 21 U.S.C. 812(b). After consideration of the analysis and recommendation of the Assistant Secretary for Health of the HHS and review of all relevant and available data, the Deputy Administrator of the DEA, pursuant to 21 U.S.C. 812(b)(4), finds that:

1. Tramadol has a low potential for abuse relative to the drugs or substances in schedule III. The abuse potential of tramadol is comparable to the schedule IV controlled substance propoxyphene;

2. Tramadol has a currently accepted medical use in treatment in the United States. Tramadol and other tramadol-containing products are approved for marketing by the FDA to manage moderate to moderately severe pain; and

3. Abuse of tramadol may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in schedule III.

Based on these findings, the Deputy Administrator of the DEA concludes that tramadol, including its salts, isomers, and salts of isomers, warrants control in schedule IV of the CSA. 21 U.S.C. 812(b)(4).

Requirements for Handling Tramadol

Upon the effective date of this final rule, any person who handles tramadol is subject to the CSA's schedule IV regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, dispensing, importing, exporting, engagement in research, and conduct of instructional activities, of schedule IV controlled substances including the following:

Registration. Any person who handles (manufactures, distributes, dispenses, imports, exports, engages in research, or conducts instructional activities with) tramadol, or who desires to handle tramadol, must be registered with the DEA to conduct such activities, pursuant to 21 U.S.C. 822, 823, 957, and 958, and in accordance with 21 CFR parts 1301 and 1312 as of August 18, 2014. Any person who currently handles tramadol and is not registered with the DEA must submit an application for registration and may not continue to handle tramadol as of August 18, 2014 unless the DEA has approved that application, pursuant to 21 U.S.C. 822, 823, 957, and 958, and in accordance with 21 CFR parts 1301 and 1312.

Disposal of stocks. Any person who does not desire or is not able to obtain a schedule IV registration must surrender all quantities of currently held tramadol in accordance with the procedures outlined in 21 CFR 1307.21 on or before August 18, 2014, or may transfer all quantities of currently held tramadol to a person registered with the DEA on or before August 18, 2014.

Security. Tramadol is subject to schedule III–V security requirements and must be handled and stored pursuant to 21 U.S.C. 821 and 823, and in accordance with 21 CFR 1301.71–1301.93 as of August 18, 2014.

Labeling and Packaging. All labels and labeling for commercial containers of tramadol must comply with 21 U.S.C. 825 and 958(e), and be in accordance with 21 CFR part 1302 as of August 18, 2014.

Inventory. Every DEA registrant who possesses any quantity of tramadol on the effective date of this final rule must take an inventory of all stocks of tramadol on hand as of August 18, 2014, pursuant to 21 U.S.C. 827 and 958, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11 (a) and (d).

Any person who becomes registered with the DEA after August 18, 2014 must take an initial inventory of all stocks of controlled substances (including tramadol) on hand on the date the registrant first engages in the handling of controlled substances, pursuant to 21 U.S.C. 827 and 958, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11 (a) and (b).

After the initial inventory, every DEA registrant must take a new inventory of all stocks of controlled substances (including tramadol) on hand every two years, pursuant to 21 U.S.C. 827 and 958, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

Records and Reports. All DEA registrants must maintain records with respect to tramadol pursuant to 21 U.S.C. 827 and 958 and in accordance with 21 CFR parts 1304 and 1312 as of August 18, 2014.

Prescriptions. All prescriptions for tramadol or products containing tramadol must comply with 21 U.S.C. 829, and be issued in accordance with 21 CFR part 1306 and subpart C of 21 CFR part 1311 as of August 18, 2014.

Importation and Exportation. All importation and exportation of tramadol must be in compliance with 21 U.S.C. 952, 953, 957, and 958, and be in accordance with 21 CFR part 1312 as of August 18, 2014.

Liability. Any activity involving tramadol not authorized by, or in violation of, the CSA, occurring as of August 18, 2014 is unlawful, and may subject the person to administrative, civil, and/or criminal action.

Regulatory Analyses

Executive Orders 12866 and 13563

In accordance with 21 U.S.C. 811(a), this scheduling action is subject to formal rulemaking procedures done ''on the record after opportunity for a hearing,'' which are conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth the criteria for scheduling a drug or other substance. Such actions are exempt from review by the Office of Management and Budget

(OMB) pursuant to section 3(d)(1) of Executive Order 12866 and the principles reaffirmed in Executive Order 13563.

Executive Order 12988

This regulation meets the applicable standards set forth in sections 3(a) and 3(b)(2) of Executive Order 12988 Civil Justice Reform to eliminate drafting errors and ambiguity, minimize litigation, provide a clear legal standard for affected conduct, and promote simplification and burden reduction.

Executive Order 13132

This rulemaking does not have federalism implications warranting the application of Executive Order 13132. The rule does not have substantial direct effects on the States, on the relationship between the national government and the States, or the distribution of power and responsibilities among the various levels of government.

Executive Order 13175

This rule does not have tribal implications warranting the application of Executive Order 13175. This rule does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal Government and Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes.

Regulatory Flexibility Act

The Deputy Administrator, in accordance with the Regulatory Flexibility Act (RFA) (5 U.S.C. 601–612), has reviewed this final rule and by approving it certifies that it will not have a significant economic impact on a substantial number of small entities. The purpose of this final rule is to place tramadol, including its salts, isomers, and salts of isomers, into schedule IV of the CSA. By this final rule, tramadol will remain in schedule IV unless and until additional scheduling action is taken to either transfer it between the schedules or to remove it from the list of schedules. *See* 21 U.S.C. 811 and 812. No less restrictive measures (i.e., non-control or control in schedule V) enable the DEA to meet its statutory obligations under the CSA.

This rule affects approximately 1.5 million DEA registrations, representing approximately 376,904 entities. The DEA estimates that 367,046 (97%) of these entities are ''small entities'' in accordance with the RFA and SBA size standards. 5 U.S.C. 601(6) and 15 U.S.C. 632.

In accordance with the RFA, the DEA evaluated the impact of this rule on small entities. Specifically, the DEA examined the registration, storage, inventory and recordkeeping, and disposal requirements for the 367,046 small entities estimated to be affected by the rule: 55 manufacturers; 1,418 distributors/importers/exporters; 50,032 pharmacies; and 315,541 entities employing or holding registrations as individual practitioners/mid-level practitioners/hospitals/clinics. Ten States currently control tramadol as a schedule IV controlled substance under State law, with requirements that meet or exceed the DEA's requirements for schedule IV controlled substances discussed in the NPRM. Entities in these States are not economically impacted by this rule.

Based on the DEA's understanding of its registrants' operations and facilities, the DEA estimates a non-recurring expense for system modification and initial inventory cost of $245.01 for all entities and an additional $10,000 for secure storage for 50% of distributors, importers, and exporters. As discussed in the EIA prepared in association with the development of this final rule, manufacturers, pharmacies, physician offices/hospitals/clinics/other health care facilities, and 50% of distributors, importers, and exporters are assumed to meet the requirement of the rule without the need to expand secure storage area. The DEA estimates these costs, on an annualized basis, will have significant economic impact (cost greater than 1% of annual revenue) on 0 of 55 (0%) of small manufacturers; 50 of 1,418 (3.5%) of small distributors; 107 of 50,032 (0.2%) small business pharmacies; and 661 of 315,541 (0.2%) of individual practitioners/mid-level practitioners/hospitals/clinics, totaling 818 of 367,046 (0.2%) of all small entities. The percentage of small entities with significant economic impact is not substantial, and therefore, this rule will not result in significant economic impact on a substantial number of small entities.

Unfunded Mandates Reform Act of 1995

In accordance with the Unfunded Mandates Reform Act (UMRA) of 1995 (2 U.S.C. 1501 *et seq.*), the DEA has determined and certifies pursuant to UMRA that this action would not result in any Federal mandate that may result ''in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100 million or more (adjusted for inflation) in any one year * * *.'' Therefore, neither a Small Government Agency Plan nor any other action is required under provisions of UMRA of 1995.

Paperwork Reduction Act of 1995

This action does not impose a new collection of information requirement under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3521). This action would not impose recordkeeping or reporting requirements on State or local governments, individuals, businesses, or organizations. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Congressional Review Act

This rule is not a major rule as defined by section 804 of the Small Business Regulatory Enforcement Fairness Act of 1996 (Congressional Review Act (CRA)). This rule will not result in: an annual effect on the economy of $100 million or more; a major increase in costs or prices for consumers, individual industries, Federal, State, or local government agencies, or geographic regions; or significant adverse effects on competition, employment, investment, productivity, innovation, or on the ability of United States-based companies to compete with foreign-based companies in domestic and export markets. However, pursuant to the CRA, the DEA has submitted a copy of this final rule to both Houses of Congress and to the Comptroller General.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, 21 CFR part 1308 is amended as follows:

PART 1308—SCHEDULES OF CONTROLLED SUBSTANCES

■ 1. The authority citation for 21 CFR part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), unless otherwise noted.

■ 2. Amend § 1308.14 by adding a new paragraph (b)(3) to read as follows:

§ 1308.14 Schedule IV.

* * * * *

(b) * * *

(3) 2-[(dimethylamino)methyl]-1-(3-methoxyphenyl)cyclohexanol, its salts, optical and geometric isomers and salts of these isomers (including tramadol)—9752

* * * * *

Dated: June 27, 2014.

Thomas M. Harrigan,

Deputy Administrator.

[FR Doc. 2014–15548 Filed 7–1–14; 8:45 am]

BILLING CODE 4410–09–P

DEPARTMENT OF THE TREASURY

Internal Revenue Service

26 CFR Part 1

[TD 9674]

RIN 1545–BM07

Guidelines for the Streamlined Process of Applying for Recognition of Section 501(c)(3) Status

AGENCY: Internal Revenue Service (IRS), Treasury.

ACTION: Final and temporary regulations.

SUMMARY: This document contains final and temporary regulations that provide guidance to eligible organizations seeking recognition of tax-exempt status under section 501(c)(3) of the Internal Revenue Code (Code). The final and temporary regulations amend current regulations to allow the Commissioner of Internal Revenue to adopt a streamlined application process that eligible organizations may use to apply for recognition of tax-exempt status under section 501(c)(3). The text of the temporary regulations also serves as the text of the proposed regulations (REG–110948–14) set forth in the notice of proposed rulemaking on this subject in the Proposed Rules section in this issue of the **Federal Register**.

DATES: *Effective date:* These regulations are effective on July 1, 2014.

Applicability date: For dates of applicability, *see* §§ 1.501(a)–1T(f)(1), 1.501(c)(3)–1T(h)(1), 1.508–1T(c)(1).

FOR FURTHER INFORMATION CONTACT: James R. Martin or Robin Ehrenberg at (202) 317–5800 (not a toll-free number).

SUPPLEMENTARY INFORMATION:

Background

Section 508 requires an organization seeking tax-exempt status under section 501(c)(3), as a condition of its exemption, to notify the Secretary of the Treasury (or his delegate) that it is applying for recognition of exempt status in the manner prescribed in the Treasury Regulations, unless it is specifically excepted from the requirement. Section 1.508–1(a) describes the process for giving notice, and requires that an organization ''submit[ ] a properly completed and executed Form 1023, exemption application.'' Section 1.501(c)(3)–1(b)(1)(v) states that an organization must, to establish its exemption, submit a detailed statement of its proposed activities with and as a part of its application for exemption. Similarly, § 1.501(a)–1(b)(1)(iii) provides that an organization described in section 501(c)(3) shall submit with, and as part of, an application, a detailed statement of its proposed activities. Section 1.501(a)–1(b)(2) states that the Commissioner may require any additional information deemed necessary for a proper determination of whether a particular organization is exempt, and when deemed advisable in the interest of an efficient administration of the internal revenue laws, the Commissioner may, in the cases of particular types of organizations, prescribe the form in which the proof of exemption shall be furnished.

Detailed procedures for applying for recognition of exemption are set out in Rev. Proc. 2014–9, 2014–2 IRB 281, and in the instructions to Form 1023, ''Application for Recognition of Exemption Under Section 501(c)(3) of the Internal Revenue Code.'' *See* § 601.601(d)(2)(ii)(*b*) of this chapter.

Explanation of Provisions

The Treasury Department and the IRS have considered how the process of meeting the notice requirement of section 508 can be made more efficient for certain smaller organizations. The IRS is developing a streamlined form and process for these organizations. Accordingly, this Treasury decision amends §§ 1.501(a)–1, 1.501(c)(3)–1, and 1.508–1 to permit eligible organizations to use a streamlined process, described in guidance published in the Internal Revenue Bulletin, to meet the notice requirements of section 508.

Specifically, this Treasury decision amends §§ 1.501(a)–1 and 1.501(c)(3)–1 to authorize the Treasury Department and the IRS to prescribe, in applicable regulations or other guidance published in the Internal Revenue Bulletin, an exception to the requirement that an organization applying for tax-exempt status provide a detailed statement of its proposed activities. This document also amends the § 1.501(a)–1 provisions relating to the Commissioner's ability to revoke a determination because of a change in the law or regulations, or for other good cause, to reference the Commissioner's authority to retroactively revoke a determination under section 7805(b). No substantive change is intended by this amendment. This Treasury decision also amends the requirement in § 1.501(a)–1(b)(3) that an organization claiming to be exempted from filing annual returns file a statement supporting its claim with and as a part of its application. This amendment would provide flexibility for the Treasury Department and the IRS to prescribe in published guidance other methods of notifying the IRS that the organization is claiming an annual filing exemption.

In addition, this document amends § 1.508–1 to provide that eligible organizations may use Form 1023–EZ, ''Streamlined Application for Recognition of Exemption Under Section 501(c)(3) of the Internal Revenue Code,'' to notify the Commissioner of their applications for tax-exempt status under section 501(c)(3). This Treasury decision also amends §§ 1.501(a)–1 and 1.508–1 to state that the office to which applications should be submitted will be published in the Internal Revenue Bulletin or instructions to the Form 1023 or Form 1023–EZ.

Finally, this Treasury decision makes certain technical revisions to the regulations. In § 1.501(a)–1, the reference to ''internal revenue district'' is removed because such reference has been made obsolete by the enactment of the Internal Revenue Service Restructuring and Reform Act of 1998, Public Law 105–206, 112 Stat. 685. References to a district director in §§ 1.501(a)–1, 1.501(c)(3)–1, and 1.508–1 are also modified, as those positions no longer exist within the IRS. Proposed regulations in the Rules and Regulations section of this issue of the **Federal Register** use the text of these temporary regulations as the text of the proposed regulations. Treasury and the IRS seek comments on all aspects of the proposed rules, including whether additional technical revisions are necessary. Simultaneously with the publication of this Treasury decision, the Treasury Department and the IRS will release for publication a Revenue Procedure that provides procedures for applying for recognition of exemption using Form 1023–EZ.

Special Analyses

It has been determined that this Treasury decision is not a significant regulatory action as defined in Executive Order 12866, as supplemented by Executive Order 13563. Therefore, a regulatory assessment is not required. It also has been determined that section 553(b) of the Administrative Procedure Act (5 U.S.C. chapter 5) does not apply to these regulations. For the applicability of the

Attachment 7

NOTE

Experience with a pharmacy technician medication history program

JULIE B. COOPER, MICHELLE LILLISTON, DEANNE BROOKS, AND BRUCE SWORDS

Purpose. The implementation and outcomes of a pharmacy technician medication history program are described.

Summary. An interprofessional medication reconciliation team, led by a clinical pharmacist and a clinical nurse specialist, was charged with implementing a new electronic medication reconciliation system to improve compliance with medication reconciliation at discharge and capture compliance-linked reimbursement. The team recommended that the pharmacy department be allocated new pharmacy technician full-time-equivalent positions to assume ownership of the medication history process. Concurrent with the implementation of this program, a medication history standard was developed to define rules for documentation of what a patient reports he or she is actually taking. The standard requires a structured interview with the patient or caregiver and validation with outside sources as indicated to determine which medications to document in the medication history. The standard is based on four medication administration category rules: scheduled, as-needed, short-term, and discontinued medications. The medication history standard forms the core of the medication history technician training and accountability program. Pharmacy technicians are supervised by pharmacists, using a defined accountability plan based on a set of medical staff approved rules for what medications comprise a best possible medication history. Medication history accuracy and completeness rates have been consistently over 90% and rates of provider compliance with medication reconciliation rose from under 20% to 100% since program implementation.

Conclusion. A defined medication history based on a medication history standard served as an effective foundation for a pharmacy technician medication history program, which helped improve provider compliance with discharge medication reconciliation.

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Patients interact with a healthcare system in various inpatient and outpatient settings, creating a constantly evolving medication list and opportunities for medication errors.[1] Medication reconciliation is an iterative process in which the patient's best possible medication list is documented, verified, and compared to the current list of prescribed medications with the intent of optimizing pharmaceutical care and reducing medication errors.[2] The effect of this dynamic process on patient safety outcomes has been extensively evaluated, but the magnitude of benefit is variable.[3] Inconsistent, incomplete, or inaccurate medication histories are well described in the literature, with clinically important error rates ranging from 11% to 59%.[1-3]

Without an accurate and complete medication history, it is impossible to conduct a clinically effective medication reconciliation.[2,4] According to the Joint Commission's National Patient Safety Goals (NPSGs), the foundation of meaningful medication reconciliation is the acquisition of a complete and accurate home medication history, documenting what a patient actually takes, within 24 hours of the first encounter for all admissions and at outpatient visits.[5] The process to acquire the best possible medication history necessitates a structured patient interview and the use of additional sources for data verification.[4,6] Clinicians face many challenges when trying to obtain a complete medication history, including a patient's health literacy and knowledge of medications, as well as time limitations.[7] Despite healthcare

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providers' perceptions, interviewing patients is a reliable method of acquiring the best possible medication history.[7-9] Medication lists documented in electronic medical records (EMRs), in claims databases, and by patients on standardized forms have not been shown to be reliable without additional patient interview.[10-13] However, many health systems remain reluctant to invest resources in this patient safety initiative, and less-rigorous alternatives continue to be evaluated to fulfill minimum requirements for medication reconciliation.[14,15]

Obtaining an accurate medication history, which is the foundation for effective medication reconciliation, is a resource-intensive process, and the literature available on this topic provides little guidance on best practices for obtaining a complete medication history.[3,15-19] As a result, the pharmacist often has to use his or her clinical judgment to determine the best method for collecting the most-relevant information.[20]

Identifying one person to own the role of documenting the best possible medication history has been proposed as a means of optimizing resource utilization by eliminating redundant efforts of multiple clinicians.[21] Pharmacist involvement with medication reconciliation has been demonstrated to be cost-effective, but pharmacist resources are limited and expensive.[3,20,22] With training, pharmacy technicians have been shown to effectively document the best possible medication history.[23-25] Pharmacy technician training is challenging, and supervision in this decentralized role has not been well described. Pharmacy technician programs have used structured patient interviews, standardized forms, and pharmacist verification to ensure accuracy.[23-26] Regardless of who documents the patients' medication history, standardization and accountability of what medications to document in a best possible medication history are necessary to ensure a consistent, complete, and accurate medication history as a foundation for effective medication reconciliation.

This article describes the implementation of and experience with a pharmacy medication history program in which pharmacy technicians complete the best possible medication history for new admissions, surgical preadmissions, and emergency department (ED) visits for a five-hospital, 1035-bed community health system. This program is based on a structured interview process using a medication history standard that defines specific rules for which medications to document in the best possible medication history and is coupled with a defined process for pharmacy technician training and accountability.

Needs assessment

In 2005, an interprofessional medication reconciliation team consisting of nurses, pharmacists, hospital administrators, and a physician champion was charged with implementing a program to comply with the Joint Commission's NPSG for medication reconciliation.[5] At our institution, physicians are responsible for conducting medication reconciliation, but not all of them performed this task. A provider survey revealed that the primary reason physicians did not perform medication reconciliation was their perception of the poor quality of the medication history documented by nurses. To address this issue, the medication reconciliation team evaluated three models for obtaining the most complete patient medication history: nursing-only documentation, pharmacy technician documentation, and a blended model in which nurses documented the medication history and consulted a pharmacist to review the history in specific high-risk patients (patients taking more than 10 medications or taking antiretrovirals, anticoagulants, or antiseizure medications). The team also created a medication reconciliation order form for physicians to use when conducting medication reconciliation on admission and at discharge.

In 2006, the blended model was selected as the preferred model for obtaining medication histories because it offered an incremental improvement in the quality of information gathered. The blended model was problematic, however, due to limited accountability and a lack of guidance provided to nurses about how to document a medication history. Wide variances in the quality of the medication histories remained despite pharmacist intervention in 10% of medication histories across the health system. Overall rates of medication reconciliation remained low with wide variability, from 80% for surgeons admitting patients for planned procedures to less than 20% for specialists caring for patients admitted via the ED. However, the health system maintained the blended model for medication history documentation due to the human resource cost associated with alternatives.

In 2008, an interprofessional heart failure core measures team consisting of physicians, nurses, pharmacists, and hospital administrators was created to develop an action plan for addressing major barriers to compliance with the Joint Commission's heart failure core measures. Since 2006, the health system had developed reimbursement contracts linked to full compliance with specific Joint Commission core measures. In 2008, the system was failing to meet these standards due to the inability to comply with the medication reconciliation requirements for this patient population.[27] Key barriers identified were the multiple medication history lists in patients' charts and a lack of physician compliance with medication reconciliation at discharge. The heart failure core measures team reported to hospital administration

that without significant changes in the system's medication reconciliation process, potential reimbursement would be lost.

As a result, in 2008, the interprofessional medication reconciliation team was reconvened, led by a clinical pharmacist and a clinical nurse specialist, with new administrative and physician champions. The team was charged with implementing a new electronic medication reconciliation system to improve compliance with medication reconciliation at discharge and capture compliance-linked reimbursement. In light of the challenges associated with the blended model for obtaining medication histories, the medication reconciliation team recommended that the pharmacy department be allocated new pharmacy technician full-time-equivalent (FTE) positions to assume ownership of the medication history process. The team believed that the use of pharmacy technicians would be a cost-effective strategy for improving the quality of medication histories. To ensure quality and accountability, the team developed specific standards for completing patient medication histories, which were approved by the medical staff.

Resources obtained

In 2008, the pharmacy department's request for additional staff to conduct medication histories for the health system was based on the average time it took to complete a best possible medication history. Based on internal studies, it was determined that a single technician completing medication histories for admitted patients on multiple nursing units could complete, on average, 16 medication histories per shift. Thus, dividing the average admissions per day by 16 was the foundation of pharmacy technician FTE estimates. It was also determined that program implementation, training, and supervision of a systemwide pharmacy medication history program would require a minimum of one pharmacist FTE. In January 2009, the pharmacy department's request for additional staff (total of four pharmacy technician FTEs) was approved. The technicians were responsible for completing admission medication histories for all nonsurgical admissions to Moses H. Cone Memorial Hospital, a 517-bed community teaching hospital and the flagship hospital for Cone Health.

After success with the initial implementation, the program was expanded with incremental FTE increases by campus. In 2010, 5 additional FTEs were allocated for completing telephone medication histories for presurgical patients. Rates of medication histories per shift were measured in a pilot study at an average of 20 medication histories per eight-hour shift; efficiency was limited by a nearly 50% rate of being unable to reach the patient on the first attempted telephone call. By the end of 2011, a total of 10.5 FTEs had been allocated for admission medication histories on all Cone Health campuses systemwide. In 2012, 17 additional FTEs were allocated for program expansion to all ED visits systemwide (four EDs) during hours when ED arrivals per hour were greater than four based on an average productivity of 25 medication histories per eight-hour shift. Efficiency was improved in this environment due to a lower average number of medications per patient and the close geographic proximity of patients.

Pharmacy now completes medication histories for all admitted inpatients, all surgical preadmissions, and a large proportion of ED visits within our five-hospital, 1035-bed community health system.

Establishing standards

Over the course of multiple inquiries into the quality of medication histories documented by nurses in our health system, the key quality barrier identified was the lack of a standard set of expectations regarding what should be documented on a patient's home medication list on admission. As a result, we established a set of standards for documenting medication histories, which were compiled into a document called the medication history standard. Our goals were to establish accountability for completing a high-quality best possible medication history and improve patient safety.

It is not always feasible to obtain a complete list of a patient's prescribed medications, especially when he or she arrives at the hospital during hours when physicians' offices are closed. Documenting such a list is further complicated by the fact that most patients have multiple physicians and thus multiple lists of prescribed medications. Ultimately, most patients have two lists of medications—a prescribed list and a list of what the patient is actually taking. Focusing on what the patient actually takes protects the patient from adverse events resulting from admission orders for medications they are not taking and gives providers information on compliance on which to base management decisions on admission and education at discharge.

The interprofessional medication reconciliation team, in collaboration with community physicians, wrote the medication history standard that was subsequently approved by the pharmacy and therapeutics committee and the medical executive committee of Cone Health. The medication history standard requires a structured interview with the patient or caregiver and any necessary follow-up with other sources to determine which medications to document in the best possible medication history. Documented medications are defined under the following four categories: scheduled, as-needed, short-term, and discontinued medications.

Scheduled medications are medications the patient takes on a regular

basis and are included on the list if the patient has taken a dose in the past 30 days. If a patient takes a medication with a frequency greater than monthly (e.g., medroxyprogesterone injections administered every three months), the medication will be included as a scheduled medication if a dose was taken within the period of that frequency.

As-needed medications taken within 30 days of hospitalization are also included in the medication history along with information about specific symptoms and frequency. A subcategory of as-needed medications called "emergency medications" was added shortly after program implementation, allowing for the documentation of specific emergency medications even if the patient had never used the medication. Examples of emergency medications used on an as-needed basis include sublingual or spray nitroglycerin, injectable epinephrine, and albuterol inhaler.

Short-term medications are taken on a regular basis for a brief duration (e.g., an antibiotic). If a patient has taken a dose of a short-term medication in the seven-day period before admission, it will be included in the best possible medication history with details about the start and planned stop dates.

Discontinued medications are medications recently taken in any of the three preceding categories, mentioned by a patient or still in his or her possession, that have been discontinued by a prescribing physician or intentionally by the patient for a specific reason (e.g., an intolerable adverse effect). If a patient indicates that a prescribing physician stopped a medication, the drug will not be included in the best possible medication history. If a patient indicates that he or she intentionally stopped a medication for a specific reason other than inability to acquire the medication, the medication will not be included in the best possible medication history.

Training and evaluation

The medication history standard forms the basis by which medication histories are measured for quality, as well as the foundation for training pharmacy technicians to obtain medication histories. Additional elements of the training program include detailed guidance on documentation, workflow, and performance expectations. The technicians begin their training with a half-day shadowing program in which they observe an experienced pharmacy technician obtaining patient medication histories. The program also includes a three-hour interactive lecture highlighting the medication history standard and key elements of a complete medication history. Initial skills demonstration is accomplished through a half day of simulated medication histories via role-playing with a pharmacist using standardized patient scripts. Each technician then performs a minimum of 10 directly observed medication histories. This phase of the training can be accomplished in less than a week. In the next phase of training, a pharmacist completes indirect observation for 100% of the technician's medication histories and provides timely feedback until the measured rates of both accuracy and completeness exceed 90%.

An evaluation form was developed to assist the pharmacists with both direct and indirect observations of the technician's performance (Figure 1). During direct observation, a pharmacist enters a patient's room with a technician and observes the technician taking the best possible medication history. For indirect observation, a pharmacist reviews the medication history documented in the EMR after it has been completed. Accuracy is defined as the number of correctly documented medications divided by the total number of medications. Completeness is defined as the number of completed elements of a structured medication history interview divided by the total number of required elements.

Management of pharmacy technicians

In 2009, the first four pharmacy technicians volunteered to learn to take medication histories. Since program inception, the staff of medication history–trained technicians has grown through the hiring of new staff members and by training existing pharmacy technicians. The culture of integrated staffing in the department of pharmacy led to a natural rotation between dispensing and medication history roles. Integrated staffing maintains a sense of the pharmacy team and limits burnout. Key qualifications sought for new technician hires include strong communication skills, time management, work ethic, and computer skills. North Carolina does not require pharmacy technician certification, but Cone Health requires certification within one year of hire. In 2011, medication history taking was established as a new major work activity for pharmacy technicians, emphasizing the importance of the investment to train and supervise technicians in this function.

After the initial training period, all pharmacy technicians receive ongoing supervision of their performance in taking medication histories. For each technician, minimums of 10 directly observed histories and 20 indirectly observed histories are reviewed annually. The three objective measures for the evaluation of this activity are individual rates for accuracy, completeness, and volume of medication histories per shift. Direct and indirect observations are used to follow up on skill development. Technicians are given face-to-face feedback for directly and indirectly observed histories as well as quarterly reports detailing their performance measures. A team of clinical pharmacists, staffing an eight-hour medication history shift five days per week, supervises the technicians.

Figure 1. Evaluation form used by pharmacists to assist with both direct and indirect observations of pharmacy technician's performance when completing a medication history.

Evaluation of Medication History

MR#_____

Historian: _____

Observer: _____

Date history taken: _____

Direct Observation Only			Comments
1. Gel in/wash out (and observed other contact precautions as required)?	☐ yes	☐ no	
2. Acknowledged the patient and used 2 patient identifiers upon room entry?	☐ yes	☐ no	
3. Introduced himself/herself to patient and/or family/caregiver?	☐ yes	☐ no	
4. Explained intent, described duration based on number of meds and asked the patient if it would be OK to discuss home medications with others room?	☐ yes	☐ no	
5. Home medication entered into computer while in room with patient?	☐ yes	☐ no	
6. Used interpreter as necessary? Correctly determined need to use outside resources?	☐ yes	☐ no	
7. Asked if patient takes any other OTCs and/or herbal medications? Specifically asked about patches, creams, injectables, eye drops & inhalers?	☐ yes	☐ no	
8. Asked open-ended questions? Asked adequate follow-up questions?	☐ yes	☐ no	
9. Observed MED RULE for SAD medications?	☐ yes or N/A	☐ no	
10. Thanked the patient and asked if he/she had questions before exiting room?	☐ yes	☐ no	
11. Used references for drug knowledge (e.g., had to look up a dose form, etc., via Micromedex, Epocrates, etc.)?	☐ yes or N/A	☐ no	
12. Correctly categorized medications for inclusion on medication history: Scheduled, PRN, Stopped & Short Term	☐ yes	☐ no	
13. Correctly identified and documented stopped medications.	☐ yes	☐ no	
14. Took history efficiently (average should be 5 meds in 7 minutes)? Time (min) _____ Number of medications_____ Time divided by number of medications = average minutes/ med _____	☐ yes	☐ no	
Direct or Indirect Observation: *Completeness Rate:* IO = # of yes (15-24)/10, or DO = # of yes (1-24)/24			
15. Documented allergies AND reactions?	☐ yes	☐ no	
16. Documented primary pharmacy & info source for each medication?	☐ yes	☐ no	
17. Documented last dose for each medication (and time for beta-blocker)?	☐ yes	☐ no	
18. Selected correct medication for each entry? Duplicate medications?	☐ yes	☐ no	
19. Documented indications and time-based frequency for each PRN medication?	☐ yes or N/A	☐ no	
20. "Additional Instruction" comments adequate and appropriate?	☐ yes	☐ no	
21. All medications include doses, strengths, and frequencies? Corrected outpatient medication entered incorrectly?	☐ yes	☐ no	
22. Changed medication history status to "in progress" and marked as reviewed upon completion?	☐ yes	☐ no	
23. Follow-up plan adequately documented?	☐ yes or N/A	☐ no	
24. "Pharmacist Review Pending" order entered for qualifying criteria?	☐ yes or N/A	☐ no	
25. Number of medications correct /total number of medications (*Accuracy Rate*)	_____/_____		

Additional Comments. ☐ See Attached Report

8/21/13 Cone Health

Technicians needing improvement are given an action plan along with individualized coaching by a pharmacist. Currently, over 80 technicians have successfully completed the medication history training program systemwide, and over 90% of the existing technician staff has been successfully trained to complete medication histories.

Based on structured evaluation, including both direct and indirect observations of technicians' medication histories, the accuracy and completeness rates have remained consistently over 90%. In our largest facility (517 beds), medication histories are provided 24 hours per day for an average of 79 admissions, 60 surgical preadmissions, and over 200 ED visits daily. As of 2012, technicians completed an average of 21 medication histories per shift at an accuracy rate of 92.59% and a completeness rate of 92.18%.

In 2012, a new EMR was implemented, requiring complete staff reeducation on workflow and the syntax of medication history documentation. The rules for the standard remained unchanged. Accuracy and completeness rates fell below 80% during the first quarter of implementation but have since risen and remain above 90%. The maintenance of medication history quality through a medical record transition demonstrated the value of a medication history standard as the foundation for accountability and training.

Challenges to establishing workflow

In 2009, Cone Health had three distinct EMRs for the ED, inpatient setting, and ambulatory care clinics. None of these records allowed for easy identification of patients being admitted. Medication history staffing began with a single pharmacy technician completing best possible medication histories in the ED for patients who were to be admitted. Due to patient identification challenges, histories were primarily completed on the floor after admission. Admitted patients were identified by an e-mail that was automatically sent by the hospital registration system to a designated medication history inbox. As the program expanded and staff grew to more than one medication history technician per shift, designated work areas were established based on geographic location to optimize timely completion of best possible medication histories. The e-mail system was utilized as a communication tool for necessary follow-up (e.g., calling a patient's pharmacy after it opened). Despite the challenging system limitations, the rate of patients whose best possible medication histories were not completed by pharmacy within 24 hours of admission was less than 1% in 2012.

Patient identification—a key limitation to program efficiency—was dramatically improved with the implementation of a single EMR. The status of the medication history was integrated into a universally accessible list of all inpatients, the ED track board, and the operating room schedule. Universal availability of the status of the medication history allows a team of medication history technicians working in remote geographic areas of the hospital to collaborate and complete best possible medication histories in a timely manner. Follow-up information is now documented directly on the medication history screen, making it easily accessible to all clinicians. Workflow challenges are now primarily linked to integrating an expanded staff of medication history technicians into an evolving workflow in a recently renovated and expanded ED and on multiple campuses.

Program impact on medication reconciliation

The metrics evaluated during initial implementation of the medication history program were rate of provider compliance with discharge medication reconciliation, provider time spent completing discharge medication reconciliation, and rate of compliance with heart failure core measures. Rates of provider compliance with medication reconciliation at discharge rose from 25% in 2006 to 89% in December 2010 and to over 90% in October 2011, despite the absence of an administrative utilization mandate for community physicians. When transitioning to the new EMR, the use of computerized prescriber order entry was mandated for all community physicians. Since the implementation of a new fully integrated EMR, health system rates of compliance with medication reconciliation have been 100%. In 2009, a single cardiology nurse practitioner recorded times for completion of discharge medication reconciliation for 20 patients before and after implementation, demonstrating a significant reduction in the total time for a complicated medical discharge (from 30 to 23 minutes [$p = 0.007$, Student's t test]). Full compliance with the heart failure core measures rose from 84% in the quarter before implementation to 95% in the quarter after implementation and has since remained above 95% for the health system.

Discussion

After determining that the poor quality of the gathered medication histories was the key barrier to provider compliance with medication reconciliation, a pharmacy technician–driven medication history program was implemented. The program was built upon a compliance-based medication history standard written by an interprofessional group of pharmacists, physicians, and nurses.

After the implementation of a fully integrated EMR in 2012, the medication history standard required adaptation to accommodate the specific documentation syntax of the new system. Full pharmacy department ownership of medication history entry for the majority of ED visits

before EMR implementation facilitated the transition to computerized prescriber order entry by reducing the number of hard stops physicians encountered when entering admission orders. Standardization has also reduced the time pharmacists spend in order verification.

However, the lack of an established and nationally standardized definition of a best possible medication history has presented challenges with the new EMR. Specifically, the EMR does not allow for robust documentation of medications the patient is not taking or taking differently than prescribed. As a result, to protect patient safety in the inpatient setting, prescribed medications that the patient is either not taking or taking differently than prescribed must be reentered into the EMR. This workflow removes important audit information from easily accessible lists in the EMR (e.g., original prescription date, refills), increasing the time required for the ambulatory care clinician attempting to perform detailed medication reconciliation. Postimplementation optimization of the new EMR is ongoing to maximize patient outcomes across the continuum of care.

Establishing a highly accountable pharmacy medication history program was a complex, multifaceted process with many challenges and setbacks. It took four years to convince our health system of the value of a high-quality best possible medication history as the cornerstone of patient safety. Physician leadership systemwide has been essential for program implementation and expansion. Provider utilization of electronic tools was key to the ultimate clinical utility of a best possible medication history documented by pharmacy. The lack of resources allocated for provider training slowed implementation. The success of the pharmacy medication history program at this health system lies not only in standardization but also in accountability. The exceptional pharmacy technician staff of our health system have stepped up and grown dramatically since program inception. Pharmacists' ownership of best possible medication history accountability and ongoing role in medication reconciliation have also been critical to maintaining quality. The best possible medication history is at the heart of medication safety; taking the time to recruit, train, and retain the right technicians has been a sound investment.

In the rapidly evolving healthcare marketplace, the importance of patient safety and optimizing pharmaceutical care cannot be overemphasized, as the rate of errors is high without a system in place for prevention, especially in the ED.[1,17-19] Without standardization of the documented best possible medication history, it may be difficult to demonstrate the clinical utility and cost-effectiveness of medication reconciliation.[3,22] Our health system is currently evaluating the cost benefit of our standardized best possible medication history service for all ED arrivals. Regardless of the outcome of this analysis, the Joint Commission requires that a medication history be documented for all patients on arrival at the health system.[5] Medication histories that are inconsistently and incorrectly documented may result in risk adverse events, especially in fully integrated EMRs.[15,16,20] A standardized best possible medication history documented once in a timely manner for each patient reduces redundancy and patient confusion and gives accurate information to the ED provider, an important decision-maker regarding the use of healthcare resources. Utilizing pharmacy technicians to staff this program significantly reduces the cost per medication history.[20,28] The investment in pharmacy technician FTEs to ensure a standardized best possible medication history for all patients has dramatically improved provider compliance with medication reconciliation.

Conclusion

A defined medication history based on a medication history standard served as an effective foundation for a pharmacy technician medication history program, which helped improve provider compliance with discharge medication reconciliation.

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Attachment 8

FDA News Release

FDA outlines expectations for human drug compounders, including registered outsourcing facilities

For Immediate Release

July 1, 2014

Release

Today, the U.S. Food and Drug Administration issued several policy documents regarding compounded drug products for human use, as part of the agency's continuing effort to implement the compounding provisions of the Drug Quality and Security Act (DQSA), enacted in November 2013. The policy documents consist of a draft interim guidance, a proposed rule, a final guidance, and two revised requests for nominations for the bulk drug substances lists.

"Providing clarity to the compounding industry on the agency's expectations for these unapproved drug products is a priority for the agency," said Janet Woodcock, M.D., director of the FDA's Center for Drug Evaluation and Research. "These actions are essential next steps in providing the compounding industry with the appropriate tools to comply with the law and advancing the FDA's efforts to continue protecting patients." The documents available today are:

- Draft interim guidance that describes the FDA's expectations regarding compliance with current good manufacturing practice (CGMP) requirements for facilities that compound human drugs and register with the FDA as outsourcing facilities under section 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act). The guidance focuses on CGMP requirements related to sterility assurance of sterile drug products and the general safety of compounded drug products.
- A proposed rule that would revise the FDA's current list of drug products that may not be compounded because the drug products have been withdrawn or removed from the market because they were found to be unsafe or not effective. The proposed rule would modify the description of one drug product on the list and add 25 drug products to the list.

  The list set forth in the proposed rule would apply to both compounders and outsourcing facilities seeking to compound drugs for human use under sections 503A and 503B, respectively.

- Final guidance for individuals or pharmacies that intend to compound drugs under section 503A, now that the FD&C Act has been amended by the DQSA. The guidance generally restates the provisions of section 503A, describes the FDA's interim policies with respect to specific provisions that require implementing regulations or other actions, and contains a non-exhaustive list of potential enforcement actions against individuals or pharmacies that compound human drug products in violation of the FD&C Act.

- Two Federal Register Notices stating the FDA is reopening the nomination process for two lists of bulk drug substances (active pharmaceutical ingredients) that may be used to compound drug products. One list is for drug products compounded in accordance with section 503A, and the other list is for drug products compounded in accordance with section 503B of the FD&C Act. In response to a December 2013 request for nominations, the agency received nominations that were not for bulk drug substances used in compounding, and that did not provide sufficient information to justify inclusion of the substances on the lists.

  The FDA is providing more detail on what information is needed to evaluate the nominations for placement on the lists.

  The draft interim guidance and proposed rule are available for public comment for 60 days, and the dockets are open for the public to nominate bulk drug substances for compounding under section 503A or 503B for 90 days.

  The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

Compliance), those steps must be done to comply with this AD; any steps that are not labeled as RC are recommended. Those steps that are not labeled as RC may be deviated from, done as part of other actions, or done using accepted methods different from those identified in the specified service information without obtaining approval of an AMOC, provided the steps labeled as RC can be done and the airplane can be put back in a serviceable condition. Any substitutions or changes to steps labeled as RC require approval of an AMOC.

(k) Related Information

(1) For more information about this AD, contact Marie Hogestad, Aerospace Engineer, Systems and Equipment Branch, ANM–130S, Seattle Aircraft Certification Office (ACO), FAA, 1601 Lind Avenue SW., Renton, WA 98057–3356; phone: 425–917–6418; fax: 425–917–6590; email: *marie.hogestad@faa.gov.*

(2) For service information identified in this AD, contact Boeing Commercial Airplanes, Attention: Data & Services Management, P. O. Box 3707, MC 2H–65, Seattle, WA 98124–2207; telephone 206–544–5000, extension 1; fax 206–766–5680; Internet *https://www.myboeingfleet.com.* You may view this referenced service information at the FAA, Transport Airplane Directorate, 1601 Lind Avenue SW., Renton, WA. For information on the availability of this material at the FAA, call 425–227–1221.

Issued in Renton, Washington, on June 24, 2014.

Jeffrey E. Duven,

Manager, Transport Airplane Directorate, Aircraft Certification Service.

[FR Doc. 2014–15505 Filed 7–1–14; 8:45 am]

BILLING CODE 4910–13–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 216

[Docket No. FDA–1999–N–0194 (Formerly 99N–4490)]

RIN 0910–AH10

Additions and Modifications to the List of Drug Products That Have Been Withdrawn or Removed From the Market for Reasons of Safety or Effectiveness

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule; withdrawal of previous proposed rule.

SUMMARY: The Food and Drug Administration (FDA or the Agency) is proposing to amend its regulations to revise the list of drug products that may not be compounded under the exemptions provided by the Federal Food, Drug, and Cosmetic Act (the FD&C Act) because the drug products have been withdrawn or removed from the market after the drug products or components of such drug products were found to be unsafe or not effective. Specifically, the proposed rule would add 25 drug products to this list of drug products and modify the description of one drug product on this list to add an exception. These revisions are necessary because new information has come to the Agency's attention since March 8, 1999, when FDA published the original list as a final rule. FDA is also withdrawing the previous proposed rule regarding additions to this list (see the **Federal Register** of January 4, 2000).

DATES: Submit either electronic or written comments on the proposed rule by September 2, 2014. The January 4, 2000, proposed rule (65 FR 256) is withdrawn as of July 2, 2014.

ADDRESSES: You may submit comments, identified by Agency name and Docket No. FDA–1999–N–0194 and/or Regulatory Information Number (RIN) number 0910–AH10, by any of the following methods:

Electronic Submissions

Submit electronic comments in the following way:

• Federal eRulemaking Portal: *http://www.regulations.gov.* Follow the instructions for submitting comments.

Written Submissions

Submit written submissions in the following ways:

• Mail/Hand delivery/Courier (for paper submissions): Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

Instructions: All submissions received must include the Agency name, Docket No. FDA–1999–N–0194, and RIN 0910–AH10 for this rulemaking. All comments received may be posted without change to *http://www.regulations.gov*, including any personal information provided. For additional information on submitting comments, see the ''Request for Comments'' heading of the **SUPPLEMENTARY INFORMATION** section of this document.

Docket: For access to the docket to read background documents or comments received, go to *http://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Edisa Gozun, Center for Drug Evaluation and Research (HFD–310), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 5199, Silver Spring, MD 20993–0002, 301–796–3110.

SUPPLEMENTARY INFORMATION:

I. Background

Section 503A of the FD&C Act (21 U.S.C. 353a) describes the conditions that must be satisfied for human drug products compounded by a licensed pharmacist or licensed physician to be exempt from the following three sections of the FD&C Act: (1) Section 501(a)(2)(B) (21 U.S.C. 351(a)(2)(B)) (concerning current good manufacturing practice); (2) section 502(f)(1) (21 U.S.C. 352(f)(1)) (concerning the labeling of drugs with adequate directions for use); and (3) section 505 (21 U.S.C. 355) (concerning the approval of drugs under new drug applications (NDAs) or abbreviated new drug applications (ANDAs)).

One of the conditions that must be satisfied to qualify for the exemptions under section 503A of the FD&C Act is that the licensed pharmacist or licensed physician does not compound a drug product that appears on a list published by the Secretary in the **Federal Register** of drug products that have been withdrawn or removed from the market because such drug products or components of such drug products have been found to be unsafe or not effective (see section 503A(b)(1)(C) of the FD&C Act).

A. Court Decisions Regarding the Pharmacy Compounding Provisions of the FD&C Act

As originally enacted, section 503A of the FD&C Act included prohibitions on the advertising and solicitation of prescriptions for any particular compounded drug, class of drug, or type of drug. Seven compounding pharmacies challenged the advertising and solicitation provisions of section 503A of the FD&C Act as an impermissible regulation of commercial speech. In February 2001, the U.S. Court of Appeals for the Ninth Circuit held that the prohibition on advertising and promotion in section 503A(c) and the provision of section 503A(a) of the FD&C Act that requires that the prescription be ''unsolicited,'' were unconstitutional restrictions on commercial speech. (See *Western States Med. Ctr.* v. *Shalala,* 238 F.3d 1090 (9th Cir. 2001).) Furthermore, the Ninth Circuit held that the advertising and solicitation provisions could not be severed from the rest of section 503A and, as a result, found section 503A of the FD&C Act to be invalid in its

entirety. In April 2002, the U.S. Supreme Court affirmed the Ninth Circuit's decision that the advertising and solicitation provisions were unconstitutional; it did not, however, rule on the severability of section 503A of the FD&C Act. (See *Thompson* v. *Western States Med. Ctr.,* 535 U.S. 357 (2002).)

In light of these decisions, FDA issued a Compliance Policy Guide in 2002 to provide guidance on FDA's approach concerning the regulation of pharmacy compounding. (See the **Federal Register** of June 7, 2002 (67 FR 39409).)

In September 2004, 10 pharmacies brought suit in the U.S. District Court for the Western District of Texas challenging FDA's authority to regulate compounded drugs. In August 2006, the District Court held, in part, that compounded human drugs are implicitly exempt from the ''new drug'' definition in section 201(p) of the FD&C Act and, as a result, are not subject to the FD&C Act's new drug approval requirements. (See *Medical Ctr. Pharm.* v. *Gonzales,* 451 F. Supp. 2d 854 (W.D. Tex. 2006).) The District Court also held that the advertising and solicitation provisions in section 503A of the FD&C Act that the Supreme Court had found to be unconstitutional were severable from the rest of that section.

The Federal Government appealed the decision of the U.S. District Court for the Western District of Texas. In July 2008, the U.S. Court of Appeals for the Fifth Circuit reversed the District Court's finding of an implicit exemption for compounded drugs from the new drug approval requirements in the FD&C Act, holding, instead, that compounded drugs fall within the definition of ''new drug'' in the FD&C Act and, therefore, are subject to regulation by FDA. (See *Medical Ctr. Pharm.* v. *Mukasey,* 536 F.3d 383 (5th Cir. 2008).) The Fifth Circuit also held that the advertising and solicitation provisions are severable from the rest of section 503A of the FD&C Act, and as a result, the other provisions of section 503A remain in effect.

The Fifth Circuit's severability ruling conflicted with the earlier Ninth Circuit decision, which held that the advertising and solicitation provisions cannot be severed from section 503A of the FD&C Act, and rendered all of section 503A void. Following a fungal meningitis outbreak in September 2012, FDA sought legislation to, among other things, resolve the split in the Circuits to clarify that section 503A of the FD&C Act was valid nationwide.

B. 2013 Drug Quality and Security Act

On November 27, 2013, President Obama signed the Drug Quality and Security Act (Pub. L. 113–54) (DQSA) that contains important provisions relating to the oversight of compounding of human drugs. This new law removes from section 503A of the FD&C Act the provisions that had been held unconstitutional by the U.S. Supreme Court in 2002. By removing these provisions, the new law clarifies that section 503A of the FD&C Act applies nationwide. In addition, the DQSA adds a new section 503B of the FD&C Act (21 U.S.C. 353b) that creates a new category of ''outsourcing facilities.'' Outsourcing facilities, as defined in section 503B of the FD&C Act, are facilities that meet certain conditions described in section 503B, including registering with FDA as an outsourcing facility. If these conditions are satisfied, a drug compounded for human use by or under the direct supervision of a licensed pharmacist in an outsourcing facility is exempt from three sections of the FD&C Act: (1) Section 502(f)(1), (2) section 505, and (3) section 582 (21 U.S.C. 360eee); but not section 501(a)(2)(B). One of the conditions in section 503B of the FD&C Act that must be satisfied to qualify for the exemptions is that the drug does not appear on a list published by the Secretary of drugs that have been withdrawn or removed from the market because such drugs or components of such drugs have been found to be unsafe or not effective (see section 503B(a)(4)).

Given that nearly identical criteria apply for a drug to be included on the list referred to in section 503A(b)(1)(C) and the list referred to in section 503B(a)(4) of the FD&C Act, FDA is proposing to revise and update the list at § 216.24 (21 CFR 216.24) for purposes of both sections 503A and 503B. Accordingly, the proposed rule that published in the **Federal Register** of January 4, 2000, which would have amended the list in § 216.24, is withdrawn (see **DATES**).

C. Regulatory History of the List

1. Original List

In the **Federal Register** of October 8, 1998 (63 FR 54082), FDA proposed a rule to establish the original list of drug products that have been withdrawn or removed from the market because the drug products or the components of such drug products were found to be unsafe or not effective (1998 proposed rule). The 1998 proposed rule was presented to the Pharmacy Compounding Advisory Committee (Advisory Committee) at a meeting held on October 14 and 15, 1998 (63 FR 47301, September 4, 1998). The Advisory Committee did not have any adverse comments on the 1998 proposed rule and did not suggest any changes. A transcript of the October 1998 Advisory Committee meeting may be found at the Division of Dockets Management (see **ADDRESSES**) and at *http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm290713.htm.*

In the **Federal Register** of March 8, 1999 (64 FR 10944), FDA published a final rule that codified the original list in § 216.24 (1999 final rule).

2. 2000 Proposed Rule and Additional Drug Products for the List in § 216.24

In the **Federal Register** of January 4, 2000 (65 FR 256), FDA proposed a rule to amend § 216.24 (2000 proposed rule). Specifically, FDA proposed to add all drug products containing aminopyrine and all drug products containing astemizole to the original list of drug products withdrawn or removed from the market because they have been found to be unsafe or not effective. After the 2000 proposed rule published, three additional drug products (cisapride, grepafloxacin, and troglitazone) were identified as candidates for addition to the list. These five drug products were presented to the Advisory Committee at a meeting held on July 13 and 14, 2000 (65 FR 40104, June 29, 2000). The Advisory Committee voted to include aminopyrine, astemizole, cisapride, grepafloxacin, and troglitazone to the list of drug products that have been withdrawn or removed from the market because they were found to be unsafe or not effective. A transcript of the July 2000 Advisory Committee meeting may be found at the Division of Dockets Management (see **ADDRESSES**) and at *http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm290713.htm.*

3. New Proposed Rule To Amend the List in § 216.24

This proposed rule would add to § 216.24 the five drug products identified in section I.C.2 and additional drug products that have been withdrawn or removed from the market since the publication of the 1999 final rule because the drug products or components of such drug products were found to be unsafe or not effective. FDA also proposes to modify the description of one drug product contained in the original list to add an exception that would allow the product to be compounded under certain

circumstances. These revisions are necessary to ensure the list of drugs in § 216.24 reflects new information that has come to the Agency's attention since FDA published the original list in the 1999 final rule. As with the original list, the primary focus of this proposed rule is on drug products that have been withdrawn or removed from the market because they were found to be unsafe. FDA may propose at a later date to add other drug products to the list that have been withdrawn or removed from the market because they were found to be not effective, or to update the list as new information becomes available to the Agency regarding products that were removed from the market because they were found to be unsafe.

This proposed rule would replace the 2000 proposed rule. The list set forth in this proposed rule would apply to compounders and outsourcing facilities seeking to qualify for the exemptions under either section 503A or section 503B of the FD&C Act. Accordingly, the 2000 proposed rule to amend § 216.24 is withdrawn. In preparing this proposed rule, FDA has taken into consideration the discussions held by the July 2000 Advisory Committee and that Advisory Committee's vote to include aminopyrine, astemizole, cisapride, grepafloxacin, and troglitazone on the list of drug products that have been withdrawn or removed from the market because they were found to be unsafe or not effective.

Additional nominations for this list can be submitted to FDA for consideration in comments to this proposed rule.

II. Procedural Issue for Comment

Section 503A of the FD&C Act describes the list in section 503A(b)(1)(C) as a list published by the Secretary in the **Federal Register** of drug products that have been withdrawn or removed from the market because such drug products or components of such drug products have been found to be unsafe or not effective. This suggests that FDA can develop the 503A(b)(1)(C) list by publishing it in the **Federal Register** and does not need to go through notice and comment rulemaking. Section 503A(c)(1) of the FD&C Act, however, states that the Secretary shall issue regulations to implement section 503A, and that before issuing regulations to implement section 503A(b)(1)(C) pertaining to the withdrawn or removed rule, among other sections, the Secretary shall convene and consult an advisory committee on compounding unless the Secretary determines that the issuance of such regulations before consultation is necessary to protect the public health. In 1998 and 1999, FDA used rulemaking to develop the original list of drug products that had been withdrawn or removed from the market, and consulted the Pharmacy Compounding Advisory Committee about the list. In 2000, FDA also proposed to amend the list through rulemaking after consultation with the Advisory Committee.

Meanwhile, new section 503B of the FD&C Act describes the list in section 503B(a)(4) as a list published by the Secretary of drugs that have been withdrawn or removed from the market because such drugs or components of such drugs have been found to be unsafe or not effective. Section 503B(c) of the FD&C Act requires that the Secretary implement through regulations, following consultation with an advisory committee, a list of drugs or categories of drugs that present demonstrable difficulties for compounding that are reasonably likely to lead to an adverse effect on the safety or effectiveness of the drug or category of drugs and therefore may not be compounded under section 503B. (See section 503B(a)(6) of the FD&C Act.) Section 503B does not, however, include any similar requirement for rulemaking or consultation with an advisory committee to establish the list of drugs that may not be compounded under section 503B of the FD&C Act because they have been withdrawn or removed from the market because such drugs or components of such drugs have been found to be unsafe or not effective.

As noted, FDA plans to publish a single list of drug products (referred to as ''the withdrawn or removed list'' or ''the list'') that cannot be compounded for human use under the exemptions provided by either section 503A or 503B of the FD&C Act because they have been withdrawn or removed from the market because such drug products or components of such drug products have been found to be unsafe or not effective. FDA invites comments on the appropriate procedure to update the list in the future. The Agency believes that the timely sharing of information about safety concerns relating to compounding drugs for human use without undue delay is essential to the protection of public health. FDA is concerned that consulting with the advisory committee and completing the rulemaking process are likely to contribute to substantial delay in updating the list to reflect current safety information. FDA therefore is seeking an alternative procedure to update the withdrawn or removed list in the future. Although FDA is publishing a proposed rule today to add 25 drugs to the list, FDA is also soliciting public input through this **Federal Register** notice on alternative procedures for updating the list and requests that this input be submitted to FDA for consideration in comments to this proposed rule. FDA will specify in the final rule the procedure it will use to update the list in the future.

III. Description of This Proposed Rule

A. Amendments to Introductory Text

FDA is proposing to add the phrase ''or section 503B(a)'' to the introductory text of § 216.24 to clarify that drug products included in the list in § 216.24 will not qualify for the exemptions under either section 503A(a) or section 503B(a) of the FD&C Act when compounded.

B. Amendments To Add Drug Products to the List

FDA is proposing to amend § 216.24 to include the 25 drug products described in the following paragraphs that have been withdrawn or removed from the market since the 1999 final rule was published (March 1999) because such drug products or components of such drug products have been found to be unsafe or not effective.

A drug product that is included in the list codified at § 216.24 is not entitled to the exemptions provided in section 503A(a) of the FD&C Act, and is subject to sections 501(a)(2)(B), 502(f)(1), and 505 of the FD&C Act, in addition to other applicable provisions. In addition, a drug that is included in the list codified at § 216.24 is not entitled to the exemptions provided in section 503B(a) of the FD&C Act, and is subject to sections 502(f)(1) and 505 of the FD&C Act, in addition to other applicable provisions.

The listed drugs are ineligible for the exemptions set forth in sections 503A and 503B of the FD&C Act because they have been withdrawn or removed from the market because they were found to be unsafe or not effective. Most drugs on the list may not be compounded in any form. There are, however, two categories of exceptions. In the first category, a particular formulation, indication, dosage form, or route of administration of a drug is explicitly excluded from an entry on the list because an approved drug containing the same active ingredient(s) has not been withdrawn or removed from the market. For such drugs, the formulation, indication, dosage form, or route of administration expressly excluded from the list may be eligible for the exemptions provided in sections 503A and 503B of the FD&C Act. In the second category, some drugs are listed only with regard to certain

formulations, concentrations, indications, routes of administration, or dosage forms because they have been found to be unsafe or not effective in those particular formulations, concentrations, indications, routes of administration, or dosage forms. For drugs that are listed with these types of limitations, any compounding of the drug will be closely scrutinized to ensure that the compounding of the drug does not create a product that is unsafe or not effective. If it appears to do so, FDA may determine that the drug is not entitled to the exemptions provided in sections 503A and 503B of the FD&C Act. Those compounding these particular drugs should take note of the reasons FDA has cited for including a drug on this list, and carefully consider these reasons when considering whether or not to compound a drug that is so listed.

The following drug products are arranged alphabetically by the established names of the active ingredients contained in the drug products and are proposed for inclusion in § 216.24. For many of the drugs, the proprietary or trade name of some or all of the drug products that contained the active ingredient are also given in the preamble paragraphs describing the withdrawn or removed drug products. In several cases, the withdrawn or removed drug products are identified according to the established name of the active ingredient, listed as a particular salt or ester of the active moiety. The following list includes a brief summary of the reasons why each drug product is being proposed for inclusion.

Alatrofloxacin mesylate: All drug products containing alatrofloxacin mesylate. Alatrofloxacin mesylate, formerly marketed as TROVAN Injection, was associated with serious liver injury. On June 9, 1999, FDA announced in a Public Health Advisory that the NDA holder agreed to a limited distribution of TROVAN (alatrofloxacin mesylate) Injection and TROVAN (trovafloxacin mesylate) tablets, 100 milligrams (mg) and 200 mg, to in-patient healthcare facilities (Ref. 1). Subsequently, in the **Federal Register** of June 16, 2006 (71 FR 34940), FDA announced that it was withdrawing the approval of the NDA for TROVAN Injection after the NDA holder notified the Agency that the drug product was no longer marketed and requested that the approval of the NDA be withdrawn.

Aminopyrine: All drug products containing aminopyrine. Aminopyrine was associated with agranulocytosis, a condition characterized by a decrease in the number of certain blood cells and lesions on the mucous membrane and skin. Some cases of agranulocytosis were fatal. In 1964, FDA declared drug products containing aminopyrine to be new drugs and invited NDAs for these drug products, but only for use as an antipyretic in serious situations where other, safer drugs could not be used. FDA received no NDAs for drug products containing aminopyrine, and those unapproved drug products were removed from the market (see the **Federal Register** of October 4, 1977 (42 FR 53954), and January 4, 2000 (65 FR 256)). Aminopyrine was presented to the Advisory Committee at the July 2000 meeting, and the Advisory Committee voted to include aminopyrine on the withdrawn or removed list (see the **Federal Register** of June 29, 2000 (65 FR 40104)).

Astemizole: All drug products containing astemizole. Astemizole, formerly marketed as HISMANAL 10-mg tablets, was associated with life-threatening heart arrhythmias. Patients with liver dysfunction or who were taking other drugs that interfered with the metabolism of astemizole were also found to be at risk of serious cardiac adverse events while taking astemizole. On June 18, 1999, the NDA holder withdrew HISMANAL (astemizole) 10-mg tablets from the market. In the **Federal Register** of August 23, 1999 (64 FR 45973), FDA announced its determination that HISMANAL (astemizole) 10-mg tablets were removed from the market for safety reasons. (See also the **Federal Register** of January 4, 2000 (65 FR 256).) Astemizole was presented to the Advisory Committee at the July 2000 meeting, and the Advisory Committee voted to include astemizole on the withdrawn or removed list (see the **Federal Register** of June 29, 2000 (65 FR 40104)).

Cerivastatin sodium: All drug products containing cerivastatin sodium. Cerivastatin sodium, formerly marketed as BAYCOL tablets, was associated with increased risk of rhabdomyolysis. Fatal rhabdomyolysis was reported most frequently when used at higher doses, when used in elderly patients, and particularly, with concomitant use of gemfibrozil (LOPID). In an August 8, 2001, ''Dear Healthcare Professional Letter,'' the NDA holder stated that it discontinued the marketing and distribution of all dosage strengths of BAYCOL (Ref. 2).

Chloramphenicol: All oral drug products containing chloramphenicol. Chloramphenicol was formerly marketed as CHLOROMYCETIN (chloramphenicol) Capsules. In a letter dated October 9, 2007, the application holder requested withdrawal of the ANDA for CHLOROMYCETIN (chloramphenicol) Capsules, 50 mg, 100 mg, and 250 mg. In the **Federal Register** of February 11, 2009 (74 FR 6896), FDA announced that it was withdrawing approval of the ANDA, effective March 13, 2009. Armenpharm, Ltd., submitted a citizen petition dated February 7, 2011 (Docket No. FDA–2011–P–0081), under § 10.30 (21 CFR 10.30), requesting that the Agency determine whether CHLOROMYCETIN (chloramphenicol) Capsules, 250 mg, were withdrawn from sale for reasons of safety or effectiveness. After considering the citizen petition, FDA determined that the drug product was withdrawn for reasons of safety or effectiveness. With the approval of additional therapies with less severe adverse drug effects, FDA determined that the risks associated with CHLOROMYCETIN (chloramphenicol) Capsules, 250 mg, as then labeled, outweighed the benefits. Furthermore, CHLOROMYCETIN (chloramphenicol) Capsules, 250 mg, may cause a number of adverse reactions, the most serious being bone marrow depression (anemia, thrombocytopenia, and granulocytopenia temporally associated with treatment). Additionally, prior to the removal of the capsule drug product from the market, a boxed warning in the prescribing information for both chloramphenicol sodium succinate injection and chloramphenicol capsules stated that serious hypoplastic anemia, thrombocytopenia, and granulocytopenia are known to occur after administration of chloramphenicol. The boxed warning also described fatal aplastic anemia associated with administration of the drug and aplastic anemia attributed to chloramphenicol that later terminated in leukemia. There is published literature that suggests that the risk of fatal aplastic anemia associated with the oral formulation of chloramphenicol may be higher than the risk associated with the intravenous formulation (see the **Federal Register** of July 13, 2012 (77 FR 41412)). FDA is not aware of any oral drug products containing chloramphenicol currently being marketed.

Cisapride: All drug products containing cisapride. Cisapride, formerly marketed as PROPULSID tablets and suspension, was associated with serious cardiac arrhythmias and death. In an April 12, 2000 ''Dear Healthcare Professional Letter,'' the NDA holder stated that it would discontinue marketing the drug as of July 14, 2000, and make the product available only through an investigational limited access program

(Ref. 3). Cisapride was presented to the Advisory Committee at the July 2000 meeting, and the Advisory Committee voted to include cisapride on the withdrawn or removed list (see the **Federal Register** of June 29, 2000 (65 FR 40104)).

Esmolol hydrochloride: All parenteral drug products containing esmolol HCl that supply 250 mg/milliliter (mL) of concentrated esmolol per 10-mL ampule. Esmolol hydrochloride (HCl), 250 mg/mL per 10-mL ampule, formerly marketed as BREVIBLOC Injection 250 mg/mL per 10-mL ampule, was associated with increased risk of medication errors resulting in serious adverse events, including deaths. The NDA holder sent a letter to FDA on June 28, 2007, notifying the Agency that the company had decided to cease the manufacture and distribution of BREVIBLOC (esmolol HCl) Injection, 250 mg/mL, 10-mL ampule. In a citizen petition dated March 27, 2008 (Docket No. FDA–2008–P–0284), submitted under § 10.30 and in accordance with 21 CFR 314.122 and 314.161, Bedford Laboratories (Bedford) requested that the Agency determine whether BREVIBLOC (esmolol HCl) Injection, 250 mg/mL, 10-mL ampule, was withdrawn from sale for reasons of safety or effectiveness. In the **Federal Register** of May 5, 2010 (75 FR 24710), FDA announced its determination that BREVIBLOC (esmolol HCl) Injection 250 mg/mL, 10-mL ampule, was withdrawn from the market for safety reasons.

Etretinate: All drug products containing etretinate. Etretinate was formerly marketed as TEGISON Capsules. In a letter dated September 23, 1999, the NDA holder requested that FDA withdraw the approval of the NDA for TEGISON (etretinate) Capsules because it had discontinued marketing the product. The letter also stated that the drug was not withdrawn for safety reasons. However, in an acknowledgement letter dated December 30, 2002, FDA informed the NDA holder that TEGISON (etretinate) Capsules was removed from the market because it posed a greater risk of birth defects than SORIATANE (acitretin), the product that replaced TEGISON (etretinate) Capsules (see the **Federal Register** of September 10, 2003 (68 FR 53384)). Subsequently, in the **Federal Register** of September 10, 2003, FDA announced it was withdrawing approval of the NDA.

Gatifloxacin: All drug products containing gatifloxacin (except ophthalmic solutions). Gatifloxacin was formerly marketed as TEQUIN tablets, injection, and oral suspension. In January 2003, FDA received revised product labeling relating to several approved supplements for TEQUIN (gatifloxacin). This revised labeling deleted references to TEQUIN injection, 10 mg/mL (200 mg), indicating that this product was no longer being marketed; therefore, the product was moved from the prescription drug product list to the ''Discontinued Drug Product List'' section of the ''Approved Drug Products With Therapeutic Equivalence Evaluations'' (the Orange Book). In response to a citizen petition from Apotex Corp. (Docket No. FDA–2005–P–0369),[1] FDA determined, as set forth in the **Federal Register** of February 3, 2006 (71 FR 5858), that TEQUIN injection, 10 mg/mL (200 mg), was not withdrawn for reasons of safety and effectiveness. On May 1, 2006, Public Citizen Research Group submitted a citizen petition (Docket No. FDA–2006–P–0081),[2] under § 10.30, requesting that FDA immediately ban TEQUIN because of the increased risk of dysglycemia (hypoglycemia, low blood sugar, and hyperglycemia, high blood sugar) in humans. In June 2006, the NDA holder announced that it would no longer market TEQUIN. In the **Federal Register** of September 9, 2008 (73 FR 52357), FDA announced its determination that all dosage forms and strengths of TEQUIN (gatifloxacin) were withdrawn from the market for safety reasons. There are currently approved gatifloxacin ophthalmic solutions on the market. Thus, FDA is proposing to include all drug products containing gatifloxacin, except ophthalmic solutions, on the withdrawn or removed list.

Grepafloxacin: All drug products containing grepafloxacin. Grepafloxacin, formerly marketed as RAXAR tablets, was associated with cardiac repolarization, manifested as QTc interval prolongation on the electrocardiogram, which could put patients at risk of Torsade de Pointes. The NDA holder sent a letter to FDA on March 5, 2003, requesting that FDA withdraw the approval of the NDA for RAXAR tablets, stating that the product was no longer being marketed. In an acknowledgment letter dated June 20, 2003, FDA stated that RAXAR (grepafloxacin) tablets had been removed from the market because of safety concerns. In a followup letter dated January 12, 2007, FDA informed the NDA holder that the RAXAR NDA should be withdrawn because of the cardiovascular risks stated previously. The NDA holder sent a letter to FDA on March 20, 2007, agreeing with FDA's determination to initiate the withdrawal of the RAXAR NDA, and FDA subsequently announced that approval of the NDA was withdrawn (see the **Federal Register** of June 14, 2007 (72 FR 32852), and July 9, 2007 (72 FR 37244)). Grepafloxacin was presented to the Advisory Committee at the July 2000 meeting, and the Advisory Committee voted to include grepafloxacin on the withdrawn or removed list (see the **Federal Register** of June 29, 2000 (65 FR 40104)).

Methoxyflurane: All drug products containing methoxyflurane. Methoxyflurane, formerly marketed as PENTHRANE Inhalation Liquid, 99.9 percent, was associated with serious, irreversible, and even fatal nephrotoxicity and hepatotoxicity in humans. In the **Federal Register** of August 16, 2001 (66 FR 43017), FDA announced that it was withdrawing the approval of the NDA after the NDA holder notified the Agency that PENTHRANE (methoxyflurane) Inhalation Liquid was no longer being marketed under the NDA and requested withdrawal of the application. In a citizen petition dated August 25, 2004 (Docket No. FDA–2004–P–0337),[3] submitted under § 10.30, and in accordance with § 314.161, AAC Consulting Group requested that the Agency determine whether PENTHRANE (methoxyflurane) Inhalation Liquid, 99.9 percent, was withdrawn from sale for reasons of safety or effectiveness. In the **Federal Register** of September 6, 2005 (70 FR 53019), FDA announced its determination that PENTHRANE Inhalation Liquid, 99.9 percent, was withdrawn from the market for safety reasons.

Novobiocin sodium: All drug products containing novobiocin sodium. Novobiocin sodium, formerly marketed as ALBAMYCIN capsule, 250 mg, was associated with adverse reactions that included relatively common skin reactions, jaundice, hepatic failure, and blood dyscrasias (neutropenia, anemia, and thrombocytopenia). Literature also revealed concerns about the development of novobiocin-resistant *Staphylococci* during treatment and a potential for drug interactions. On June

[1] This citizen petition was originally assigned docket number 2005P–0023/CP1. The number was changed to FDA–2005–P–0369 as a result of FDA's transition to its new docketing system (*http://www.regulations.gov*) in January 2008.

[2] This citizen petition was originally assigned docket number 2006P–0178. The number was changed to FDA–2006–P–0081 as a result of FDA's transition to its new docketing system (*http://www.regulations.gov*) in January 2008.

[3] This citizen petition was originally assigned docket number 2004P–0379. The number was changed to FDA–2004–P–0337 as a result of FDA's transition to its new docketing system (*http://www.regulations.gov*) in January 2008.

9, 1999, the NDA holder sent an annual report to FDA that indicated that ALBAMYCIN (novobiocin sodium) capsule, 250 mg, was no longer being manufactured, and on June 27, 2007, the NDA holder sent a letter to FDA notifying the Agency that ALBAMYCIN (novobiocin sodium) capsule, 250 mg, had been discontinued. In the **Federal Register** of February 11, 2009 (74 FR 6896), FDA announced that it was withdrawing approval of the NDA in response to the NDA holder's withdrawal request. Crixmore LLC submitted a citizen petition dated July 9, 2008 (Docket No. FDA–2008–P–0431), under § 10.30, requesting that the Agency determine whether ALBAMYCIN (novobiocin sodium) capsule, 250 mg, was withdrawn from sale for reasons of safety or effectiveness. In the **Federal Register** of January 19, 2011 (76 FR 3143), FDA announced its determination that ALBAMYCIN (novobiocin sodium) capsule, 250 mg, was withdrawn from the market for reasons of safety or effectiveness.

Oxycodone hydrochloride: All extended-release drug products containing oxycodone hydrochloride that have not been determined by FDA to have abuse-deterrent properties. OXYCONTIN (oxycodone hydrochloride) extended-release tablets were approved in multiple strengths under NDA 20–553 in 1995. The formulation was often abused by manipulating the product to defeat its extended-release mechanism, causing the oxycodone to be released more rapidly. This product was voluntarily withdrawn from sale following introduction of a reformulated version, also marketed as OXYCONTIN (oxycodone hydrochloride) extended-release tablets, which was developed with physicochemical properties intended to make the tablets more difficult to manipulate for purposes of abuse or misuse and was approved in multiple strengths under NDA 22–272 in 2010. Several parties submitted citizen petitions under § 10.30, requesting that the Agency determine whether original OXYCONTIN (oxycodone HCl) extended-release tablets were voluntarily withdrawn from sale for reasons other than safety or effectiveness.[4] In a letter to FDA dated March 19, 2013, the NDA holder requested withdrawal of approval of NDA 20–553 for original OXYCONTIN. In the **Federal Register** of April 18, 2013 (78 FR 23273), FDA published notice of its determination that original OXYCONTIN, NDA 20–553, was withdrawn from sale for reasons of safety or effectiveness. The notice concluded that ''[o]riginal OXYCONTIN . . . poses an increased potential for abuse by certain routes of administration, when compared to reformulated OXYCONTIN. Based on the totality of the data and information available to the Agency at this time, FDA concludes that the benefits of original OXYCONTIN no longer outweigh its risks.'' In the **Federal Register** of August 7, 2013 (78 FR 48177), FDA announced that it was withdrawing the approval of NDA 20–553. In addition, because the drug approval process is the most appropriate way for FDA to evaluate the effect and labeling of products with potentially abuse-deterrent properties, compounding of opioid products with potentially abuse-deterrent properties will be closely scrutinized.

Pemoline: All drug products containing pemoline. Pemoline, formerly marketed as CYLERT tablets and chewable tablets, was associated with liver failure. FDA determined that the overall risk of liver toxicity from CYLERT and generic pemoline outweighed the benefits of the drug. On October 24, 2005, FDA announced in an FDA Alert that the NDA and ANDA holders chose to stop sales and marketing of CYLERT and generic pemoline in May 2005 (Ref. 4).

Pergolide mesylate: All drug products containing pergolide mesylate. Pergolide mesylate, formerly marketed as PERMAX tablets, was associated with increased risk of heart valve damage. On March 29, 2007, FDA announced in a Public Health Advisory that the NDA and ANDA holders agreed to withdraw PERMAX and generic pergolide mesylate from the market (Ref. 5).

Phenylpropanolamine (PPA): All drug products containing PPA. A study demonstrated that PPA was associated with increased risk of hemorrhagic stroke. On November 6, 2000, FDA announced in a Public Health Advisory that it was taking steps to remove PPA from all drug products and requested that all drug companies discontinue marketing products containing PPA (Ref. 6). In response to FDA's request, companies reformulated their products to exclude PPA. In a notice published in the **Federal Register** on August 14, 2001 (66 FR 42665), FDA offered an opportunity for a hearing on a proposal to issue an order, under section 505(e) of the FD&C Act, withdrawing approval of 13 NDAs and 8 ANDAs for products containing phenylpropanolamine. (Although the August 14, 2001, notice stated that FDA proposed to withdraw approval of 16 NDAs and 8 ANDAs, the notice listed only 13 NDAs and 8 ANDAs.) FDA withdrew approval of ANDA 71–099 for BROMATAPP Extended-Release Tablets in a notice published in the **Federal Register** of February 20, 2002 (67 FR 7702) after the application holder informed FDA that the product was no longer being marketed and requested withdrawal. In the **Federal Register** of February 20, 2014 (79 FR 9744), FDA announced that the NDA and ANDA products containing PPA were no longer shown to be safe for use under the conditions that formed the basis upon which the applications were approved, and thus the Agency was withdrawing approval of 20 products containing PPA.

Polyethylene glycol (PEG) 3350, sodium chloride, sodium bicarbonate, potassium chloride, and bisacodyl: All drug products containing PEG 3350, sodium chloride, sodium bicarbonate, and potassium chloride for oral solution, and 10 mg or more of bisacodyl delayed-release tablets. PEG 3350, sodium chloride, sodium bicarbonate, and potassium chloride for oral solution, and four bisacodyl delayed-release tablets, 5 mg (20-mg bisacodyl), formerly marketed as HALFLYTELY AND BISACODYL TABLETS BOWEL PREP KIT (20-mg bisacodyl), was associated with ischemic colitis. The NDA holder informed FDA that it ceased to manufacture and market HALFLYTELY AND BISACODYL TABLETS BOWEL PREP KIT (20-mg bisacodyl) as of September 25, 2007. On July 15, 2008, FDA received a citizen petition (Docket No. FDA–2008–P–0412), submitted under § 10.30, from Foley & Lardner LLP. The petition requested that the Agency determine whether HALFLYTELY AND BISACODYL TABLETS BOWEL PREP KIT (PEG–3350, sodium chloride, sodium bicarbonate, and potassium chloride for oral solution and four bisacodyl delayed release tablets, 5 mg) (HALFLYTELY AND BISACODYL TABLETS BOWEL PREP KIT (20-mg bisacodyl)), manufactured by Braintree Laboratories, Inc. (Braintree), was withdrawn from sale for reasons of safety or effectiveness. In the **Federal Register** of

[4] Varam, Inc., Docket No. FDA–2011–P–0473 (June 9, 2011) (10, 15, 20, 30, 40, 50, 80, and 160 mg); Sheppard, Mullin, Richter & Hampton LLP, Docket No. FDA–2010–P–0540 (October 8, 2010) (10, 15, 20, 30, 40, 60, and 80 mg); Lachman Consultant Services, Inc., Docket No. FDA–2010–P–0526 (September 30, 2010) (10, 15, 20, 30, 40, 60, 80, and 160 mg). Lachman also submitted a petition in 2001 concerning just Purdue Pharma LP's 2001 withdrawal of the 160 mg strength, Docket No. FDA–2001–P–0473 (formerly Docket No. 2001P–0426) (September 18, 2001).

March 19, 2010 (75 FR 13292), FDA announced its determination that HALFLYTELY AND BISACODYL TABLETS BOWEL PREP KIT (20-mg bisacodyl) was withdrawn from the market for reasons of safety or effectiveness. Similarly, PEG 3350, sodium chloride, sodium bicarbonate, and potassium chloride for oral solution, and two bisacodyl delayed-release tablets, 5 mg (10-mg bisacodyl), formerly marketed as HALFLYTELY AND BISACODYL TABLETS BOWEL PREP KIT (10-mg bisacodyl), was associated with ischemic colitis. The NDA holder informed FDA that it ceased to manufacture and market HALFLYTELY AND BISACODYL TABLETS BOWEL PREP KIT (10-mg bisacodyl) as of July 17, 2010. On September 23, 2010, FDA received a citizen petition (Docket No. FDA–2010–P–0507), submitted under § 10.30, from Perrigo Company (Perrigo) requesting that the Agency determine whether HALFLYTELY AND BISACODYL TABLETS BOWEL PREP KIT (PEG–3350, sodium chloride, sodium bicarbonate, and potassium chloride for oral solution and two bisacodyl delayed release tablets, 5 mg) (HALFLYTELY AND BISACODYL TABLETS BOWEL PREP KIT (10-mg bisacodyl)), manufactured by Braintree, was withdrawn from sale for reasons of safety or effectiveness. In the **Federal Register** of August 17, 2011 (76 FR 51037), FDA announced its determination that HALFLYTELY AND BISACODYL TABLETS BOWEL PREP KIT (10-mg bisacodyl) was withdrawn from the market for reasons of safety or effectiveness.

Propoxyphene: All drug products containing propoxyphene. Propoxyphene, formerly marketed under various names such as DARVON and DARVOCET, was associated with serious toxicity to the heart. In a drug safety communication dated November 19, 2010, FDA announced it had requested that companies voluntarily withdraw propoxyphene from the U.S. market and that FDA was recommending against the continued use and prescribing of the pain reliever propoxyphene because new data showed that the drug can cause serious toxicity to the heart, even when used at therapeutic doses. FDA concluded that the safety risks of propoxyphene outweighed its limited benefits for pain relief at recommended doses. The Agency's recommendation was based on all available data including data from a then-new study that evaluated the effects that increasing doses of propoxyphene have on the heart. The results of the study showed that when propoxyphene was taken at therapeutic doses, there were significant changes to the electrical activity of the heart which can increase the risk for serious abnormal heart rhythms (Ref. 7). In the **Federal Register** of March 10, 2014 (79 FR 13308), FDA announced that due to this safety risk, the Agency was withdrawing approval of 54 propoxyphene products with agreement from holders of the affected applications. On that date, FDA also published a notice of opportunity for a hearing on its proposal to withdraw approval of three additional propoxyphene products for which FDA had not received correspondence from the application holders requesting that FDA withdraw approval (see the **Federal Register** of March 10, 2014 (79 FR 13310)).

Rapacuronium bromide: All drug products containing rapacuronium bromide. Rapacuronium bromide, formerly marketed as RAPLON for Injection, was associated with the occurrence of bronchospasm. In a letter dated March 27, 2001, the NDA holder announced that it voluntarily withdrew all batches of RAPLON for Injection from the market (Ref. 8). FDA subsequently announced in the **Federal Register** of March 19, 2012 (77 FR 16039) that it was withdrawing the approval of the NDA.

Rofecoxib: All drug products containing rofecoxib. Rofecoxib, formerly marketed as VIOXX, was associated with increased risk of serious cardiovascular events, including heart attack and stroke. On September 30, 2004, FDA announced in a Public Health Advisory that the NDA holder voluntarily withdrew VIOXX from the market (Ref. 9).

Sibutramine hydrochloride: All drug products containing sibutramine hydrochloride. Sibutramine hydrochloride (HCl), formerly marketed as MERIDIA oral capsules, was associated with increased risk of heart attack and stroke. In a letter dated October 12, 2010, the NDA holder requested that FDA withdraw the approval of the NDA for MERIDIA. In an acknowledgment letter dated November 1, 2010, FDA stated that the benefits of MERIDIA (sibutramine HCl) oral capsules no longer outweighed the risks in any identifiable population. FDA subsequently announced in the **Federal Register** of December 21, 2010 (75 FR 80061) that it was withdrawing approval of the NDA.

Tegaserod maleate: All drug products containing tegaserod maleate. Tegaserod maleate, formerly marketed as ZELNORM, was associated with a higher chance of heart attack, stroke, and worsening heart chest pain that can become a heart attack, compared to a placebo. On March 30, 2007, FDA announced in a Public Health Advisory that the NDA holder agreed to stop selling ZELNORM (Ref. 10). On July 27, 2007, FDA announced that it was permitting the restricted use of ZELNORM (tegaserod maleate) under a treatment investigational new drug (IND) protocol to treat irritable bowel syndrome with constipation (IBS–C) and chronic idiopathic constipation (CIC) in women younger than 55 who meet specific guidelines (Ref. 11). On April 2, 2008, FDA announced that the sponsor of ZELNORM notified FDA that it would no longer provide ZELNORM (tegaserod maleate) under a treatment IND protocol to treat IBS–C and CIC in women younger than 55; however, the sponsor agreed to continue to supply ZELNORM for use in emergency situations (Ref. 12).

Troglitazone: All drug products containing troglitazone. Troglitazone, formerly marketed as REZULIN and PRELAY Tablets, a treatment for type 2 diabetes, was shown to be more toxic to the liver than two other more recently approved drugs that offered a similar benefit. In a letter dated May 1, 2002, the holder of the NDA for REZULIN (troglitazone) Tablets requested that FDA withdraw the NDA for REZULIN (troglitazone) Tablets because it had discontinued marketing the product in March 2000. FDA subsequently announced in the **Federal Register** of January 10, 2003 (68 FR 1469) that it was withdrawing the approval of the NDA for REZULIN. In a letter dated December 31, 2002, the holder of the NDA for PRELAY (troglitazone) Tablets requested that FDA withdraw the approval of the NDA for PRELAY (troglitazone) Tablets because it never marketed the drug and had no plans to market the drug in the future. In the **Federal Register** of August 11, 2003 (68 FR 47581), FDA concluded that PRELAY was voluntarily withdrawn after review of safety data showed that REZULIN was more toxic to the liver than two other more recently approved drugs that offered a similar benefit, and FDA announced that it was withdrawing approval of the NDA for PRELAY. Troglitazone was presented to the Advisory Committee at the July 2000 meeting, and the Advisory Committee voted to include troglitazone on the withdrawn or removed list (see the **Federal Register** of June 29, 2000 (65 FR 40104)).

Trovafloxacin mesylate: All drug products containing trovafloxacin mesylate. Trovafloxacin mesylate,

formerly marketed as TROVAN tablets, 100 mg and 200 mg, was associated with serious liver injury. On June 9, 1999, FDA announced in a Public Health Advisory that the NDA holder agreed to a limited distribution of TROVAN (alatrofloxacin mesylate) Injection and TROVAN (trovafloxacin mesylate) tablets, 100 mg and 200 mg, to in-patient healthcare facilities (Ref. 1). The holders of the NDAs for TROVAN (trovafloxacin mesylate) tablets, 100 mg and 200 mg, and TROVAN/ZITHROMAX COMPLIANCE PAK (trovafloxacin mesylate/azithromycin for oral suspension) notified the Agency that the drug products were no longer marketed and requested that the approval of the NDAs be withdrawn (see the **Federal Register** of September 22, 1999 (64 FR 51325), and June 16, 2006 (71 FR 34940)). FDA announced it was withdrawing approval of the NDAs in the **Federal Register** of September 22, 1999 (64 FR 51325), and June 16, 2006 (71 FR 34940).

Valdecoxib: All drug products containing valdecoxib. Valdecoxib, formerly marketed as BEXTRA, was associated with increased risk of serious cardiovascular events and an increased risk of serious skin reactions (e.g., toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme) compared to other nonsteroidal anti-inflammatory drugs. On April 7, 2005, FDA announced in an FDA Alert that it had concluded that the overall risk versus benefit profile of BEXTRA (valdecoxib) was unfavorable and that the NDA holder had voluntarily removed BEXTRA from the market (Ref. 13). In letters dated May 27, 2011, August 8, 2011, and October 31, 2011, the holder of the NDA for BEXTRA (valdexoxib) Tablets requested that FDA withdraw the NDA for BEXTRA (valdexoxib) Tablets. FDA subsequently announced in the **Federal Register** of August 2, 2013 (78 FR 46984) that it was withdrawing approval of the NDA.

C. Amendment To Modify the Description of a Drug Product on the List

FDA is proposing to amend § 216.24 to modify the description of bromfenac sodium on the list.

Bromfenac sodium: All drug products containing bromfenac sodium (except ophthalmic solutions). The use of bromfenac sodium, formerly marketed as DURACT (bromfenac sodium) Capsules, was associated with fatal hepatic failure. The manufacturer of DURACT Capsules voluntarily withdrew the drug from the market on June 22, 1998 (see the **Federal Register** of October 8, 1998 (63 FR 54082)). On March 8, 1999, FDA included all drug products containing bromfenac sodium in the list codified at § 216.24 when FDA published the 1999 final rule (64 FR 10944). Since then, FDA has approved bromfenac ophthalmic solutions, and although one of these, XIBROM (bromfenac ophthalmic solution) 0.09%, was discontinued by the NDA holder in 2011, FDA announced its determination in the **Federal Register** of May 13, 2011 (76 FR 28045) that it was not withdrawn for reasons of safety or effectiveness. (See also Docket No. FDA–2011–P–0128.) Approved bromfenac ophthalmic solutions are currently on the market. Thus, FDA is proposing to include all drug products containing bromfenac sodium on the list with an exception for ophthalmic solutions.

For the convenience of the reader, the regulatory text of § 216.24 provided with this proposed rule includes the drug products proposed for addition and modification discussed in this document and the drug products codified by the 1999 final rule.

IV. Environmental Impact

FDA has determined under 21 CFR 25.30(h) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

V. Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866, Executive Order 13563, the Regulatory Flexibility Act (5 U.S.C. 601–612) and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104–4). Executive Orders 12866 and 13563 direct Agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The Agency believes that this proposed rule is not a significant regulatory action as defined by Executive Order 12866.

The Regulatory Flexibility Act requires Agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because small businesses are not expected to incur any compliance costs or loss of sales due to this regulation, we propose to certify that this rule will not have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that Agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing ''any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year.'' The current threshold after adjustment for inflation is $141 million, using the most current (2013) Implicit Price Deflator for the Gross Domestic Product. We do not expect this proposed rule to result in any 1-year expenditure that would meet or exceed this amount.

This rule proposes to amend § 216.24 concerning pharmacy compounding. Specifically, the proposed rule would add to or modify the list of drug products that may not be compounded under the exemptions provided by sections 503A and 503B of the FD&C Act because the drug products were withdrawn or removed from the market because such drug products or components of such drug products were found to be unsafe or not effective (see section III). The Agency is proposing to add 25 drug products to the list and to modify the description of 1 drug product on the list to add an exception. The Agency is not aware of any routine use of these drug products in pharmacy compounding and, therefore, does not estimate any compliance costs or loss of sales as a result of the prohibition against compounding these drugs for human use. However, the Agency invites the submission of comments and solicits current compounding usage data for these drug products, if they are compounded for human use.

Unless an Agency certifies that a rule will not have a significant economic impact on a substantial number of small entities, the Regulatory Flexibility Act requires Agencies to analyze regulatory options to minimize any significant economic impact of a regulation on small entities. Most pharmacies meet the Small Business Administration definition of a small entity, which is defined as having annual sales less than $25.5 million for this industry. The Agency is not aware of any routine compounding of these drug products and does not estimate any compliance costs or loss of sales to small businesses as a result of the prohibition against compounding these drugs. Therefore, the Agency proposes to certify that this proposed rule will not have a significant

economic impact on a substantial number of small entities.

VI. Paperwork Reduction Act of 1995

The submission of comments on this proposed rule and the submission of additional nominations for the list that is the subject of this rulemaking would be submissions in response to a **Federal Register** notice, in the form of comments, which are excluded from the definition of ''information'' under 5 CFR 1320.3(h)(4) of OMB regulations on the Paperwork Reduction Act (i.e., facts or opinions submitted in response to general solicitations of comments from the public, published in the **Federal Register** or other publications, regardless of the form or format thereof, provided that no person is required to supply specific information pertaining to the commenter, other than that necessary for self-identification, as a condition of the Agency's full consideration of the comment). The proposed rule contains no other collection of information.

VII. Request for Comments

Interested persons may submit either electronic comments regarding this document to *http://www.regulations.gov* or written comments to the Division of Dockets Management (see **ADDRESSES**). It is only necessary to send one set of comments. Identify comments with the docket number found in the brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at *http://www.regulations.gov.*

VIII. References

The following references have been placed on display in the Division of Dockets Management (see **ADDRESSES**) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday, and are available electronically at *http://www.regulations.gov.* (FDA has verified the Web site addresses in this reference section, but FDA is not responsible for any subsequent changes to the Web sites after this document publishes in the **Federal Register**.)

1. FDA Public Health Advisory Letter from Murray M. Lumpkin, Deputy Center Director (Review Management), Center for Drug Evaluation and Research, FDA, Re: Food and Drug Administration TROVAN (Trovafloxacin/Alatrofloxacin Mesylate) Interim Recommendations (June 9, 1999), *http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/PublicHealthAdvisories/ucm053103.htm.*
2. Letter from E. Paul Mac Carthy, Vice President, Head U.S. Medical Science, Bayer Corporation, to Healthcare Professional, Re: Market withdrawal of Baycol (cerivastatin) (August 8, 2001), *http://www.fda.gov/downloads/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/UCM173692.pdf.*
3. Letter from Jan Gheuens, Vice President, Medical Affairs, Janssen Pharmaceutica, to Healthcare Professional (April 12, 2000), PROPULSID (cisapride) Dear Healthcare Professional Letter (April 2000), *http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm175000.htm.*
4. FDA Alert—Information for Healthcare Professionals: Pemoline Tablets and Chewable Tablets (marketed as CYLERT) (October 2005), *http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm126461.htm.*
5. FDA Public Health Advisory—Pergolide (marketed as PERMAX) (March 29, 2007), *http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/PublicHealthAdvisories/ucm051285.htm.*
6. FDA Public Health Advisory—Safety of Phenylpropanolamine (November 6, 2000), *http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/PublicHealthAdvisories/ucm052236.htm.*
7. FDA Drug Safety Communication—FDA Recommends Against the Continued Use of Propoxyphene (November 19, 2010), *http://www.fda.gov/Drugs/DrugSafety/ucm234338.htm.*
8. Letter from Deborah Shapse, Medical Director, Organon, Inc., Re: Voluntary Market Withdrawal of RAPLON (rapacuronium bromide) for Injection, All Batches (March 27, 2001), *http://www.fda.gov/downloads/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/UCM173891.pdf.*
9. FDA Public Health Advisory—Safety of VIOXX (September 30, 2004), *http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm106274.htm.*
10. FDA Public Health Advisory—Tegaserod maleate (marketed as ZELNORM) (March 30, 2007), *http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/PublicHealthAdvisories/ucm051284.htm.*
11. FDA News Release, ''FDA Permits Restricted Use of Zelnorm for Qualifying Patients'' (July 27, 2007), *http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2007/ucm108956.htm.*
12. FDA—ZELNORM (tegaserod maleate) Information (April 2, 2008), *http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm103223.htm.*
13. FDA Alert—Information for Healthcare Professionals: Valdecoxib (marketed as Bextra) (April 7, 2005), *http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm124649.htm.*

List of Subjects in 21 CFR Part 216

Drugs, Prescription drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, the proposed rule that published on January 4, 2000 (65 FR 256), is withdrawn and it is proposed that 21 CFR part 216 be amended as follows:

PART 216—HUMAN DRUG COMPOUNDING

■ 1. The authority citation for 21 CFR part 216 is revised to read as follows:

Authority: 21 U.S.C. 351, 352, 353a, 353b, 355, and 371.

■ 2. The heading for part 216 is revised to read as set forth above.

■ 3. Section 216.24 is revised to read as follows:

§ 216.24 Drug products withdrawn or removed from the market for reasons of safety or effectiveness.

The following drug products were withdrawn or removed from the market because such drug products or components of such drug products were found to be unsafe or not effective. The following drug products may not be compounded under the exemptions provided by section 503A(a) or section 503B(a) of the Federal Food, Drug, and Cosmetic Act:

Adenosine phosphate: All drug products containing adenosine phosphate.

Adrenal cortex: All drug products containing adrenal cortex.

Alatrofloxacin mesylate: All drug products containing alatrofloxacin mesylate.

Aminopyrine: All drug products containing aminopyrine.

Astemizole: All drug products containing astemizole.

Azaribine: All drug products containing azaribine.

Benoxaprofen: All drug products containing benoxaprofen.

Bithionol: All drug products containing bithionol.

Bromfenac sodium: All drug products containing bromfenac sodium (except ophthalmic solutions).

Butamben: All parenteral drug products containing butamben.

Camphorated oil: All drug products containing camphorated oil.

Carbetapentane citrate: All oral gel drug products containing carbetapentane citrate.

Casein, iodinated: All drug products containing iodinated casein.

Cerivastatin sodium: All drug products containing cerivastatin sodium.

Chloramphenicol: All oral drug products containing chloramphenicol.

Chlorhexidine gluconate: All tinctures of chlorhexidine gluconate formulated for use as a patient preoperative skin preparation.

Chlormadinone acetate: All drug products containing chlormadinone acetate.

Chloroform: All drug products containing chloroform.

Cisapride: All drug products containing cisapride.

Cobalt: All drug products containing cobalt salts (except radioactive forms of cobalt and its salts and cobalamin and its derivatives).

Dexfenfluramine hydrochloride: All drug products containing dexfenfluramine hydrochloride.

Diamthazole dihydrochloride: All drug products containing diamthazole dihydrochloride.

Dibromsalan: All drug products containing dibromsalan.

Diethylstilbestrol: All oral and parenteral drug products containing 25 milligrams or more of diethylstilbestrol per unit dose.

Dihydrostreptomycin sulfate: All drug products containing dihydrostreptomycin sulfate.

Dipyrone: All drug products containing dipyrone.

Encainide hydrochloride: All drug products containing encainide hydrochloride.

Esmolol hydrochloride: All parenteral dosage form drug products containing esmolol hydrochloride that supply 250 milligrams/milliliter of concentrated esmolol per 10-milliliter ampule.

Etretinate: All drug products containing entretinate.

Fenfluramine hydrochloride: All drug products containing fenfluramine hydrochloride.

Flosequinan: All drug products containing flosequinan.

Gatifloxacin: All drug products containing gatifloxacin (except ophthalmic solutions).

Gelatin: All intravenous drug products containing gelatin.

Glycerol, iodinated: All drug products containing iodinated glycerol.

Gonadotropin, chorionic: All drug products containing chorionic gonadotropins of animal origin.

Grepafloxacin: All drug products containing grepafloxacin.

Mepazine: All drug products containing mepazine hydrochloride or mepazine acetate.

Metabromsalan: All drug products containing metabromsalan.

Methamphetamine hydrochloride: All parenteral drug products containing methamphetamine hydrochloride.

Methapyrilene: All drug products containing methapyrilene.

Methopholine: All drug products containing methopholine.

Methoxyflurane: All drug products containing methoxyflurane.

Mibefradil dihydrochloride: All drug products containing mibefradil dihydrochloride.

Nitrofurazone: All drug products containing nitrofurazone (except topical drug products formulated for dermatalogic application).

Nomifensine maleate: All drug products containing nomifensine maleate.

Novobiocin sodium: All drug products containing novobiocin sodium.

Oxycodone hydrochloride: All extended-release drug products containing oxycodone hydrochloride that have not been determined by FDA to have abuse-deterrent properties.

Oxyphenisatin: All drug products containing oxyphenisatin.

Oxyphenisatin acetate: All drug products containing oxyphenisatin acetate.

Pemoline: All drug products containing pemoline.

Pergolide mesylate: All drug products containing pergolide mesylate.

Phenacetin: All drug products containing phenacetin.

Phenformin hydrochloride: All drug products containing phenformin hydrochloride.

Phenylpropanolamine: All drug products containing phenylpropanolamine.

Pipamazine: All drug products containing pipamazine.

Polyethylene glycol 3350, sodium chloride, sodium bicarbonate, potassium chloride, and bisacodyl: All drug products containing polyethylene glycol 3350, sodium chloride, sodium bicarbonate, and potassium chloride for oral solution, and 10 milligrams or more of bisacodyl delayed-release tablets.

Potassium arsenite: All drug products containing potassium arsenite.

Potassium chloride: All solid oral dosage form drug products containing potassium chloride that supply 100 milligrams or more of potassium per dosage unit (except for controlled-release dosage forms and those products formulated for preparation of solution prior to ingestion).

Povidone: All intravenous drug products containing povidone.

Propoxyphene: All drug products containing propoxyphene.

Rapacuronium bromide: All drug products containing rapacuronium bromide.

Reserpine: All oral dosage form drug products containing more than 1 milligram of reserpine.

Rofecoxib: All drug products containing rofecoxib.

Sibutramine hydrochloride: All drug products containing sibutramine hydrochloride.

Sparteine sulfate: All drug products containing sparteine sulfate.

Sulfadimethoxine: All drug products containing sulfadimethoxine.

Sulfathiazole: All drug products containing sulfathiazole (except for those formulated for vaginal use).

Suprofen: All drug products containing suprofen (except ophthalmic solutions).

Sweet spirits of nitre: All drug products containing sweet spirits of nitre.

Tegaserod maleate: All drug products containing tegaserod maleate.

Temafloxacin hydrochloride: All drug products containing temafloxacin.

Terfenadine: All drug products containing terfenadine.

3,3′,4′,5-tetrachlorosalicylanilide: All drug products containing 3,3′,4′,5-tetrachlorosalicylanilide.

Tetracycline: All liquid oral drug products formulated for pediatric use containing tetracycline in a concentration greater than 25 milligrams/milliliter.

Ticrynafen: All drug products containing ticrynafen.

Tribromsalan: All drug products containing tribromsalan.

Trichloroethane: All aerosol drug products intended for inhalation containing trichloroethane.

Troglitazone: All drug products containing troglitazone.

Trovafloxacin mesylate: All drug products containing trovafloxacin mesylate.

Urethane: All drug products containing urethane.

Valdecoxib: All drug products containing valdecoxib.

Vinyl chloride: All aerosol drug products containing vinyl chloride.

Zirconium: All aerosol drug products containing zirconium.

Zomepirac sodium: All drug products containing zomepirac sodium.

Dated: June 25, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

[FR Doc. 2014–15371 Filed 7–1–14; 8:45 am]

BILLING CODE 4164–01–P

Attachment 9

Kaiser Permanente Pharmacy Administration
12254 Bellflower Blvd
Downey, CA 90242

June 30th, 2014

California State Board of Pharmacy
Attn: Virginia Herold, Executive Officer

1625 N. Market Blvd., N-219
Sacramento, CA 95834

RE: Request to add agenda item for upcoming Enforcement & Compounding Subcommittee Meeting

TOPIC: End-Product testing as promulgated in 16 CCR 1751.7

We are writing to request that the above topic be added as an agenda item for discussion at the next Enforcement & Compounding Subcommittee meeting scheduled.

As the law currently reads, 16 CCR 1751.7(a) states that "*The end product shall be examined on a periodic sampling basis as determined by the pharmacist-in-charge to assure that it meets required specifications*".

Several recent inspections at Kaiser Permanente facilities around the state have yielded orders of correction as to this requirement. Kaiser Permanente believes that inspections of our facilities with respect to meeting this requirement have been inconsistent and unpredictable, often fluctuating with the assignment of the inspector involved. We wish to highlight the inconsistencies and present the organizational stance and process for meeting the intent of this regulation.

Sincerely,

Kaiser Permanente Pharmacy Administration

562.658.3669 (office)

Kind Regards,

Tony H. Wang, Pharm.D., J.D.
Director of Pharmacy Regulatory Affairs
National Pharmacy Compliance
12254 Bellflower Blvd.
Downey, CA 90242

Attachment 10

Inspection Findings (6/26/14 – 9/5/14)

140 Sterile Compounding Inspections

- 66 Hospital/LSC
- 63 Annual/new inspections of current licensed sterile compounders
- 11 Non-resident Inspections

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137 violations were found in 58 of these pharmacies

Inspection Outcomes (6/27/14 – 9/5/14)

137 non-compliance issues were recorded in 57 pharmacies

	Violations	
Hospital/LSC (28)	55	40.1%
PHY/LSC (21)	48	35.0%
NRP/NSC (8)	34	24.8%

Top Violations in HSP/LSC (N=55)
(6/26/14 – 9/5/14)

• Compounding records incomplete	13	23.6%
• Ceiling, walls, surfaces not disinfected weekly	11	20.0%
• Compounding self-assessment not completed	4	7.3%

Top Violations in PHY/LSC (N=48)
(6/26/14 – 9/5/14)

• Master formula incomplete	4	33.3%
• Ceiling, walls, surfaces not disinfected weekly	3	25.0%
• Compounding self-assessment not completed	3	25.0%

Top Violations in NRP/NSC (N=34)
(6/26/14 – 9/5/14)

• Compounding self-assessment not completed	6	17.6%
• Ceiling, walls, surfaces not disinfected weekly	3	8.8%
• P&P's not reviewed annually by PIC	3	8.8%

Inspections to be Completed (9/1/14 – 12/31/14)

In CA

9/1/14 expiration	=	46 (completed)
10/1/14 expiration	=	43
11/1/14 expiration	=	273
12/1/14 expiration	=	49

Non-resident

9/1/14 expiration	=	11 (completed)
10/1/14 expiration	=	7 (scheduled)
11/1/14 expiration	=	10
12/1/14 expiration	=	7

Attachment 11

Cappello, Susan@DCA

From: Pharmacy_Subscriberlist@DCA
Sent: Thursday, December 19, 2013 2:08 PM
To: PHARM-GENERAL@LISTSERV.DCA.CA.GOV
Cc: Pharmacy_Subscriberlist@DCA
Subject: Recall notice - Abrams Royal Pharmacy

Abrams Royal Pharmacy is recalling all unexpired lots of sterile products dispensed nationwide due to concerns of lack of sterility assurance. Sterile products are injectable medications, IVs, eye drops, pellet implants, nasal sprays, inhalation solutions, and eye ointments.

All recalled products have a label that includes Abrams Royal Pharmacy's name and phone as well as a lot number. While not every label contains an expiration date, consumers can call the pharmacy with the lot number and learn the expiration date.

The recall was issued after a single, isolated report of an adverse event involving a patient in California who received a compounded medication from the pharmacy. Out of an abundance of caution, Abrams Royal is recalling all sterile products within expiry. If there is microbial contamination in products intended to be sterile, patients are at risk for serious, potentially life-threatening infections.

The recalled products were distributed to health care facilities, physicians, and patients from June 17, 2013 through December 17, 2013.

To return product or request assistance related to this recall, users should contact Abrams Royal at 214-349-8000, Monday through Friday, between 9:00 a.m. and 7:00 p.m. CST, and on Saturday between 9:00 a.m. and 3:00 p.m. CST.

Customers that have product which is being recalled should stop using it and contact the pharmacy to arrange for return of unused product. Consumers should contact their physician or health care provider if they have experienced any problems that may be related to taking or using these products. Adverse reactions may be reported to the FDA's MedWatch program via:

Online: www.fda.gov/medwatch/report.htm
Mail: use postage-paid, pre-addressed Form FDA 3500 found at www.fda.gov/MedWatch/getforms.htm.
Fax: 1-800-FDA-0178

Cappello, Susan@DCA

From: Pharmacy_Subscriberlist@DCA
Sent: Monday, December 23, 2013 4:21 PM
To: PHARM-GENERAL@LISTSERV.DCA.CA.GOV
Cc: Pharmacy_Subscriberlist@DCA
Subject: Order to Cease and Desist – Abrams Royal Pharmacy - ISSUED: December 23, 3013

Abrams Royal Pharmacy shall immediately **CEASE AND DESIST** from compounding sterile injectable products for shipment into California. This cease and desist order shall remain in effect for 30 days or until the date of a hearing seeking an interim suspension order, whichever is earlier. Pursuant to Business and Professions Code section 4127.3, subdivision (c), within 15 days of the receipt of this notice you may request a hearing before the president of the board to contest the cease and desist order.

Additionally Abrams Royal Pharmacy shall contact **EACH PRESCRIBER AND PATIENT** in California for whom Abrams Royal Pharmacy has prepared sterile injectable medications to determine if the patient or prescriber has any such preparation in his/her possession. Any such preparation in the possession of prescribers/patients shall be recalled. The product is to be returned to Abrams Royal Pharmacy.

To view the Order to Cease and Desist go to: http://www.pharmacy.ca.gov/enforcement/fy1213/abrams.pdf

Cappello, Susan@DCA

From: Pharmacy_Subscriberlist@DCA
Sent: Wednesday, January 08, 2014 11:42 AM
To: PHARM-GENERAL2@LISTSERV.DCA.CA.GOV
Cc: Pharmacy_Subscriberlist@DCA
Subject: SafeSpout and SafeShower Filtration Products by Nephros: Class I Recall - Exposure to Bacteria or Virus

AUDIENCE: Risk Manager, Biomedical Engineer

ISSUE: The Nephros non-medical water filtration SafeSpout and SafeShower products may pose risks to health potentially resulting in adverse health events or death. Exposure to harmful bacteria may occur when the fiber filter or the sealing compound, holding the fiber in place, breaks apart. If the filter breaks, patients could be exposed to bacteria or viruses, which could result in infection or death. To date, reports of one death and one infection are associated with this recall.

This recall involves all production lots of the following point-of-use (POU) filters, manufactured between July 2011 and September 2013 and distributed between October 2011 and October 2013:

SafeSpout 70-0233, 70-0238
SafeShower HH (Hand Held) 70-0237
SafeShower FH (Fixed Head) 70-0236

BACKGROUND: The Nephros SafeSpout and SafeShower are intended to filter water for washing and drinking. They are intended to be installed at the end of a standard sink faucet or shower head.

RECOMMENDATION: If you are in possession of any of the filters identified above, please remove them from use immediately. See the Recall Notice for additional information.

Healthcare professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program:

- Complete and submit the report Online: www.fda.gov/MedWatch/report.htm
- Download form or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178

[01/06/2014 - Recall Notice - FDA]

Related MedWatch Alert:

[01/07/2014 - Nephros Filtration Products: Class I Recall - Labeling Promoting Medical Claims]

Cappello, Susan@DCA

From: General Board of Pharmacy Subscriber List <PHARM-GENERAL@LISTSERV.DCA.CA.GOV> on behalf of Pharmacy_Subscriberlist@DCA
Sent: Friday, February 14, 2014 3:50 PM
To: PHARM-GENERAL@LISTSERV.DCA.CA.GOV
Subject: FDA MedWatch - L-citrulline by Medisca: Alert - Potentially Subpotent Product

L-citrulline by Medisca: Alert - Potentially Subpotent Product

AUDIENCE: Medical Geneticist, Pediatrics, Pharmacy

ISSUE: FDA is notifiying health care professionals, patients, and caregivers of adverse events reported in patients who were administered L-citrulline repackaged and distributed by Medisca Inc. L-citrulline is used to treat certain urea cycle disorders, rare genetic disorders primarily diagnosed in children. FDA has received adverse event reports associated with potentially subpotent L-citrulline. Subpotent L-citrulline in patients with certain urea cycle defects can lead to high ammonia levels, which is serious and potentially life-threatening.
In addition to the identified lot number 96453, FDA is investigating reports that may include additional lot numbers.

BACKGROUND: Medisca supplies pharmacies nationwide with L-citrulline. The product is sold to pharmacies and clinics in containers filled with powdered L-citrulline, and it may be compounded into tablets, capsules, or liquids by pharmacies, or remain a powder.

RECOMMENDATION: FDA recommends health care professionals quarantine lots of L-citrulline from Medisca and not administer to patients until FDA provides additional information.

Patients should contact their physician or health care provider if they have concerns about the use of L-citrulline.

FDA asks health care professionals, patients, and caregivers to report adverse reactions or quality problems experienced with the use of L-citrulline packed by any companies, including Medisca, to the FDA's MedWatch Adverse Event Reporting program:

- Complete and submit the report online at http://www.fda.gov/medwatch/report.htm
- Download and complete the reporting form, then submit it via fax at 1-800-FDA-0178

Read the MedWatch safety alert, including a link to the FDA Statement, at:
http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm385978.htm

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https://www.dca.ca.gov/webapps/pharmacy/subscribe.php

Cappello, Susan@DCA

From: Pharmacy_Subscriberlist@DCA
Sent: Tuesday, February 18, 2014 7:32 AM
To: PHARM-GENERAL@LISTSERV.DCA.CA.GOV
Cc: Pharmacy_Subscriberlist@DCA
Subject: L-citrulline by Medisca: Alert - Potentially Subpotent Product

UPDATED 02/17/2014. FDA has tested samples from recalled lots of Medisca's L-citrulline product, and were analyzed by several laboratory methods to identify the ingredient that was repackaged by Medisca and labeled as L-citrulline. FDA has found that the samples contain N-acetyl-leucine, which is used to treat a certain type of dizziness (acute vestibular vertigo). No L-citrulline was found in the samples FDA tested.

UPDATED 02/15/2014. FDA alerts health care professionals and patients that Medisca is voluntarily recalling certain lots of its L-citrulline product after testing indicated that it does not contain any L-citrulline

- Testing by Medisca indicated that L-citrulline, lot numbers 95482/A, 95482/B, 95482/C, 95482/D and 96453/A, 96453/B, 96453/C, 96453/D do not contain L-citrulline. Pharmacists should see updated FDA Statement below for more product details.
- Medisca is voluntarily recalling all L-citrulline product with the above lot numbers.
- Health care professionals should discontinue dispensing from these lots, contact patients, and return all unused product to Medisca Inc.
- Patients and caregivers should stop using any product with these lot numbers.
- FDA has received several adverse event reports associated with Medisca's L-citrulline product. FDA is investigating reports that may include additional lot numbers, continues to investigate the full scope of this issue and will continue to provide additional information as it becomes available.

[Posted 02/14/2014]

AUDIENCE: Medical Geneticist, Pediatrics, Pharmacy

ISSUE: FDA is notifiying health care professionals, patients, and caregivers of adverse events reported in patients who were administered L-citrulline repackaged and distributed by Medisca Inc. L-citrulline is used to treat certain urea cycle disorders, rare genetic disorders primarily diagnosed in children. FDA has received adverse event reports associated with potentially subpotent L-citrulline. Subpotent L-citrulline in patients with certain urea cycle defects can lead to high ammonia levels, which is serious and potentially life-threatening.

In addition to the identified lot number 96453, FDA is investigating reports that may include additional lot numbers.

BACKGROUND: Medisca supplies pharmacies nationwide with L-citrulline. The product is sold to pharmacies and clinics in containers filled with powdered L-citrulline, and it may be compounded into tablets, capsules, or liquids by pharmacies, or remain a powder.

RECOMMENDATION: FDA recommends health care professionals quarantine lots of L-citrulline from Medisca and not administer to patients until FDA provides additional information.

Patients should contact their physician or health care provider if they have concerns about the use of L-citrulline.

FDA asks health care professionals, patients, and caregivers to report adverse reactions or quality problems experienced with the use of L-citrulline packed by any companies, including Medisca, to the FDA's MedWatch Adverse Event Reporting program:

- Complete and submit the report online at www.fda.gov/medwatch/report.htm
- Download and complete the reporting form, then submit it via fax at 1-800-FDA-0178

[02/14/2014 - Statement - FDA]

Cappello, Susan@DCA

From: Pharmacy_Subscriberlist@DCA
Sent: Tuesday, July 22, 2014 8:20 AM
To: PHARM-GENERAL@DCALISTS.CA.GOV
Cc: Pharmacy_Subscriberlist@DCA
Subject: Order to Cease and Desist issued to Unique Pharmaceuticals LTD

The Board of Pharmacy has issued an Order to Cease and Desist effective July 21, 2014 to Unique Pharmaceuticals LTD., located at 5920 S. General Bruce Dr., Temple, TX 97502.

Unique Pharmaceuticals LTD shall immediately Cease and Desist from compounding sterile injectable products for shipment into California.

Cappello, Susan@DCA

From: General Board of Pharmacy Subscriber List <PHARM-GENERAL@DCALISTS.CA.GOV> on behalf of Board of Pharmacy <pharmacy.subscriberlist@DCA.CA.GOV>
Sent: Monday, September 08, 2014 9:03 AM
To: PHARM-GENERAL@DCALISTS.CA.GOV
Subject: Recall notice - Advance Outcome Management Pharmacy Services

During the semi-annual testing of sterile cleanrooms and anteroom, the air samples from the anteroom tested positive for microorganisms. Surface and air samples taken from the biosafety cabinets used in sterile compounding showed no bacterial or fungal contamination. Although these results may have been due to the testing procedures themselves, as a precaution Advance Outcome Management Pharmacy Services, are recalling ALL Sterile Compounded Products.

Please immediately check inventory, quarantine, and discontinue distribution of the affected product and contact your wholesaler for directions.

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