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STATE AND CONSUMER SERVICES AGENCY
DEPARTMENT OF CONSUMER AFFAIRS
ARNOLD SCHWARZENEGGER, GOVERNOR

LICENSING COMMITTEE
WORKGROUP ON COMPOUNDING

Ken Schell, Pharm.D.
John Tilley, R.Ph.

March 3, 2004
1:30 p.m. – 4:00 p.m.
Holiday Inn Oakland Airport
500 Hegenberger Road
Oakland, CA 94621
(510) 562-5311

MEETING MATERIALS

Attachment A	Guidance for FDA Staff and Industry Compliance Policy Guides Manual Sec. 460.200 – Pharmacy Compounding (May 2002)
Attachment B	"Compounding Under Siege" *Drug Topics,* January 6, 2003
Attachment C	Letter from Department of Health Services dated July 18, 2002
Attachment D	Letter from the International Academy of Compounding Pharmacists dated August 8, 2002
Attachment E	Letter from John Cronin, Pharm.D., J.D. dated September 3, 2002
Attachment F	Pharmacy Law Related to Compounding
Attachment G	1995 Board Guidelines for Distinguishing Compounding from Manufacturing

ATTACHMENT A

Guidance for FDA Staff and Industry

Compliance Policy Guides Manual

Sec. 460.200
Pharmacy Compounding

Submit written comments regarding this guidance document to the Dockets Management Branch (HFA-305), 5630 Fishers Lane, rm.1061, Rockville, MD 20852.

Additional copies of this document may be obtained by sending a request to the Division of Compliance Policy (HFC-230), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, or from the Internet at: http://www.fda.gov/ora/compliance_ref/cpg/default.htm

U.S. Department of Health and Human Services
Food and Drug Administration
Office of Regulatory Affairs
Center for Drug Evaluation and Research
May 2002

Compliance Policy Guide[1]
Compliance Policy Guidance for FDA Staff and Industry
CHAPTER - 4
SUB CHAPTER - 460

Sec. 460.200 Pharmacy Compounding

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

INTRODUCTION

This document provides guidance to drug compounders and the staff of the Food and Drug Administration (FDA) on how the Agency intends to address pharmacy compounding of human drugs in the immediate future as a result of the decision of the Supreme Court in Thompson v. Western States Medical Center, No. 01-344, April 29, 2002. FDA is considering the implications of that decision and determining how it intends to regulate pharmacy compounding in the long term. However, FDA recognizes the need for immediate guidance on what types of compounding might be subject to enforcement action under current law. This guidance describes FDA's current thinking on this issue.

BACKGROUND

On March 16, 1992, FDA issued a compliance policy guide (CPG), section 7132.16 (later renumbered as 460.200) to delineate FDA's enforcement policy on pharmacy compounding. That CPG remained in effect until 1997 when Congress enacted the Food and Drug Administration Modernization Act of 1997.

On November 21, 1997, the President signed the Food and Drug Administration Modernization Act of 1997 (Pub. L. 105-115) (the Modernization Act). Section 127 of the Modernization Act added section 503A to the Federal Food, Drug, and Cosmetic Act (the Act), to clarify the status of pharmacy compounding under Federal law. Under section 503A, drug products that were compounded by a pharmacist or physician on a customized basis for an individual patient were entitled to exemptions from three key provisions of the Act: (1) the adulteration provision of section 501(a)(2)(B) (concerning the good manufacturing practice requirements); (2) the misbranding provision of section 502(f)(1) (concerning the labeling of drugs with adequate directions for use); and (3) the new drug provision of section 505 (concerning the approval of drugs under new drug or abbreviated new drug applications). To qualify for these statutory exemptions, a compounded drug

[1] This guidance has been prepared by the Office of Regulatory Policy and the Office of Compliance in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration.

product was required to satisfy several requirements, some of which were to be the subject of FDA rulemaking or other actions.

Section 503A of the Act took effect on November 21, 1998, one year after the date of the enactment of the Modernization Act. In November, 1998, the solicitation and advertising provisions of section 503A were challenged by seven compounding pharmacies as an impermissible regulation of commercial speech. The U.S. District Court for the District of Nevada ruled in the plaintiffs' favor. FDA appealed to the U.S. Court of Appeals for the Ninth Circuit. On February 6, 2001, the Court of Appeals declared section 503A invalid in its entirety (Western States Medical Center v. Shalala, 238 F.3rd 1090 (9th Cir. 2001)). The government petitioned for a writ of certiorari to the U.S. Supreme Court for review of the circuit court opinion. The Supreme Court granted the writ and issued its decision in the case on April 29, 2002.

The Supreme Court affirmed the 9th Circuit Court of Appeals decision that found section 503A of the Act invalid in its entirety because it contained unconstitutional restrictions on commercial speech (i.e., prohibitions on soliciting prescriptions for and advertising specific compounded drugs). The Court did not rule on, and therefore left in place, the 9th Circuit's holding that the unconstitutional restrictions on commercial speech could not be severed from the rest of section 503A. Accordingly, all of section 503A is now invalid.

FDA has therefore determined that it needs to issue guidance to the compounding industry on what factors the Agency will consider in exercising its enforcement discretion regarding pharmacy compounding.

DISCUSSION

FDA recognizes that pharmacists traditionally have extemporaneously compounded and manipulated reasonable quantities of human drugs upon receipt of a valid prescription for an individually identified patient from a licensed practitioner. This traditional activity is not the subject of this guidance.[2]

FDA believes that an increasing number of establishments with retail pharmacy licenses are engaged in manufacturing and distributing unapproved new drugs for human use in a manner that is clearly outside the bounds of traditional pharmacy practice and that violates the Act. Such establishments and their activities are the focus of this guidance. Some "pharmacies" that have sought to find shelter under and expand the scope of the exemptions applicable to traditional retail pharmacies have claimed that their manufacturing and distribution practices are only the regular course of the practice of pharmacy. Yet, the practices of many of these entities seem far more consistent with those of drug manufacturers and wholesalers than with those of retail pharmacies. For example, some firms receive and use large quantities of bulk drug substances to manufacture large quantities of unapproved drug products in advance of receiving a valid prescription for them. Moreover, some firms sell to physicians and patients with whom they have only a remote professional relationship. Pharmacies engaged in activities analogous to manufacturing and distributing drugs for human use may be held to the same provisions of the Act as manufacturers.

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[2] With respect to such activities, 21 U.S.C. 360(g)(1) exempts retail pharmacies from the registration requirements of the Act. The exemption applies to "Pharmacies" that operate in accordance with state law and dispense drugs "upon prescriptions of practitioners licensed to administer such drugs to patients under the care of such practitioners in the course of their professional practice, and which do not manufacture, prepare, propagate, compound, or process drugs or devices for sale other than in the regular course of their business of dispensing or selling drugs or devices at retail" (emphasis added). See also 21 U.S.C. §§ 374(a)(2) (exempting pharmacies that meet the foregoing criteria from certain inspection provisions) and 353(b)(2) (exempting drugs dispensed by filling a valid prescription from certain misbranding provisions).

POLICY:

Generally, FDA will continue to defer to state authorities regarding less significant violations of the Act related to pharmacy compounding of human drugs. FDA anticipates that, in such cases, cooperative efforts between the states and the Agency will result in coordinated investigations, referrals, and follow-up actions by the states.

However, when the scope and nature of a pharmacy's activities raise the kinds of concerns normally associated with a drug manufacturer and result in significant violations of the new drug, adulteration, or misbranding provisions of the Act, FDA has determined that it should seriously consider enforcement action. In determining whether to initiate such an action, the Agency will consider whether the pharmacy engages in any of the following acts:

1. Compounding of drugs in anticipation of receiving prescriptions, except in very limited quantities in relation to the amounts of drugs compounded after receiving valid prescriptions.

2. Compounding drugs that were withdrawn or removed from the market for safety reasons. Appendix A provides a list of such drugs that will be updated in the future, as appropriate.

3. Compounding finished drugs from bulk active ingredients that are not components of FDA approved drugs without an FDA sanctioned investigational new drug application (IND) in accordance with 21 U.S.C. § 355(i) and 21 CFR 312.

4. Receiving, storing, or using drug substances without first obtaining written assurance from the supplier that each lot of the drug substance has been made in an FDA-registered facility.

5. Receiving, storing, or using drug components not guaranteed or otherwise determined to meet official compendia requirements.

6. Using commercial scale manufacturing or testing equipment for compounding drug products.

7. Compounding drugs for third parties who resell to individual patients or offering compounded drug products at wholesale to other state licensed persons or commercial entities for resale.

8. Compounding drug products that are commercially available in the marketplace or that are essentially copies of commercially available FDA-approved drug products. In certain circumstances, it may be appropriate for a pharmacist to compound a small quantity of a drug that is only slightly different than an FDA-approved drug that is commercially available. In these circumstances, FDA will consider whether there is documentation of the medical need for the particular variation of the compound for the particular patient.

9. Failing to operate in conformance with applicable state law regulating the practice of pharmacy

The foregoing list of factors is not intended to be exhaustive. Other factors may be appropriate for consideration in a particular case.

Other FDA guidance interprets or clarifies Agency positions concerning nuclear pharmacy, hospital pharmacy, shared service operations, mail order pharmacy, and the manipulation of approved drug products.

REGULATORY ACTION GUIDANCE:

District offices are encouraged to consult with state regulatory authorities to assure coherent application of this guidance to establishments that are operating outside of the traditional practice of pharmacy.

FDA-initiated regulatory action may include issuing a warning letter, seizure, injunction, and/or prosecution. Charges may include, but need not be limited to, violations of 21 U.S.C. §§ 351(a)(2)(B), 352(a), 352(f)(1), 352(o), and 355(a) of the Act.

Issued: 3/16/1992
Reissued: 5/29/2002

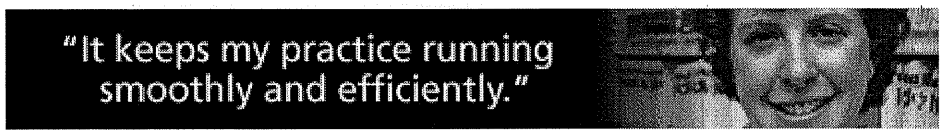
APPENDIX A

LIST OF COMPOUNDING DRUGS THAT WERE WITHDRAWN OR REMOVED FROM THE MARKET FOR SAFETY REASONS

Adenosine phosphate: All drug products containing adenosine phosphate.
Adrenal cortex: All drug products containing adrenal cortex.
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.
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.
Chlorhexidine gluconate: All tinctures of chlorhexidine gluconate formulated for use as a patient reoperative 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 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.
Fenfluramine hydrochloride: All drug products containing fenfluramine hydrochloride.
Flosequinan: All drug products containing flosequinan.
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.
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.
Oxyphenisatin: All drug products containing oxyphenisatin.
Oxyphenisatin acetate: All drug products containing oxyphenisatin acetate.
Phenacetin: All drug products containing phenacetin.
Phenformin hydrochloride: All drug products containing phenformin hydrochloride.

Pipamazine: All drug products containing pipamazine.
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.
Reserpine: All oral dosage form drug products containing more than 1 milligram of reserpine.
Sparteine sulfate: All drug products containing sparteine sulfate.
Sulfadimethoxine: All drug products containing sulfadimethoxine.
Sulfathiazole: All drug products containing sulfathiazole (except 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.
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.
Urethane: All drug products containing urethane.
Vinyl chloride: All aerosol drug products containing vinyl chloride.
Zirconium: All aerosol drug products containing zirconium.
Zomepirac sodium: All drug products containing zomepirac sodium.

ATTACHMENT B



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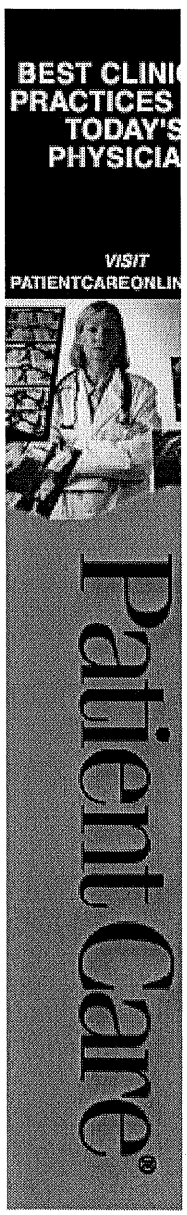

COVER STORY

COMPOUNDING UNDER SIEGE

As more reports surface about improperly compounded drugs, will new restrictions be placed on the practice?

The long-smoldering debate about pharmacy compounding has flared into a raging controversy, fanned by media coverage of patients dying from improperly compounded drugs and calls for more regulation of what critics see as one area of practice run amok.

The media have focused the public spotlight in recent months on errors and contaminated drugs traced back to pharmacies doing large-scale compounding. Major daily newspaper articles and national network news programs have portrayed the practice in unflattering terms, referring to makeshift labs, minimal oversight, and bad medicine that add up to a prescription for disaster.

The most recent uproar was triggered when four North Carolina patients were sickened and one died from fungal meningitis found in methylprednisolone injections compounded by Urgent Care Pharmacy in Spartansburg, S.C. The state pharmacy board shut down the compounding operation of the pharmacy, which recalled the contaminated drug. Tests by the Food & Drug Administration and the Centers for Disease Control & Prevention found that unopened vials from three separate lots were contaminated.

The South Carolina pharmacy board inspection of Urgent Care found improper operation of an autoclave, inadequate cleanroom practices based on ASHP's guidelines, and no testing for sterility or quality, according to

CDC's *Morbidity and Mortality Review (MMR)* of Dec. 13, 2002. The FDA issued a nationwide alert against use of all Urgent Care compounded drugs.

After reviewing the Urgent Care incident, the *MMR* report stated, "Clinicians should consider the possibility of improperly compounded medications as a source of infection in patients after epidural or intra-articular injections."

By pointing the finger at pharmacies compounding sterile injectables, the CDC underscored what some critics have been saying all along. To them, such large-scale compounding is a dangerous, unregulated practice conducted outside good manufacturing practices that puts patients at risk.

"Compounding has become a very big industry, and we don't know the scope of it, but our patients are vulnerable," said Sarah Sellers, Pharm.D., an Illinois-based consultant on policy and regulation. "We're going to have to start considering in our differential diagnoses whether treatment failure is due to exposure to substandard [compounded] drugs. England has identified extemporaneous compounding as an added risk to the provision of pharmaceutical care, and so they basically prohibit compounding."

Another risk factor for patients is that compounding pharmacies cannot vouch for the quality of the bulk chemicals they buy, said Sellers, who served on the Pharmacy Compounding Advisory Committee of the Center for Drug Evaluation & Research (CDER) in the FDA. She also raised the specter of counterfeit bulk chemicals making their way to patients.

"We don't have a good idea of the quality of the chemicals," said Sellers. "When the bulk [chemical] jars get to the pharmacy, the pharmacists rely on their sixth sense to determine the potency and quality of the chemicals. Repackagers have been found taking expired drugs and repacking them with new expiration dates. Right now we might not even be able to determine where the bulk chemical was actually manufactured and when. If you're not starting with a quality material, no matter what you're doing in your compounding process, you're not going to end up with a quality product."

The charge that pharmacy organizations have been apologists for compounding's bad actors rings true for Carmen Catizone, executive director, National Association of Boards of Pharmacy. "One argument that's difficult to refute is that if you have a pharmacy shipping 40,000 doses, even those for individual patients, at some point that mom-and-pop pharmacy has become a manufacturer," he said. "I don't care if they're doing it right and following all the state laws, when you make a certain quantity, it leaves the 'old shoe box.' That's a belief we can't get pharmacy to accept, and that creates problems."

It wouldn't matter how much the American Pharmaceutical Association condemned compounding's bad apples, it wouldn't be enough for some critics, countered Susan Winckler, v.p.-policy and communication and general counsel. "APhA's challenge is that when we defend compounding,

some people think we defend *all* who are compounding," she said. "That's incorrect, but you have some people certainly interpreting our words that way."

If patients are getting substandard drugs, lay out the evidence, said L. D. King, executive director, International Academy of Compounding Pharmacists (IACP). "It's estimated that 1% of all prescriptions are compounded, which is quite a huge number," he said. "When you put it in the perspective of the number of incidents of substandard drugs leading to patient harm, it's a very safe practice."

The champions of compounding may point to its safety record, but that's misleading because no one is keeping track of adverse events, according to Larry Sasich, Pharm.D., M.P.H., research analyst, Public Citizen Research Group. "There is no reporting requirement and, for all practical purposes, no regulatory oversight of these pharmacists," he said. "We could be knocking off a few people here and a few people there and nobody knows about it. I am ashamed of the position organized pharmacy has taken. I think the public's esteem for the profession is going to suffer tremendously because the profession hasn't spoken up. It was just a matter of time before we began to see problems, and it's beginning to float into view in the public periscope. And there is interest in doing something on Capitol Hill."

Sure enough, six members of Congress recently sounded an alarm about hospitalizations and deaths traced to compounding pharmacies. The Representatives wrote that "compounding should not be a loophole to circumvent the established role of the FDA in ensuring the highest level of quality for the nation's drug supply" in an Oct. 21, 2002, letter to the new FDA commissioner, Mark McClellan.

"While we believe the practice of pharmacy compounding in which a pharmacist modifies a prescription on an individual patient basis has a time-honored and important role to play in our healthcare delivery system, we share the FDA's concern that when 'the scope and nature of a pharmacy's activities raise the kinds of concerns normally associated with a drug manufacturer,' enforcement action is necessary to protect the health of the public," the letter continued. "We urge you to vigorously enforce against such practices."

The 900-lb. gorilla

Congressional calls for the FDA to get more involved are not music to the profession's ears. Pharmacy organizations have been squabbling for years with the FDA over regulation of compounding. When manning the ramparts against the federal agency, such organizations take the stance that compounding is a traditional right of pharmacists and only the state pharmacy boards have the authority to regulate it.

The ongoing battle culminated in a Supreme Court decision last spring that

struck down section 503A of the Food & Drug Administration Modernization Act of 1997. Compounding pharmacists had sued over being barred from advertising that they compounded specific drugs. The Supreme Court agreed and its decision knocked down the entire section, not just the commercial speech aspect.

As a result, the FDA issued a compounding policy guidance document last June laying out its stance on drawing the line between compounding and manufacturing. Noting that the agency recognized traditional compounding, the FDA stated its belief "that an increasing number of establishments with retail pharmacy licenses are engaged in manufacturing and distributing unapproved new drugs for human use in a manner that is clearly outside the bounds of traditional pharmacy practice."

Despite FDA protestations of leaving regulation of traditional compounding to the states, the National Community Pharmacists Association doesn't buy it. Standing up for independent pharmacists who make up the bulk of compounders, NCPA believes that "the FDA has no authority to regulate pharmacy compounding because it's just not their business," said John Rector, general counsel, senior v.p.-government affairs. "We say if the FDA finds people manufacturing who are not licensed to do so, bust them. They don't need jurisdiction over pharmacy compounding to sanction or respond to those manufacturers without proper credentials. The FDA seems to be on the warpath because it lost its intrusive authority regarding compounding."

While pharmacy is adamant that the FDA has no legal authority over compounding, the agency begs to differ in two areas: manufacturing masquerading as compounding and patient safety, said David Horowitz, CDER director of compliance. "We cannot allow compounders to compound large volumes of drugs and engage in activities that are more similar to drug manufacturing without being regulated as drug manufacturing," he said. "A tougher issue for us to come to grips with is those that might not be large-volume compounders but that might raise significant public health issues. In those cases, we want to work with the states and support their actions, and, if necessary, take FDA action."

Most compounding advocates contend that state pharmacy boards are the proper regulatory watchdogs. IACP's King pointed out that one-third of the states are in the process of revising their regulations. "The states are becoming more sophisticated about regulating compounding," he said. "As the states become more equipped to address compounding, we hope the FDA will feel less inclined to get involved."

State pharmacy boards already have a blueprint for good compounding practices developed by NABP, said Catizone. However, he added, "some states have implemented them; others ignore them. There is no uniformity, just a patchwork of standards and regulation."

While critics contend that state pharmacy boards merely react to complaints instead of actively policing compounding pharmacies, the hard

facts of regulatory life dictate how boards operate. There simply is no money in strapped state budgets to pay for more inspectors. "The criticism is why can't the boards be more proactive and monitor for compounding and enforce the standards and put some of these people out of business?" said Catizone "But it's a matter of resources. I don't know how the boards can justify inspecting every pharmacy that's compounding."

Despite pharmacy's fear of the FDA, the agency is really not that powerful, given its own lack of resources, said Public Citizen's Sasich. "Most people think the FDA is a 900-lb. bureaucratic gorilla with a big stick, but it's really pretty weak," he said.

Credentials, please

One move pharmacy is mulling over to give a jittery public a yardstick is the creation of a credential that compounding pharmacists could earn and perhaps accreditation of compounding sites by an outside organization. For instance, King said IACP has held discussion with the Board of Pharmaceutical Specialties and the National Institute for Standards in Pharmacist Credentialing.

BPS is "very anxious" to work with the compounding community to create a certification program for compounding as a special advanced practice area, said executive director Richard Bertin, Ph.D. The next step is up to a group to petition BPS to recognize compounding as a new specialty, followed by national hearings and a review process.

"Right now there is no way that the patient, payer, healthcare professionals, or others in pharmacy can really identify those compounders with the appropriate level of skills and knowledge for what they're doing," said Bertin. "Sooner rather than later, they need a credential that will be believable and give them the credibility they need in the pharmacy community and beyond, which may be even more important."

There may be some reluctance among compounders to commit to BPS certification because the process is rigorous and costly, said Bertin. "My impression is that there's a little bit of fear of the BPS process. Some are concerned that if there is certification, somewhere along the line regulators will want to mandate that *all* compounders have that certification. There is interest, but I think they're trying to see whether there are other alternatives that, quite frankly, might be cheaper and easier."

APhA has also been working closely with IACP and others to figure out whether certification is the way to go, said Winckler. While simple compounding might not justify a certificate credential, she feels, "if a pharmacist is going to get into sterile product preparation, there should be a certification program, so he or she can say, 'Here's my knowledge in this area.' "

On another front, the U.S. Pharmacopeia has proposed a new general

chapter on good compounding practices to give compounders and regulators detailed information on compounding, including the compounder's responsibilities, training requirements, procedures and documentation, and the facilities and equipment needed. There is also a table indicating various levels of the difficulty of compounding the preparation.

Wish lists

Most of the players interested in compounding have a wish list for the direction in which they'd like to see the practice move. Of course, most of them would go their separate ways.

New legislation that spells out what cannot or should not be done by compounding pharmacists is the top wish for Public Citizen's Sasich. "The first thing I'd start out with is a list of drugs that cannot be safely manufactured in a back room of the pharmacy or outside a regulated facility under good manufacturing guidelines," he said. "At the top of that list would be sterile products, including injections and inhalation solutions. Then there has to be some kind of public disclosure of the fact that compounded drugs have not been tested for safety and effectiveness and are not produced under good manufacturing practices."

APhA's Winckler would second the notion that patients should know when they're taking a compounded drug and why. She would also like to see the profession pull together a resource of all compounding regulations to evaluate what's working.

For NABP, the top job is getting the state boards of pharmacy, the profession, and the FDA to agree on the distinction between compounding and manufacturing, said NABP's Catizone, "and then getting the bad players out of the system."

The FDA wants to work with the states, the U.S. Pharmacopeia, and other stakeholders to develop a new legislative framework. "We intend to pursue the possibility of new legislation," said Horowitz, "because we believe that both the compounding community and consumers would be better off if there were greater clarity than we can achieve using our compounding policy guide."

Representing 1,800 compounding pharmacists, IACP wants the FDA to help the profession understand the differences between compounding and manufacturing, said King. He also favors further development of standards for compounding practice. "The bottom line is that we have to make medication that is safe and effective for our patients," he said. "And we'll do everything in our power to make sure that exists."

Carol Ukens

Bad news

In recent years, compounding has been involved in several incidents that captured media attention and triggered calls for more regulation, including the following:

• In North Carolina, one patient died and three became ill from fungal meningitis traced to methylprednisolone compounded by Urgent Care Pharmacy of Spartansburg, S.C. In September 2002, the pharmacy recalled the contaminated product. State and federal inspections found several instances of nonadherence to sterile technique. However, when Urgent Care refused to recall *all* its compounded products, the Food & Drug Administration issued a national alert advising against use of any products compounded by the pharmacy.

• On Sept. 20, the FDA put Med-Mart Pulmonary Services of Novato, Calif., on notice that it was operating as a drug manufacturer, not a retail pharmacy. Citing concerns about "large-scale production of massive quantities of inhalation solutions," the FDA threatened actions such as seizure and/or injunction if the firm did not provide a plan to correct numerous operational deficiencies.

• Although Robert Courtney's dilution of chemotherapy drugs was not strictly compounding, the finer points of the Kansas City pharmacist's operation were lost on the media and the public following discovery of his criminal actions in August 2001. He was recently sentenced to 30 years in prison.

• Last July, two pharmacists and six healthcare professionals were convicted in Miami of defrauding Medicare of millions of dollars with bogus billing for compounded aerosol medications through South Beach Pharmacy, LaModerna Pharmacy, and/or CDC of South Florida Inc. The compounded drugs contained little or no active ingredients.

• On Sept. 18, 2002, the U.S. Department of Justice sent a letter to Pharmaceutical Compounding Centers of America (PCCA) informing the Houston firm that the huge volume of chemicals it had supplied to Miami pharmacies should have been a "red flag" that there was Medicare fraud going on. The firm was also informed that its actions "have assisted in the systematic defrauding of the Medicare Trust Fund."

• PCCA was also the target of an FDA warning letter in July 2001 taking the firm to task for violations of good manufacturing practices, including failure to ensure against cross contamination between cephalosporins and penicillin repackaged on common equipment. The FDA also alleged that PCCA had been repacking and distributing bulk drugs that had been removed from the market, such as phenacetin, dipyrone, and adenosine phosphate.

• On April 10, 2002, the FDA warned three pharmacies that the nicotine

lollipops and lip balm they were selling were illegal because they were compounded without an Rx and were made from nicotine salicylate, which is not approved for compounding.

• Last June, Portage Pharmacy, Portage, Mich., issued a class I recall of 791 vials of compounded drugs, including methylprednisolone, due to contamination and a class II recall of 175 vials of other compounded medications due to lack of assurance of sterility.

• Two patients in Michigan who had received compounded medication for spinal injection became ill with *Chryseomonas* meningitis last year, according to CDC.

• In March 2001, four Atlanta patients had severe adverse reactions to a compounded thyroid drug prescribed for Wilson's syndrome, a quack diagnosis created by a Florida doctor who lost his license. One R.Ph. was put on probation for five years and the owner-R.Ph. surrendered his license. He had been sanctioned in 1986 for felony convictions for mail fraud and misbranding and adulteration of drugs.

• Thirteen people were hospitalized and three others died from meningitis traced to contaminated betamethasone compounded by Doc's Pharmacy in Walnut Creek, Calif., in May 2001. The pharmacist-owner's license was revoked for one year, but a young pharmacist who co-owned the pharmacy later committed suicide following a 90-day license suspension.

Compounding flunks FDA test

Among 29 samples taken from 12 compounding pharmacies that advertise their wares over the Internet, 10 failed to meet standard quality tests, according to small study by the Food & Drug Administration.

• The 34% failure rate for the compounded samples was "significant," compared with the 2% failure rate among drug manufacturers, according to researchers in the FDA's Center for Drug Evaluation & Research. Nine of the 10 failures were for subpotency; the other was for contamination.

• More than half the samples had less than 70% of the potency stated on the labeling. Three additional samples failed an initial test but there was insufficient product for retesting, so they were not counted among the failures.

• The FDA study is on the Web at **www.fda.gov/cder/pharmcomp/communityPharmacy/default.htm** .

Carol Ukens. Cover Story: COMPOUNDING UNDER SIEGE. *Drug Topics* 2003;1:44.

ATTACHMENT C

State of California—Health and Human Services Agency

Department of Health Services

California Department of Health Services

DIANA M. BONTÁ, R.N., Dr. P.H.
Director

RECEIVED BY CALIF.
BOARD OF PHARMACY

2002 JUL 22 PM 2:51

GRAY DAVIS
Governor

July 18, 2002

John Jones, R.Ph., President
California State Board of Pharmacy
400 R Street, Suite 4070
Sacramento, CA 95814

Dear Mr. Jones:

The California Department of Health Services' (DHS) Food and Drug Branch (FDB) and The California State Board of Pharmacy (BOP) have over the years worked cooperatively on numerous issues. Pharmacy compounding has been one of these issues. Due to many recent events relative to pharmacy compounding, 1) U.S. Food and Drug Administration (FDA) issuing of a Compliance Policy Guide; 2) U.S. Supreme Court decision on the compounding provisions of the FDA Modernization Act of 1997; 3) chaptering of Senate Bill 293 (Torlakson) - pharmacy compounding of sterile injectable drug products; and 4) BOP's draft standards for sterile compounding, FDB would like to revisit with the BOP the issue of pharmacy compounding, including criteria used by BOP to determine when pharmacy compounding falls outside the scope of pharmacy practice. Because FDB is responsible for licensing California's drug manufacturers, it is important for us to understand how the BOP notifies individuals when pharmacy compounding activities fall outside the scope of pharmacy practice.

FDA has requested comments on their Compliance Policy Guide for pharmacy compounding. FDB believes combined comments on this Compliance Policy Guide by DHS and BOP may be more useful to FDA than comments by the individual agencies. A meeting would determine if combined comments are feasible and would serve as a starting point in their preparation.

FDB participated in preparing BOP's "Guidelines for Distinguishing Compounding from Manufacturing" published in the mid-1990's. With the many recent events identified above, FDB is unsure of the status of this guideline. A meeting would clarify this.

Since the agenda for the July 24 & 25, 2002 BOP meeting includes the topic of pharmacy compounding, you may wish to discuss our request at that time. Uncertainties with the state budget prohibit FDB from attending this meeting.

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If you have any questions regarding this request, please contact me or Glen Lawrence, Chief, Drug Safety Unit at (916) 445 – 2264.

Sincerely,

James M. Waddell, Acting Chief
Food and Drug Branch

cc: Ms. Patty Harris, Executive Officer
California State Board of Pharmacy
400 R Street, Suite 4070
Sacramento, CA 95814

Glen Lawrence, Chief
Drug Safety Unit
Food and Drug Branch

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www.consumerenergycenter.org/flex/index.html

ATTACHMENT D

International Academy of Compounding Pharmacists

P.O. Box 1365
Sugar Land, Texas 77487

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1-800-927-4227

www.iacprx.org
iacpinfo@iacprx.org

2002 AUG 12 PM 3:41

August 8, 2002

Patricia F. Harris, Executive Officer
California State Board of Pharmacy
400 R Street, Ste 4070
Sacramento, CA 95814

Dear Patricia F. Harris:

In May 2002, the U.S. Food and Drug Administration (FDA) issued a Compliance Policy Guide (CPG) Manual Section 460.200, entitled "Pharmacy Compounding." In this guidance, FDA provides nine policy factors (which we have attached to this document for your convenience) designed to differentiate between manufacturing and pharmacy compounding. FDA's publication of the CPG follows the U.S. Supreme Court decision, Tommy Thompson v. Western States Medical Center, in which the Court held that Section 503A, the compounding portion of the Food, Drug and Cosmetic Act (FDCA) added by the 1997 Food and Drug Administration Modernization Act, is unconstitutional. This now defunct legislation formally exempted pharmacy compounding from new drug approval and good manufacturing provisions of the FDCA. In the absence of legislation, FDA is seeking to once again assert its regulatory oversight of pharmacy compounding. IACP and other pharmacy organizations have questioned under what authority FDA issued the CPG. FDA has clear authority over the practice of manufacturing. However, the practice of pharmacy, including pharmacy compounding, is traditionally regulated by State Boards of Pharmacy. The CPG should be limited to providing guidance regarding the distinction between pharmacy compounding and manufacturing. However, this guidance clearly oversteps regulation of manufacturing and manufacturing under the guise of compounding and encroaches on the practice of legitimate pharmacy compounding of medications for individual patients.

IACP is also concerned that there was no comment period for the CPG prior to its release. Normally FDA will issue this type of guidance for public comment before it becomes official. However, in this case FDA determined that "prior public participation [was] not feasible or appropriate." Such a comment period is essential to ensure that FDA does not overstep its role into the areas of pharmacy practice. We are hopeful that FDA will revise the guidance after receiving comments from the profession.

The International Academy of Compounding Pharmacists (IACP) is an international, non-profit association protecting and promoting the art and skill of pharmaceutical compounding. IACP represents more than 1,600 pharmacists – and their patients, who benefit from compounded medications. IACP's mission includes increasing awareness of the importance of compounding by providing accurate information on the benefits of compounding and providing assistance to pharmacists in improving their compounding activities. We have recently assisted a number of states in their efforts to update their regulations for pharmacy compounding.

We appreciate the opportunity to share our concerns with you and look forward to working with you on issues related to pharmacy compounding that we may encounter in the future. If we can be of any assistance, or if you have any questions, please do not hesitate to contact me.

Sincerely,

L.D. King
Executive Director

Attachments (2)

International Academy
of Compounding Pharmacists

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Sugar Land, Texas 77487

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August 8, 2002

Dockets Management Branch (HFA-305)
Food and Drug Administration
Room 1061
5630 Fishers Lane
Rockville, Maryland 20852

Re: Docket No. 02D-0242: Compliance Policy Guides Manual Section 460.200, "Pharmacy Compounding"

Dear Sir or Madam:

The International Academy of Compounding Pharmacists ("IACP") appreciates the opportunity to comment on the Food and Drug Administration's ("FDA") Compliance Policy Guide ("CPG") Manual Section 460.200, entitled "Pharmacy Compounding." IACP's mission includes increasing awareness of the importance of compounding by providing accurate information on the benefits of compounding and providing assistance to pharmacists in improving their compounding activities. In this capacity, IACP wishes to address a number of issues in this Compliance Policy Guide. IACP submits these comments on behalf of its 1600 member compounding pharmacists and their patients, who benefit from compounded medications.

Initially, IACP objects to the publication of this guidance without public comment. Although FDA claimed that the CPG needed to be implemented immediately, pursuant to 21 C.F.R. § 10.115(g)(2) ("FDA will not seek your comment before it implements a Level 1 guidance document if the agency determines that prior public participation is not feasible or appropriate"),[1] IACP is hard-pressed to understand why the agency had "an urgent need to explain how, in light of the Supreme Court decision, it will exercise its enforcement discretion in regard to compounded human drugs."[2] The haste is unwarranted in that every state in the Ninth Circuit had been operating without Section 503A of the Federal Food, Drug, and Cosmetic Act ("FDCA") for months following the Ninth Circuit's decision in Western States Medical Center v. Shalala, 238 F.3d 1090 (9th Cir. 2001). Moreover, the practice of pharmacy, including compounding, is heavily regulated by the State Boards of Pharmacy. There was thus no need for the precipitous action taken by the agency. It was both appropriate and feasible for the FDA to allow public comment before publication of a final guidance.

FDA has spoken of how it wishes to work in a more cooperative and open manner with the pharmacy community. The abrupt issuance of the CPG in final form is inconsistent with the

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1 See 67 Fed. Reg. 39,409, 39,410 (June 7, 2002).

2 Id.

agency's purported objective of receiving meaningful input from interested parties. Accepting comments after the fact is not a substitute for soliciting comments before publication.

In addition, giving the public and regulated industry the opportunity to comment prior to release of the CPG would have helped FDA resolve some of the ambiguities that must now be addressed after the fact. The document issued has created unnecessary controversy and confusion, much of which, we believe, could have been avoided by allowing even a brief period for public comment. IACP requests that all future policy guides relating to pharmacy compounding (and revisions of such documents) be released for comment prior to the publication of the final guidance.

Seeking public comment may have helped the agency avoid a fundamental tension within the CPG. Although the FDA indicated that the CPG is intended to delineate the line between drug manufacturers and pharmacies engaged in compounding,[3] the CPG actually conflates two separate and distinct issues: first, distinguishing compounding from manufacturing and second, how to compound in a safe manner. Some of the factors in the CPG, which will be discussed in more detail below, even though they do not relate to the ostensible objective of the CPG, address the "safety" issue, not the scope and scale of the compounding activities.

For example, not obtaining written assurance from a supplier that each lot of a drug substance has been made in an FDA-registered facility, not ensuring that drug components meet official compendia requirements, or compounding a product that used bulk active ingredients that are not components of FDA-approved drugs, are each a factor listed in the CPG. However, there is virtually no relationship between those factors and whether a pharmacy is a manufacturer. Although the Supreme Court was not speaking of these variables in Western States, its language requiring that there be an appropriate "fit" between the regulatory goal and the means to achieve it

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[3] See CPG § 460.200 at 3 ("FDA believes that an increasing number of establishments with retail pharmacy licenses are engaged in manufacturing and distributing unapproved new drugs for human use in a manner that is clearly outside the bounds of traditional pharmacy practice and that violates the Act. Such establishments and their activities are the focus of this guidance.") There are two points worth noting here. First, IACP questions the basis for the statement that there are an "increasing number" of pharmacies acting as manufacturers. This language was taken almost verbatim from the 1992 CPG, and is thus ten years old. Unless FDA has information to support this assertion, it should be deleted from the CPG. Second, although this is not the forum for an extended discussion of this issue, as IACP, and others, demonstrated in their briefs in the Western States appeal before the United States Supreme Court, pharmacy compounding does not result in an unapproved new drug. Historically, pharmacy compounding was exempted from the new drug requirements of the FDCA. Brief of the International Academy of Compounding Pharmacists, *amicus curiae*, in Thompson v. Western States Medical Center, No. 01-344, 2-5 (2002).

is also appropriate here.[4] Factors 2 (compounding drugs that were withdrawn or removed from the market for safety reasons), 3 (compounding from bulk active ingredients that are not components of FDA-approved drugs), 4 (receiving, storing, or using drug substances without obtaining written assurance from the supplier that each lot has been made in an FDA-registered facility), and 5 (receiving, storing, or using drug components not guaranteed or otherwise determined to meet compendia requirements) all address safety issues, not whether a pharmacy is acting as a manufacturer. In many instances, factor 9 (failing to operate in conformance with applicable state law regulating the practice of pharmacy) may have no bearing on either issue.

Whatever FDA's statutory power over pharmacies may be, IACP believes that FDA has no authority to set national safety standards for pharmacies that are not "manufacturers." While Congress clearly has the power to impose these requirements upon pharmacists, FDA, in the absence of legislation, does not. IACP does not believe this to be the forum to discuss this issue in depth. We strongly believe, however, that Congress never authorized FDA to act as the National Board of Pharmacy.

Congress authorized FDA to regulate manufacturers and set standards for safety and efficacy for new drugs produced by manufacturers. Conversely, as IACP demonstrated in its brief to the Supreme Court, Congress never intended FDA to regulate pharmacies to the same extent as manufacturers. That is why pharmacies are exempt from registration and listing requirements and the detailed inspections that manufacturers must undergo.[5] Whatever power FDA might have over pharmacists who have become manufacturers, there is no statutory basis for FDA to assert that it has the authority to prescribe standards for traditional pharmacies engaged in extemporaneous compounding.

According to the guidance, the CPG applies only to pharmacists who are manufacturing under the guise of compounding. The CPG distinctly excludes those pharmacists engaged in traditional compounding pharmacy (as stated in the discussion of the CPG) and, thus, no part of the CPG should be enforced against those pharmacists, provided they are not manufacturers. However, the criteria of the CPG do not operate this way. A pharmacist who compounds a single prescription from a bulk drug that is not the subject of an FDA-approval, without getting an assurance that the drug came from an FDA-registered facility or a guarantee that it met compendia standards has failed three of the nine criteria. That pharmacist could not possibly be considered a manufacturer. He is operating within the practice of pharmacy, subject to regulation by the State Boards of Pharmacy. Yet the CPG wrongly treats these factors as having a bearing on whether a pharmacist is a manufacturer in disguise. The stated objective of the CPG and its factors are at odds with one another.

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4 Western States, slip op. at 13-14; dissent at 11.

5 FDCA § 510(g)(1); 704(a)(2)(A).

IACP urges FDA to defer to the State Boards of Pharmacy and standard-setting organizations such as the U.S. Pharmacopeia ("USP") and the National Association of Boards of Pharmacy ("NABP") for the regulation of compounding practices. State Boards of Pharmacy and the cited organizations have been effectively regulating the practice of compounding pharmacy for many years through state pharmacy law and regulations, and USP Chapter 795 "Pharmacy Compounding" and NABP's Good Compounding Practices.[6] Therefore we believe that factors 2, 3, 4, and 5 should be removed from the CPG as irrelevant to its professed objective of regulating those pharmacies that "are engaged in manufacturing and distributing unapproved new drugs for human use in a manner that is clearly outside the bounds of traditional pharmacy practice and that violates the Act."[7] CPG § 460.200 at 3.

Although the CPG lists extraneous factors, it omits the core of pharmacy: receiving a valid prescription or order from a licensed health care professional. IACP has long maintained that the pharmacist-physician-patient triad relationship is central to whether a pharmacy is acting as a pharmacy. IACP recommends that FDA drop factors 2,3,4, and 5, and include a factor relating to the existence of the triad relationship.

Specific Issues

IACP has additional concerns with the nine factors that FDA has stated it will consider when determining if the agency will initiate enforcement action.

Factor 1: The initial factor indicates that FDA will consider enforcement action when a pharmacy engages in "compounding of drugs in anticipation of receiving prescriptions, *except in very limited quantities* in relation to the amounts of drugs compounded after receiving valid prescriptions." See CPG Sec. 460.200 Pharmacy Compounding (emphasis added). This statement represents a significant change from FDA's prior position in its 1992 Compliance Policy Guide for Pharmacy Compounding, CPG Sec. 7132.16, which stated that FDA would consider enforcement action if a pharmacy were engaged in "compounding *inordinate amounts* of drugs in anticipation of receiving prescriptions . . .." The language in the 2002 CPG is also more restrictive than the Food and Drug Administration Modernization Act ("FDAMA") Section 503A, which was consistent with the 1992 Compliance Policy Guide. IACP believes that the change from allowing anticipatory compounding except in "inordinate amounts" (with evidence of prescription trends) to

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6 National Association of Boards of Pharmacy, Good Compounding Practices Applicable to State Licensed Pharmacies, Appendix C.

7 Although we have commented on these factors, we urge FDA to drop them from the CPG. Factor 9 should be clarified so that FDA utilizes state law only to the extent that the law addresses the manufacturer versus compounding issue.

disallowing anticipatory compounding except in "very limited quantities," is unduly restrictive and significantly limits the ability of compounding pharmacists to run effective practices and to meet their patients' needs.

The phrase "very limited" may lead FDA to take action based on what has been regarded as acceptable anticipatory compounding, or cause pharmacists to unduly curtail anticipatory compounding based on historical prescribing patterns. IACP recognizes that the phrase "inordinate amounts," by itself, was not well defined. The same is true, though, for "very limited." IACP suggests that this section be revised to say "limited quantities based on historical prescribing patterns."

Anticipatory compounding is a well-accepted, beneficial component of traditional compounding. See, e.g. Ohio Admin. Code § 4729-9-21 ("A limited quantity may be compounded in anticipation of prescription drug orders based on routine, regularly observed prescribing patterns"); 22 Tex. Admin. Code § 291.31 (defining compounding to include "[t]he preparation, mixing, assembling, packaging, or labeling of a drug or device: . . . in anticipation of prescription drug orders based on routine, regularly observed prescribing patterns").

The NABP Model Rules state that:

> Pharmacists may compound drugs in very limited quantities prior to receiving a valid prescription based on a history of receiving valid prescriptions that have been generated solely within an established pharmacist/patient/prescriber relationship, and provided that they maintain the prescriptions on file for all such products compounded at the pharmacy (as required by State law). The compounding of inordinate amounts of drugs in anticipation of receiving prescriptions without any historical basis is considered manufacturing.

Although the NABP guidelines refer to "very limited quantities," they specifically reference a history of prescription patterns to determine what is a "very limited quantity." Further, the NABP guidelines state that a pharmacist is engaged in manufacturing only when the pharmacist compounds "inordinate amounts of drugs" in anticipation of prescriptions and there is no historical basis for the anticipatory compounding. Thus, the NABP guidelines use the context of historical practice, whereas the CPG uses the more restrictive, absolute standard of "very limited."[8]

Additionally, this factor could have negative effects on drug quality if it forces pharmacists to compound multiple small batches of a drug product as opposed to a single, large batch. Producing multiple small batches of drug products may incur a greater risk of error and contamination than preparing a single batch of greater quantity. Compounding in larger batches

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8 As stated above, we also recommend removing the modifier "very" as unnecessarily restrictive.

may permit sterile compounding pharmacies to conduct sterility testing in advance of receiving prescriptions, thereby enabling pharmacies to determine sterility of the compounded product prior to releasing the product to the consumer. Patient-by-patient compounding precludes this testing. There are situations when larger batches can be tested and validated more efficiently because of the number of samples that have to be tested, the sensitivity of the analytical balances (minimum amounts that can be accurately weighed) and the measuring/mixing capabilities of the compounding equipment based on dilution factors.

Compounding pharmacists strive to assure maximum accuracy and safety in all compounded preparations regardless of batch sizes. Compounding pharmacies should not be restricted from preparing appropriate amounts of pharmaceutical products based on physician refill instructions and routine, historical prescribing patterns.

Allowing pharmacists who receive regular prescriptions for a drug the flexibility to compound sufficient quantities of that drug could under certain circumstances enhance quality and lead to greater efficiencies. This can benefit the patient, by permitting faster access to the medication, and also give the pharmacist more time for other necessary activities, such as patient counseling. Given the substantial nationwide shortage of pharmacists,[9] having pharmacists compound multiple small batches of the same medication may not be the most productive use of pharmacists' time.

Factor 2: The second factor references a list of drug substances that "were withdrawn from the market for safety reasons." While IACP generally agrees with the purpose of this factor,[10] we do have several concerns. First, it is IACP's position that there should be notice and an opportunity to comment before a drug is added to this "negative" list. A few recent additions to the list of drugs withdrawn from the market for safety reasons received no public input prior to their addition to the list. For example, three drug products – Cisapride, Grepafloxacin, and Troglitazone – were listed in the May 2002 CPG. These products had not previously appeared on the list of drug substances withdrawn from the market for safety reasons. In addition to the lack of opportunity to comment on the CPG overall, there was no public comment period given on these drug products before they were added to the list of drugs prohibited for use in compounding.

Many of the drug products that are withdrawn are limited to certain doses, dosage forms, or indications. Public comment is critical to ensure the limitations on the use of the drug product are appropriate and take into consideration the differences between compounding and manufacturing.

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9 Bureau of Health Professions, Health Resources and Services Administration, Report to Congress: The Pharmacist Workforce: A Study of the Supply and Demand for Pharmacists, 4-6 (2000).

10 However, as noted above, IACP also believes this factor to be unrelated to the pharmacist-manufacturer dichotomy.

Section 503A required that FDA receive public input before adding a drug to this list. IACP believes that this process allows for better decision-making. There have occasionally been instances where FDA has reversed its stance on an identified drug following public comment. For example, FDA decided not to add parenteral drug products containing neomycin sulfate to the list of drug substances withdrawn from the market for safety reasons following the public comment period.[11] Thus, IACP requests that the FDA procedure for modifying the lists adhere to its good guidance practices and permit a proposal stage, to allow for review and comments by the public, before the issuance of additions to any list.

Factor 3: The third factor in the CPG unnecessarily restricts those ingredients that may be used to compound drug products. Under Section 503A, compounding pharmacists were permitted to compound using three sources of bulk drug ingredients – bulk drugs that have been components of FDA-approved drug products, bulk drugs that complied with the standards of an applicable USP or National Formulary ("NF") monograph, and bulk drugs that appeared on the list of drug substances that may be used in pharmacy compounding.[12] However, the May 2002 Compliance Policy Guide references only bulk drug substances that are components of FDA-approved drug products. The reduction of approved bulk drug sources from three primary sources to one significantly reduces the ability of pharmacists to compound to meet patients' needs. IACP therefore recommends that FDA restore the approved bulk drug sources to the three sources cited in Section 503A.

The lack of the USP and the "Positive List"[13] as sources of approved bulk drug substances are both glaring omissions in the CPG. The USP should clearly be a source for approved drugs. Some old drugs that have been grandfathered have not been approved by FDA, but have a long history of compounding use. As worded, the CPG would exclude the use of many bulk drug substances that have USP monographs but are not found in the Orange Book, FDA's defined source of approved drug substances. Examples include histamine diphosphate, phenobarbital, chloral hydrate, oxytetracycline dihydrate, estriol, collodion flexible, potassium permanganate, menadione and tinidazole. Some of these listed drug actives are even commercially available through finished drug products. Allowing use of only bulk drug substances that are components of FDA-approved drugs is evidently an inadequate provision for pharmacy compounding or even manufacturing.

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11 See 64 Fed. Reg. 10944, 10946 (Mar. 8, 1999). Adding a drug to the list, and then soliciting comments is not an adequate substitute. This sequence may lead to patients foregoing necessary therapy for as long as the product is listed.

12 FDCA § 503A(b)(i)).

13 Ibid.

Also, the FDA has already approved a proposed list of bulk drug substances that do not have USP monographs and that are not components of FDA-approved drug products. This list includes several commonly compounded drug products, such as metronidazole benzoate, caffeine citrate, and cantharidin. Just as the negative list places limits on access to drugs that are potentially unsafe, the positive list provides access to compounded drugs that potentially offer benefits to patients. FDA has previously recognized the necessity of expanding approved bulk drug sources through the provision of this positive list and an identified procedure for future additions to this list. There is no reason why these previous provisions should now be revoked. The symmetry found in FDAMA, Section 503A should be maintained.[14]

Additionally, the third factor discusses "bulk active ingredients that are not components of FDA-approved drugs . . .." The use of the present tense could be read as implying that pharmacists may not compound using active ingredients that were present in FDA-approved drugs, but that are no longer commercially available. FDA should revise this factor to clarify that pharmacists may compound using bulk active ingredients that are used in FDA-approved drugs, or were, at one time, present in FDA-approved drugs, as long as the drug products were not withdrawn from the market for safety reasons. Drug companies discontinue products for many reasons unrelated to safety, such as market position. The election by a drug manufacturer to stop selling an unprofitable but safe drug should have no impact on the ability of pharmacists to compound that drug to fill prescriptions.

Factor 4: The fourth factor requires that pharmacies obtain written assurance from suppliers that each lot of the drug substance has been made in an FDA-registered facility. This paper-trail requirement imposes an additional burden on the pharmacist that is unrelated to whether they are a manufacturer.

Furthermore, it is unclear who the "supplier" is. Does the wholesaler or importer of a bulk ingredient qualify as the supplier? Must the certification come from the manufacturer of the ingredient even though the pharmacist is very unlikely to have contact with that entity? After all, pharmacists rarely have contact directly with manufacturers. What should a pharmacy do if the manufacturer is not identified? Returning a drug that a pharmacy has received for lack of this piece of information will mean that prescriptions will go unfilled. That surely is not in the best interest of patients. IACP therefore recommends that if this factor is retained, pharmacists should be able to satisfy this requirement through receiving from their immediate supplier any documentation that accompanies the drug, such as a statement on a Certificate of Analysis that the ingredient was manufactured in an FDA-registered facility.

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[14] This discussion, though, underscores how the CPG has muddled safety issues with delineating compounding from manufacturing.

The FDCA and FDA require that manufacturers register.[15] Pharmacists who compound should not be asked to serve as tools for enforcing this requirement directed at manufacturers.

Additionally, the terminology in factor four, "without first obtaining," is problematic. This phraseology could be interpreted to require pharmacists to receive written assurance prior to the receipt of a drug product. This interpretation would result in detrimental delays in providing patients with access to crucial medications. If the documentation required by factor four is maintained, the word "first" or the words "receiving" and "storing" should be removed to prevent excessive delays in drug delivery.

Factor 5: The fifth factor, prohibiting the "receiving, storing, or using drug components not guaranteed or otherwise determined to meet official compendia requirements," should be deleted as unrelated to the nominal purpose of the CPG. If retained, it needs to be clarified. FDA should explicitly state that this refers solely to active pharmaceutical ingredients that have USP monographs.

IACP agrees that it is generally better for pharmacists to use USP grade ingredients, when a USP monograph exists. In many cases, though, there are no monographs. Some older drugs were never subjects of monographs. Some newer drugs will eventually be covered by monographs, but it can take a long time for monographs to be written. Neither situation is a reason to preclude filling prescriptions that call for use of that compounded drug. This is more of a safety issue that is better addressed by the State Boards of Pharmacy, USP, and NABP. It is not a question of whether a pharmacy is engaged in manufacturing.

In any event, pharmacists should be able to rely on the designation of USP on an ingredient label. The labeled designation should suffice as the "guarantee," without need for anything more. If a company represents a drug as meeting USP standards but it does not, FDA has ample authority to proceed against the supplier.[16] This is a regulation matter to be addressed with manufacturers of ingredients, not pharmacists.

Factor 6: The sixth factor addresses the use of "commercial scale manufacturing or testing equipment for compounding drug products." IACP is concerned with any limitation on testing equipment. Pharmacists should not be deterred from using even highly sophisticated testing equipment that enhances product quality. The FDA has no reason to restrict testing of products to ensure quality and safety. IACP recommends removing <u>any</u> reference to testing equipment.

The restriction on commercial scale equipment is also a source of concern. The CPG provides no bright line test to determine whether a particular piece of equipment is of "commercial scale." Some pharmaceutical manufacturers make small quantities of certain drug products (<u>e.g.,</u>

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15 FDCA § 510(b); 21 U.S.C. § 360(b).

16 <u>See, e.g.</u>, FDCA § 501(b); 21 U.S.C. § 351(b).

orphan drugs). There may be some overlap in scale or quantity in equipment that a manufacturer possesses and the equipment that a compounding pharmacist who receives numerous prescriptions might need to operate his or her business effectively. IACP recommends that the FDA remove this language in the CPG. Section 503A did not contain this provision. If FDA retains this factor, FDA should include examples of equipment that it considers to be of commercial scale or provide an explanation of how the agency will determine whether a piece of equipment is of "commercial scale."

Also, FDA should never use sophistication of equipment as a surrogate endpoint for whether a pharmacy is a manufacturer. Pharmacists who use advanced technology will have an enhanced ability to compound properly. More pharmacists are using automated equipment, such as automated mixing and dispensing equipment, to facilitate compounding and increase the quality of compounded drugs. FDA should not confuse scale, which relates to volume and quantity, with sophistication or complexity, which relates to quality.

Factor 7: The seventh factor, "compounding drugs for third parties who resell to individual patients or offering compounded drug products at wholesale to other state licensed persons or commercial entities for resale," is also problematic. IACP agrees with FDA that pharmacies may not sell to wholesalers or distributors for resale, but believes that the current language is overbroad.

Many physicians and institutions request from pharmacists compounded drugs for use in the office or institution that are not commercially available. Many of these drug products – such as most injectable drug products – must be administered in the provider's office. FDA recognized this fact by including cantharidin on the "positive" "List of Drug Substances That May Be Used in Pharmacy Compounding" with the restriction that the drug be administered topically "in the professional office setting only."[17] There is clearly a need for some provision for licensed institution and office use of compounded drugs. Pharmacists, however, cannot ensure that the purchaser will not resell the product once it is dispensed to the purchaser.

IACP recommends that the FDA instead adopt the approach of some State Boards of Pharmacy, which require compounding pharmacists to attach a label to their compounded product which reads "FOR OFFICE USE ONLY" and "NOT FOR RESALE."[18] With the affixing of this label, the pharmacist declares his or her intent that the product is not to be resold to a third party provider. However, pharmacists should not be held accountable for the actions of the purchaser, which is beyond their control.

The CPG should also clarify that it is permissible if a pharmacist dispenses a drug for office use, and the physician then charges his or her patient for that drug (or a hospital charges its patient). A pharmacy should not sell to a hospital or physician with the intention that the hospital

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17 64 Fed. Reg.998, 1002 (Jan. 7, 1999).

18 See, e.g., Ark. Admin. Code 07-02-002(L)(3); 22 Tex. Admin. Code § 291.33(i)(2)(D)(i).

or physician will sell to another entity. The hospital or physician, though, may charge the patient for the drug which it received from the pharmacist and which that hospital or physician then administered or dispensed.

Factor 8: IACP is concerned with the lack of definition of the phrase "commercially available FDA-approved drug product." IACP recommends that FDA clarify this provision using a clause similar to section 503A(b)(2). The definition of a commercially available drug should read: "the term 'essentially a copy of a commercially available drug product' does not include a drug product in which there is a change which produces a significant difference, as determined by the prescribing practitioner, between the compounded drug and the comparable commercially available drug product." Without such a definition, this factor offers no guidance to the pharmacy profession. The definition chosen by Congress was appropriate, and FDA should similarly adopt it.[19]

FDA should also clarify that a product is not commercially available if health care providers cannot obtain the product from the FDA-approved manufacturer. In many instances, pharmacies compound drugs that are in short supply, are temporarily unavailable, or, although they have not been withdrawn for safety reasons, are off the market. If a pharmacist receives prescriptions for copies of FDA-approved drugs, is told by the health care provider that the health care provider is unable to obtain the FDA-approved product through normal chains of commercial distribution, and the pharmacist verifies this status, the pharmacist should be permitted to compound the product. Otherwise, patients will be denied access to necessary medications. Unfortunately, many drug products that have been approved by FDA are in short supply or are temporarily not being produced; compounding by pharmacists can fill these gaps.

Finally, IACP recommends that FDA delete the requirement of "documentation of the medical need for the particular variation of the compound for the particular patient." A prescription from a licensed practitioner for a compounded drug should be sufficient documentation of the medical need. It is inappropriate for FDA to demand more documentation from a licensed practitioner of the medical need of a particular patient. Pharmacists have never been required to receive documentation of medical need beyond the prescription. FDA should not interfere with the practice of pharmacy and disrupt the interaction between physicians and pharmacists by the imposition of this brand new requirement. IACP also believes that requiring physicians to justify the decision to prescribe a particular drug for a patient is utterly without any statutory basis. Physicians are free to prescribe off-label uses without documentation.[20] They are

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19 Congress' definition did refer to an "identified individual patient." This language could have been construed as precluding compounding for office use. IACP endorses FDA's recognition in the CPG that there should be no prohibition against compounding for office use.

20 21 C.F.R. § 312.2(d).

equally free to prescribe compounded medication without written explanations.[21] (This is a state board of pharmacy/state medical issue.)

Factor 9: The ninth factor of the CPG relates to whether pharmacists "fail[] to operate in conformance with applicable state laws regulating the practice of pharmacy." While IACP agrees that pharmacists must act in conformance with applicable pharmacy laws, FDA should clarify that this factor relates to those aspects of state pharmacy law that indicate whether the pharmacy is acting as a manufacturer. State boards of pharmacy impose numerous requirements on pharmacies, such as the need to pay its registration fee in a timely manner,[22] establishing a pharmacist to pharmacy technician ratio[23] and the need to notify the board of pharmacy of the designated pharmacist-in-charge.[24] There are numerous other requirements of state pharmacy law that have no bearing on whether a pharmacy is acting as a manufacturer. The failure to comply with every single element of a statute or regulation does not mean that a pharmacy is a manufacturer. Thus, if a specific state law violation indicates that a pharmacy is a manufacturer, FDA may appropriately consider it in assessing a pharmacy's status. Otherwise, enforcement should rest solely with the State Boards of Pharmacy.

We appreciate the opportunity to provide the FDA with comments on this issue.

Respectfully submitted,

L.D. King
Executive Director
International Academy of Compounding Pharmacists

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21 This element also creates an extraordinary practical challenge: how to evaluate a physician's rationale. It places FDA in the unprecedented position of second-guessing decisions by doctors, effectively leading FDA to regulate the practice of medicine. See Chaney v. Heckler, 718 F.2d 1174 (D.C. Cir. 1984); rev'd, 470 U.S. 821 (1985) (legislative history of FDCA "expressed a specific intent to prohibit FDA from regulating physicians' practice of medicine"). The prescription should suffice; nothing more is needed.

22 See, e.g., Cal. Bus. & Prof. Code §§ 4400, 4401; Cal. Code Regs. tit. 16 § 1749.

23 See, e.g., Cal. Bus. & Prof. Code § 4115(g); Cal. Code Regs. tit. 16 § 1793.7(f).

24 See, e.g., Cal. Bus. & Prof. Code § 4113(a); Cal. Code Regs. tit. 16 § 1709.

ATTACHMENT E

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Of Counsel: ALLEN D. EMMEL*

September 3, 2003

Enforcement Committee
c/o Patricia Harris, Executive Officer
California State Board of Pharmacy
400 R. Street, Suite 4070
Sacramento CA 95814

Re: Compounding Issues: Labels and Central Fill

Dear Enforcement Committee:

On behalf of several clients and the Compounding Pharmacists Section of the California Pharmacists Association, thank you for putting these issues on the agenda for the next Enforcement Committee Meeting.

1. Labels on Compounded Products.
An issue that has been brought to the attention of several compounding pharmacists involves the appropriate content of labels of compounded products. There is widespread agreement with the Board that current label requirements reflect information that is needed by consumers when they receive compounded products. The problem arises when the compounded product is provided in multiple units of a dosage form – i.e. suppositories, single dose vials, etc. – for which individual product labels are either not feasible, cost prohibitive or even a hindrance to treatment. For instance, many creams are dispensed in application syringes that contain multiple doses of the product. Graduations on the syringes are used to measure the individual dose. Because of their size, placing a label on each syringe would obstruct these graduations, making accurate dosing difficult or impossible.

The question raised is: What, if any, information does the Board feel should be included on individual units of compounded products that are dispensed to patients?

In the opinion of the pharmacists we surveyed, this should be a matter for the individual discretion of the compounding pharmacist. In many cases, individual doses should contain some sort of label to indicate the active ingredients. The form of this label will vary depending on the dispensing unit and available space. In other cases, a label on individual doses will result in little or no benefit and will cause more problems than it solves. In the case of compounded tablets and capsules, identification of any kind on individual doses simply isn't practical.

In any case, the patient should be made aware of the situation and advised to always keep the doses in the box, bag or container in which it was dispensed and which is labeled with the information that may be needed by a family member or emergency personnel in the event of a problem.

To clarify existing law and resolve any conflicts that may arise, we ask that the Board of Pharmacy weigh in on this issue. We welcome the opportunity to participate in a dialog to reach a reasonable and agreeable guideline for labels on compounded products.

2. Compounding in Central Fill Pharmacies

Many pharmacists and pharmacies are specializing in compounded products. The value of these products is broadly recognized. The Board's recent activities with regard to compounding of sterile injectable products has provided needed focus on the systems and facilities needed for the safe compounding of sterile injectables.

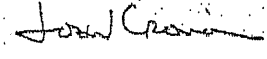
For a large number of compounded products, similar, if less stringent, systems and facilities are needed for the preparation of products to assure consistency in preparation and potency. Pharmacies that specialize in this practice have invested in those systems and facilities and, as evidenced by the growth in this area of practice, the products they compound are accepted as effective and safe.

We believe consumers should have improved access to compounded products. A safe and cost-effective way to accomplish this is to allow compounding pharmacies to act as central fill pharmacies for compounded products in the same way as is allowed for other prescriptions under CCR 1707.4. The Board has authorized similar activity for parenteral products for many years (cf B&P sec. 4123). We believe allowing central filling of compounded products under the provisions of 1707.4 will improve access for consumers, reduce costs and result in the provision of more consistent, safer and more effective compounded products.

We ask the Board to move forward on this proposal and are willing to work with the Board to resolve any problems that stand in the way of this application of section 1707.4.

I look forward to discussing these proposals further at the upcoming Enforcement Committee meeting.

Sincerely,



John Cronin, Pharm.D., J.D.

ATTACHMENT F

(b) Drugs purchased pursuant to Section 256b of Title 42 of the United States Code and received by a pharmacy shall be segregated from the pharmacy's other drug stock by either physical or electronic means. All records of acquisition and disposition of these drugs shall be readily retrievable in a form separate from the pharmacy's other records.
(c) Drugs obtained by a pharmacy to be dispensed to patients of a covered entity pursuant to Section 256b of Title 42 of the United States Code that cannot be distributed because of a change in circumstances for the covered entity or the pharmacy shall be returned to the distributor from which they were obtained. For the purposes of this section, a change in circumstances includes, but is not limited to, the termination or expiration of the contract between the pharmacy and the covered entity, the closure of a pharmacy, disciplinary action against the pharmacy, or closure of the covered entity.
(d) A licensee that participates in a contract to dispense preferentially priced drugs pursuant to this section shall not have both a pharmacy and a wholesaler license.
(e) Neither a covered entity nor a pharmacy shall be required to obtain a license as a wholesaler based on acts reasonably necessary to fully participate in the drug purchase program established by Section 256b of Title 42 of the United States Code.

Article 7.5 – Injectable Sterile Drug Products

4127. The board shall adopt regulations establishing standards for compounding injectable sterile drug products in a pharmacy.

4127.1. (a) A pharmacy shall not compound injectable sterile drug products in this state unless the pharmacy has obtained a license from the board pursuant to this section. The license shall be renewed annually and is not transferable.
(b) A license to compound injectable sterile drug products may only be issued for a location that is licensed as a pharmacy. Furthermore, the license to compound injectable sterile drug products may only be issued to the owner of the pharmacy license at that location. A license to compound injectable sterile drug products may not be issued until the location is inspected by the board and found in compliance with this article and regulations adopted by the board.
(c) A license to compound injectable sterile drug products may not be renewed until the location has been inspected by the board and found to be in compliance with this article and regulations adopted by the board.
(d) Pharmacies operated by entities that are licensed by either the board or the State Department of Health Services and that have current accreditation from the Joint Commission on Accreditation of Healthcare Organizations, or other private accreditation agencies approved by the board, are exempt from the requirement to obtain a license pursuant to this section.
(e) The reconstitution of a sterile powder shall not require a license pursuant to this section if both of the following are met:
(1) The sterile powder was obtained from a manufacturer.
(2) The drug is reconstituted for administration to patients by a health care professional licensed to administer drugs by injection pursuant to this division.
(f) This section shall become effective on the earlier of July 1, 2003, or the effective date of regulations adopted by the board pursuant to Section 4127.

4127.2. (a) A nonresident pharmacy may not compound injectable sterile drug products for shipment into the State of California without a license issued by the board pursuant to this section. The license shall be renewed annually and shall not be transferable.
(b) A license to compound injectable sterile drug products may only be issued for a location that is licensed as a nonresident pharmacy. Furthermore, the license to compound injectable sterile drug products may only be issued to the owner of the nonresident pharmacy license at that location. A license to compound injectable sterile drug products may not be issued or renewed until the board receives the following from the nonresident pharmacy:
(1) A copy of an inspection report issued by the pharmacy's licensing agency, or a report from a private accrediting agency approved by the board, in the prior 12 months documenting the pharmacy's compliance with board regulations regarding the compounding of injectable sterile drug products.
(2) A copy of the nonresident pharmacy's proposed policies and procedures for sterile compounding.
(c) Nonresident pharmacies operated by entities that are licensed as a hospital, home health agency, or a skilled nursing facility and have current accreditation from the Joint Commission on Accreditation of Healthcare Organizations, or other private accreditation agencies approved by the board, are exempt from the requirement to obtain a license pursuant to this section.
(d) This section shall become effective on the earlier of July 1, 2003, or the effective date of regulations adopted by the board pursuant to Section 4127.

4127.3. (a) Whenever the board has a reasonable belief, based on information obtained during an inspection or investigation by the board, that a pharmacy compounding injectable sterile drug products poses an immediate threat to the

public health or safety, the executive officer of the board may issue an order to the pharmacy to immediately cease and desist from compounding injectable sterile drug products. The cease and desist order shall remain in effect for no more than 30 days or the date of a hearing seeking an interim suspension order, whichever is earlier.
(b) Whenever the board issues a cease and desist order pursuant to subdivision (a), the board shall immediately issue the owner a notice setting forth the acts or omissions with which the owner is charged, specifying the pertinent code section or sections.
(c) The order shall provide that the owner, within 15 days of receipt of the notice, may request a hearing before the president of the board to contest the cease and desist order. Consideration of the owner's contest of the cease and desist order shall comply with the requirements of Section 11425.10 of the Government Code. The hearing shall be held no later than five days from the date the request of the owner is received by the board. The president shall render a written decision within five days of the hearing. In the absence of the president of the board, the vice president of the board may conduct the hearing permitted by this subdivision. Review of the decision of the president of the board may be sought by the owner or person in possession or control of the pharmacy pursuant to Section 1094.5 of the Code of Civil Procedure.
(d) Failure to comply with a cease and desist order issued pursuant to this section shall be unprofessional conduct.

4127.4. Notwithstanding any other provision of law, a violation of this article, or regulations adopted pursuant thereto, may subject the person or entity that committed the violation to a fine of up to two thousand five hundred dollars ($2,500) per occurrence pursuant to a citation issued by the board.

4127.5. The fee for the issuance of a license, or renewal of a license, to compound sterile drug products shall be five hundred dollars ($500) and may be increased to six hundred dollars ($600).

4127.6. This article shall become operative upon the allocation of positions to the board for the implementation of the provisions of this article in the annual Budget Act.

Article 9 – Hypodermic Needles and Syringes

4140. No person shall possess or have under his or her control any hypodermic needle or syringe except when acquired in accordance with this article.

4141. No person shall furnish hypodermic needles or syringes, by sale or otherwise, without a license issued by the board, except as otherwise provided by this article.

4142. Except as otherwise provided by this article, no hypodermic needle or syringe shall be sold at retail except upon the prescription of a physician, dentist, veterinarian, or podiatrist.

4143. This article shall not apply to the sale of hypodermic syringes and needles at wholesale by pharmacies, drug wholesalers, drug manufacturers or manufacturers and dealers in surgical instruments to pharmacies, physicians, dentists, podiatrists, veterinarians, or persons to whom a license has been issued under this article.

4144. A person may sell or obtain hypodermic needles and hypodermic syringes without a prescription or permit, for uses that the board determines are industrial, and that person shall not be required to comply with Section 4145 or 4146.

4145. Notwithstanding any other provision of law, a pharmacist or physician may, without a prescription or a permit, furnish hypodermic needles and syringes for human use in the administration of insulin or adrenaline; a pharmacist or veterinarian may, without a prescription or license, furnish hypodermic needles and syringes for use on poultry or animals; and a person may, without a prescription or license, obtain hypodermic needles and syringes from a pharmacist or physician for human use in the administration of insulin or adrenaline, or from a pharmacist, veterinarian, or licenseholder, for use on poultry or animals; if all of the following requirements are met:
(a) No needle or syringe shall be furnished to a person who is unknown to the furnisher and unable to properly establish his or her identity.
(b) The furnisher, at the time furnishing occurs, makes a record of the furnishing in the manner required by Section 4146.

4146. Any furnishing of a hypodermic syringe or hypodermic needle without a prescription shall, at the time of furnishing, be recorded in a book by the furnisher. The record of furnishing shall consist of the date and hour of the furnishing, the type or kind, size, and quantity of syringe or needle furnished, the purpose and use for which the needle or syringe was obtained, the signature of the furnisher, and the signature and address of the person to whom the needle or syringe was furnished. The record book shall be available for inspection by any authorized officer of the law.

(a) For each prescription for a Schedule II controlled substance, the dispensing pharmacy shall provide the following information: the full name and address of the patient; the gender and date of birth of the patient; the DEA (Drug Enforcement Administration) number of the prescriber; the triplicate prescription number; the pharmacy prescription number; the pharmacy license number; the NDC (National Drug Code) number and the quantity of the controlled substance; the ICD-9 (diagnosis code), if available; the date of issue of the prescription, the date of dispensing of the prescription, and the state medical license number of any prescriber using the DEA number of a government exempt facility.

(b) The above information shall be provided in the following format:

(1) For each pharmacy with the capacity to do so, by on-line transmission at least every 30 days and no later than the 18th calendar day of the month following the month in which the prescription is dispensed.

(2) For each pharmacy which does not have the capacity to transmit the information on-line, on a three and one-half inch diskette in a ASCII format or one-half inch nine track magnetic 1600 BPI tape or any other medium approved by the Board of Pharmacy, which diskette, tape or medium shall be mailed or delivered to a location specified by The Board of Pharmacy, at least every 30 days and no later than the 18th calendar day of the month following the month in which the prescription is dispensed.

(3) For each pharmacy without the capacity to comply with either subsection (b)(1) or (2), the original triplicate shall be transmitted to the Department of Justice by the end of the month in which the prescription was filled.

For each pharmacy which submits hard copy pursuant to this subdivision and which pharmacy averages more than 25 triplicate prescriptions per month in any six months, the Board of Pharmacy or its designee may thereafter require that pharmacy to comply with subsections (b)(1) and (2).

(4) As to a prescription which is partially filled or dispensed, the period for compliance with subsections (1), (2), or (3) shall be measured from the earlier of the following dates and times: the prescription is either (1) completely dispensed or (2) can no longer be dispensed.

(c) Every pharmacy which has made a submission as required by this section by July 18, 1998, shall receive a reduction of $75 on its next renewal fee for licensure of the pharmacy by the board. Every pharmacy shall be in compliance with this section and Health and Safety Code section 11165 by September 18, 1998.

Authority cited: Sections 4005, Business and Professions Code. Reference: Sections 11164 and 11165, Health and Safety Code.

§1715.6. Reporting Drug Loss.

The owner shall report to the Board within thirty (30) days of discovery of any loss of the controlled substances, including their amounts and strengths.

Authority cited: Section 4005, Business and Professions Code. Reference: Sections 4081 and 4332, Business and Professions Code.

§1716. Variation from Prescriptions.

Pharmacists shall not deviate from the requirements of a prescription except upon the prior consent of the prescriber or to select the drug product in accordance with Section~~.6~~ 4073 of the Business and Professions Code.

Nothing in this regulation is intended to prohibit a pharmacist from exercising commonly-accepted pharmaceutical practice in the compounding or dispensing of a prescription.

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4040, Business and Professions Code.

§1716.1. Compounding Unapproved Drugs for Prescriber Office Use.

As used in Business and Professions Code Section 4052(a)(1), the following terms have the indicated meaning concerning the compounding of unapproved drugs for prescriber office use:

(a) "Reasonable quantity" means that quantity of an unapproved drug which:

(1) is sufficient for that prescriber's office use consistent with the expiration date of the product as set forth in section 1716.2(a)(3); and

(2) is reasonable considering the intended use of the compounded medication and nature of the prescriber's practice; and

(3) for any individual prescriber and for all prescribers taken as a whole, is an amount which the pharmacy is capable of compounding in compliance with pharmaceutical standards for identity, strength, quality and purity of the compounded medication.

(b) "Compounded medication" means medications actually compounded by the pharmacy supplying them to a prescriber.

(c) "Prescriber office use" means application or administration in the prescriber's office, or for distribution of not more than a 72-hour supply to the prescriber's patients as estimated by the prescriber.

Authority cited: Section 4005, Business and Professions Code. Reference: Sections 4027, 4033, 4050, 4051, 4052, 4059, 4170 and 4171, Business and Professions Code.

§1716.2. Record Requirements--Compounding for Future Furnishing.

(a) For the purpose of compounding in quantities larger than required for immediate dispensing by a prescriber or for future dispensing upon prescription, a pharmacy shall maintain records that include, but are not limited to:

(1) The date of preparation.

(2) The lot numbers. These may be the manufacturer's lot numbers or new numbers assigned by the pharmacy. If the lot number is assigned by the pharmacy, the pharmacy must also record the original manufacturer's lot numbers and expiration dates, if known. If the original manufacturer's lot numbers and expiration dates are not known, the pharmacy shall record the source and acquisition date of the components.

(3) The expiration date of the finished product. This date must not exceed 180 days or the shortest expiration date of any component in the finished product unless a longer date is supported by stability studies in the same type of packaging as furnished to the prescriber. Shorter dating than set forth in this subsection may be used if it is deemed appropriate in the professional judgment of the responsible pharmacist.

(4) The signature or initials of the pharmacist performing the compounding.

(5) A formula for the compounded product. The formula must be maintained in a readily retrievable form.

(6) The name(s) of the manufacturer(s) of the raw materials.

(7) The quantity in units of finished products or grams of raw materials.

(8) The package size and the number of units prepared.

Authority cited: Section 4005, Business and Professions Code. Reference: Sections 4005, 4051, 4059, 4081 and 4332, Business and Professions Code.

§1717. Pharmaceutical Practice.

(a) No medication shall be dispensed on prescription except in a new container which conforms with standards established in the official compendia.

Notwithstanding the above, a pharmacist may dispense and refill a prescription for non-liquid oral products in a clean multiple-drug patient medication package (patient med pak), provided:

(1) a patient med pak is reused only for the same patient;

(2) no more than a one-month supply is dispensed at one time; and

(3) each patient med pak bears an auxiliary label which reads, "store in a cool, dry place."

(b) In addition to the requirements of Section 4036, Business and Professions Code, the following information shall be maintained for each prescription on file and shall be readily retrievable:

(1) The date dispensed, and the name or initials of the dispensing pharmacist. All prescriptions filled or refilled by an intern pharmacist must also be initialed by the preceptor before they are dispensed.

(2) The brand name of the drug or device; or if a generic drug or device is dispensed, the distributor's name which appears on the commercial package label; and

(3) If a prescription for a drug or device is refilled, a record of each refill, quantity dispensed, if different, and the initials or name of the dispensing pharmacist.

(4) A new prescription must be created if there is a change in the drug, strength, prescriber or directions for use, unless a complete record of all such changes is otherwise maintained.

(c) Promptly upon receipt of an orally transmitted prescription, the pharmacist shall reduce it to writing, and initial it, and identify it as an orally transmitted prescription. If the prescription is then dispensed by another pharmacist, the dispensing pharmacist shall also initial the prescription to identify him or herself. All orally transmitted prescriptions shall be received and transcribed by a pharmacist prior to compounding, filling, dispensing, or furnishing.

Chart orders as defined in Section 4019 of the Business and Professions Code are not subject to the provisions of this subsection.

Board of Pharmacy
Proposed Revisions to Title 16 CCR 1751 et seq.

Article 7. Sterile Injectable Compounding

Amend Section 1751. Sterile Injectable Compounding Area ~~for Parenteral Solutions~~

(a) The pharmacy shall have a designated area for the preparation of sterile injectable products ~~for dispensing~~ which shall meet the following standards:

~~a.~~ (1) Clean Room and Work Station Requirements, shall be in accordance with Section ~~490A.7.1~~ 490A.3.1 of Title 24 of the California Code of Regulations.

~~b.~~ (2) Walls, ceilings, and floors shall ~~be~~ have cleanable, nonporous surfaces and be constructed in accordance with Section 490A.7.2 of Title 24 of the California Code of Regulations.

~~c.~~ (3) Be ventilated in a manner in accordance with Section ~~505.11~~ 505.12 of Title 24 of the California Code of Regulations.

~~d.~~ (4) Be certified annually by a qualified technician who is familiar with the methods and procedures for certifying laminar air flow hoods and clean room requirements, in accordance with standards adopted by the ~~Federal Standard 209(b), Clean Room and Work Station Requirements, Controlled Environment, as approved by the Commission, Federal Supply Service~~, United States General Services Administration. ~~, as amended May 30, 1976 (available from the U.S. General Services Administration, Specifications Activity, Printed Materials Supply Division, Building 197, Naval Weapons Plant,Washington,D.C. 20407).~~ Certification records must be retained for at least 3 years.

~~e.~~ (5) The pharmacy shall be arranged in accordance with Section ~~490A.7.3~~ 490A.3 of Title 24 of the California Code of Regulations. Items related to the compounding of sterile injectable products ~~parenteral solutions~~ within the compounding area ~~may not be stored in corrugated cardboard boxes and~~ shall be stored in such a way as to maintain the integrity of an aseptic environment.

~~f.~~ (6) A sink with hot and cold running water shall be in accordance in Section ~~490A.7.4~~ 490A.3.4 of Title 24 of the California Code of Regulations.

~~g.~~ (7) There shall be a refrigerator and/or freezer of sufficient capacity to meet the storage requirements for all material requiring refrigeration.

NOTE
Authority cited: Section 4005, Business and Professions Code.
Reference: Section 4005, Business and Professions Code; and Section 18944(a), Health and Safety Code.

Add Section 1751.01 Facility and Equipment Standards for Sterile Injectable Compounding from Non-Sterile Ingredients

(a) On and after January 1, 2005 this subdivision shall apply to any pharmacy compounding sterile injectable products from one or more non-sterile ingredients. The aseptic processing of such products shall occur in one of the following environments:

(1) A class 100 laminar airflow hood within a class 10,000 cleanroom. The cleanroom must have a positive air pressure differential relative to adjacent areas.

(2) A class 100 cleanroom. The cleanroom must have a positive air pressure differential relative to adjacent areas.

(3) A barrier isolator that provides a class 100 environment for compounding.

(b) No sterile injectable product shall be prepared if it is known, or reasonably should be known, that the compounding environment fails to meet criteria specified in the pharmacy's written policies and procedures for the safe compounding of sterile injectable drug products.

(c) During the preparation of sterile injectable products, access to the designated area or cleanroom must be limited to those individuals who are properly attired.

(d) All equipment used in the designated area or cleanroom must be made of a material that can be easily cleaned and disinfected.

(e) Exterior workbench surfaces and other hard surfaces in the designated area, such as walls, floors, ceilings, shelves, tables, and stools, must be disinfected weekly and after any unanticipated event that could increase the risk of contamination.

NOTE

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code; and Section 18944(a), Health and Safety Code.

Add Section 1751.02. Policies and Procedures

(a) Written policies and procedures associated with the pharmacy's preparation and dispensing of sterile injectable products shall include, but not be limited to:

(1) Compounding, filling, and labeling of sterile injectable compounds..

(2) Labeling of the sterile injectable product based on the intended route of administration and recommended rate of administration.

(3) Equipment and supplies.

(4) Training of staff in the preparation of sterile injectable products.

(5) Procedures for handling cytotoxic agents.

(6) Quality assurance program.

(7) Record keeping requirements.

(b) The ingredients and the compounding process for each preparation must be determined in writing before compounding begins and must be reviewed by a pharmacist.

(c) Pharmacies compounding sterile injectable products from one or more non-sterile ingredients must have written policies and procedures that comply with the following:

(1) Immediately available to all personnel involved in these activities and board inspectors.

(2) All personnel involved must read the policies and procedures before compounding sterile injectable products, and any additions, revisions, and deletions to the written policies and procedures must be communicated to all personnel involved in sterile compounding.

(3) Policies and procedures must address at least the following:

(A) Competency evaluation.

(B) Storage and handling of products and supplies.

(C) Storage and delivery of final products.

(D) Process validation.

(E) Personnel access and movement of materials into and near the controlled area.

(F) Use and maintenance of environmental control devices used to create the critical area for manipulation of sterile products (e.g., laminar-airflow

workstations, biological safety cabinets, class 100 cleanrooms, and barrier isolator workstations).
(G) Regular cleaning schedule for the controlled area and any equipment in the controlled area and the alternation of disinfectants. Pharmacies subject to an institutional infection control policy may follow that policy as it relates to cleaning schedules and the alternation of disinfectants in lieu of complying with this subdivision.
(H) Disposal of packaging materials, used syringes, containers, and needles to enhance sanitation and avoid accumulation in the controlled area.
(I) For sterile batch compounding, written policies and procedures must be established for the use of master formulas and work sheets and for appropriate documentation.
(J) Sterilization.
(K) End-product evaluation and testing.

NOTE

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code.

Amend Section 1751.2. Labeling Requirements

In addition to existing labeling requirements, a pharmacy which compounds sterile ~~parenteral~~ injectable products shall include the following information on the labels for those products:
a. Telephone number of the pharmacy, except for sterile injectable products dispensed for inpatients of a hospital pharmacy.
b. Name and concentrations of ~~all~~ ingredients contained in the sterile injectable ~~parenteral~~ product ~~including primary solution~~.
c. Instructions for storage and handling.
d. All cytotoxic agents shall bear a special label which states "Chemotherapy-Dispose of Properly."

NOTE
Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code.

Amend Section 1751.3. Record keeping Requirements

(a) In addition to the medication profile required by section 1707.1, pharmacies ~~Pharmacies~~ which ~~both~~ compound sterile injectable products ~~parenteral solutions and dispense those solutions~~ shall have ~~on the premises or readily accessible~~ an immediately retrievable patient profile ~~record~~ for each patient being treated with compounded sterile injectable products ~~with parenteral therapy~~. ~~In addition to existing record keeping requirements, the~~ The following records shall be maintained when dispensing compounded sterile injectable products:

~~(a) Records of furnishing of all prescriptions and medical supplies;~~

~~(b)~~ (1) Information relevant to the patient's ~~parenteral~~ sterile injectable drug therapy shall include but not be limited to:

~~(1)~~ (A) Patient's body weight.

~~(2)~~ (B) Primary diagnosis related to need for prescribed therapy; secondary diagnosis if available.

~~(3)~~ (C) Summary of most recent hospitalization and/or previous history related to the diagnosis for which the sterile injectable drug is prescribed.

~~(4) Medication history, including current diet/medication regimen and drug/food allergies.~~

~~(c)~~ (2) Progress notes documenting pharmacist contact with the patient or physician relative to compounded sterile injectable drug ~~parenteral~~ therapy.

~~(d)~~ (3) Laboratory data relevant to the pharmacist's management of the patient's treatment with compounded sterile injectable drug ~~parenteral~~ therapy.

(b) Pharmacies compounding sterile injectable products for future use pursuant to section 1716.1 shall, in addition to those records required by section 1716.2, have records indicating the name, lot number, amount, and date on which the products were provided to a prescriber.

(c) In addition to the records required by subdivisions (a) and (b), for sterile products compounded from one or more non-sterile ingredients the following records must be maintained for at least three years:

(1) The training and competency evaluation of employees in sterile product procedures.

(2) Refrigerator and freezer temperatures.

(3) Certification of the sterile compounding environment.

(4) Other facility quality control logs specific to the pharmacy's policies and procedures (e.g., cleaning logs for facilities and equipment).

(5) Inspection for expired or recalled pharmaceutical products or raw ingredients.

(6) Preparation records including the master work sheet, the preparation work sheet, and records of end-product evaluation results.

NOTE

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code.

Amend Section 1751.4. ~~Protective Clothing~~ Attire

(a) When preparing cytotoxic agents, gowns and gloves shall be worn.

(b) When compounding sterile products from one or more non-sterile ingredients the following standards must be met:

(1) Cleanroom garb consisting of a low-shedding coverall, head cover, face mask, and shoe covers must be worn inside the designated area at all times.

(2) Cleanroom garb must be donned and removed outside the designated area.

(3) Hand, finger, and wrist jewelry must be eliminated. If jewelry cannot be removed then it must be thoroughly cleaned and covered with a sterile glove.

(4) Head and facial hair must be kept out of the critical area or be covered.

(5) Gloves made of low-shedding materials are required.

(c) The requirements of this subdivision do not apply if a barrier isolator is used to compound sterile injectable products from one or more non-sterile ingredients.

NOTE

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code.

Amend Section 1751.5. Training of Staff, Patient, and Caregiver

(a) Consultation shall be available to the patient and/or primary caregiver concerning proper use of ~~parenterals~~ sterile injectable products and related supplies furnished by the pharmacy.
(b) The pharmacist in charge shall be responsible to ensure all pharmacy personnel engaging in compounding sterile injectable drug products ~~parenteral solutions~~ shall have training and demonstrated competence in the safe handling and compounding of sterile injectable products,~~parenteral solutions~~ including cytotoxic agents if the pharmacy compounds products with cytotoxic agents.
(c) Records of training and demonstrated competence shall be available for each individual and shall be retained for three years beyond the period of employment.
(d) The pharmacist-in-charge shall be responsible to ~~insure~~ ensure the continuing competence of pharmacy personnel engaged in compounding sterile injectable products ~~parenteral solutions~~.
(e) Pharmacies that compound sterile products from one or more non-sterile ingredients must comply with the following training requirements:

1) The pharmacy must establish and follow a written program of training and performance evaluation designed to ensure that each person working in the designated area has the knowledge and skills necessary to perform their assigned tasks properly. This program of training and performance evaluation must address at least the following:

(A) Aseptic technique.
(B) Pharmaceutical calculations and terminology.
(C) Sterile product compounding documentation.
(D) Quality assurance procedures.
(E) Aseptic preparation procedures.
(F) Proper gowning and gloving technique.
(G) General conduct in the controlled area.
(H) Cleaning, sanitizing, and maintaining equipment used in the controlled area.
(I) Sterilization techniques.
(J) Container, equipment, and closure system selection.

(2) Each person assigned to the controlled area must successfully complete practical skills training in aseptic technique and aseptic area practices. Evaluation must include written testing and a written protocol of periodic routine performance checks involving adherence to aseptic area policies and procedures. Each person's proficiency and continuing training needs must be reassessed every 12 months. Results of these assessments must be documented and retained in the pharmacy for three years.

NOTE

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code.

Amend Section 1751.6. Disposal of Waste Material

Pharmacies ~~providing parenteral services~~ compounding sterile injectable products shall have written policies and procedures for the disposal of infectious materials and/or materials containing cytotoxic residues. The procedures shall include cleanup of spills and shall be in conformance with local health jurisdiction. ~~The pharmacy shall ensure the return of such materials or shall communicate the proper destruction of such materials to the caregiver.~~

NOTE

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code.

Amend Section 1751.7. Quality Assurance and Process Validation

(a) There shall be 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:

~~a.~~ (1) Cleaning and sanitization of the parenteral medication preparation area.

~~b.~~ (2) Written documentation that the end product has been tested on a periodic sampling basis for microbial contamination and steps taken in the event that testing for contamination proves positive.

~~c. If manufacturing of parenteral products is performed using nonsterile chemicals, extensive end product testing must be documented prior to the release of product from quarantine. This process must include testing for sterility and pyrogens.~~

~~d.~~ (3) The storage of compounded parenteral products in the pharmacy and periodic documentation of refrigerator temperature.

~~e.~~ (4) Steps to be taken in the event of a drug recall.

~~f.~~ (5) Written justification of the chosen expiration dates for compounded parenteral products.

(b) Each individual involved in the preparation of sterile injectable products from one or more non-sterile ingredients must successfully complete a validation process before being allowed to prepare sterile products. The validation process shall be carried out in the same manner as normal production, except that an appropriate microbiological growth medium is used to test the sterility of a final product. The same personnel, procedures, equipment, and materials are 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, or whenever improper aseptic techniques are observed. Revalidation must be documented.

NOTE

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code.

Repeal Section 1751.8. Policies and Procedures

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code.

Amend Section 1751.9. Reference Materials

There shall be current and appropriate reference materials regarding the compounding of sterile injectable products located in or immediately available to the pharmacy.

~~Such references shall include information on:~~

~~a. The drugs and chemicals used in parenteral therapy services and~~

~~b. All parenteral therapy, manufacturing, dispensing, distribution, and counseling services provided.~~

NOTE

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code.

ATTACHMENT G

Board Guidelines for Distinguishing Compounding from Manufacturing

The following information was adopted as guidelines by the board in 1994. It was developed by a committee composed of individuals from the Board of Pharmacy, Department of Health Services, Food and Drug Administration, and pharmacy practitioners from throughout the state.

Many licensees of the board have asked for guidance from the board as to when product preparation by a pharmacy will be considered to be manufacturing.

At the outset it should be understood that all compounding by a pharmacy is considered manufacturing by the federal Food and Drug Administration (FDA) and the California Department of Health Services (DHS). DHS licenses and FDA registers or licenses businesses engaged in certain compounding activities.

Under current federal (21 United States Code (U.S.C.) §§ 301 et seq.) and state law (Health and Safety Code §§26000 et seq.) any manipulation of a drug product or component which alters its original state, including repackaging or relabeling, constitutes manufacturing, including what has been traditionally considered pharmacy compounding (21 Code of Federal Regulations (C.F.R.) § 207.3(a)(8): Health and Safety Code §26019). All pharmacies must comply with those laws. As noted above, federal and state food and drug laws, as well as California's Pharmacy Law, do recognize compounding as a proper function of pharmacy practice and exempt pharmacies engaged in legitimate compounding from licensure or registration as manufacturers; however, even where the pharmacy need not be registered or licensed, the pharmacy must still comply with federal and state requirements for the preparation, packaging, repackaging, safety, efficacy, labelling and use of drugs.

The Board of Pharmacy has jurisdiction over anyone who handles or prepares a dangerous drug, whether for sale, retail or otherwise, in this state. The board licenses wholesalers and pharmacies, both in-state and out-of-state, which ship or retail dangerous drugs within or into this state.

The FDA and DHS have and retain authority over manufacturing, including compounding, even by those exempt from licensure and registration, but, in the exercise of their discretion, both the FDA and DHS have chosen to target that pharmacy compounding which is outside the bounds of traditional pharmacy practice and leave day-to-day regulation of traditional pharmacy practices to state boards of pharmacy.

As to what a pharmacy or pharmacist may do and still be within the practice of pharmacy, the Board of Pharmacy believes that, in addition to any other act authorized by the Pharmacy Law (Business and Professions Code sections 4000 et seq.) and board regulations (commencing with section 1700 of the California Code of Regulations), a pharmacist may;

1. compound:
   a. pursuant to a prescription or chart order, for a dangerous drug or an over the counter product; or
   b. in a reasonable quantity in anticipation of prescriptions based upon existing practitioner, patient and pharmacist relationships; or
   c. products for prescriber office use, pursuant to Business and Professions Code section 4046 (c)(1) and sections 1716.1 and 1761.2 of the California Code of Regulations and related statutes and regulations.
2. in anticipation of prescriptions, repackage a reasonable quantity of dangerous drugs from bulk to unit of use for dispensing and retail sale to consumers
3. reconstitute a finished pharmaceutical pursuant to approved labeling. The board believes a proper definition of pharmacy compounding is:

> the preparing, mixing or assembling of a dangerous drug or device by a pharmacy

From July 7, 1993, until January 5, 1995, a committee of the board has examined the issue of when what a pharmacy calls compounding may actually be manufacturing beyond the scope of the pharmacy license and has identified factors which are set out below and for which this article provides illustrations and examples. These factors and the statements in this article reflect the official position of the Board of Pharmacy.

The issue arises when a pharmacy considers what it is doing to be within the compounding exception permitted by a pharmacy license, and either a regulatory agency takes the position it is really not exempt or the pharmacy is concerned the agency might think so (if the activity is not subject to the exemption from registration or licensure, it would require registration or licensure as a drug manufacturer).

Each licensee should understand the following are guidelines only, intended to advise licensees of the kind of factors the board will look to. The presence of any one factor does not necessarily mean the conduct is outside the scope of pharmacy practice; similarly, the absence of any one factor does not necessarily mean the conduct is within the scope of pharmacy practice. Each licensee should also be aware of the authority and interpretations of that authority by the federal Food an Drug Administration and the state Department of Health Services. (For further information of FDA regulations and policy on compounding, you may wish to read FDA Compliance Policy Guide 7132.16 and An Introduction to FDA Drug Regulation: A Manual for Pharmacists [G.P.O. #1990-266-430/20424]).

Certain conduct is per se-that is, absolutely-not within the scope of pharmacy practice and requires a manufacturer's license from the Department of Health Services and registration or licensure by the federal Food and Drug Administration.

Each licensee should be advised that while the board is considering whether any existing laws and regulations need revision, unless or until a law or regulation is revised, it remains in effect and will be enforced by the appropriate agency, including the Board of Pharmacy, the Department of Health

*See **Compounding**, Page 17*

Be Alert to Large Orders for OTCs Used in Methamphetamine Production

The Drug Enforcement Administration and the state's Bureau of Narcotics Enforcement have become concerned with the increasing use of ephedrine, pseudoephedrine, and phenylpropanolamine for illicit laboratory production of methamphetamine and methcathinone.

These agencies advise that pharmacies receiving requests for large or bulk quantities of these products in OTC capsule or tablet form should question the intent of such orders. Additionally, if there appears to be noticeable interest in or unusually active sales of these products, pharmacists should keep ephedrine, pseudoephedrine (especially the 60mg strength having minimal binders), and phenylpropanolamine behind the pharmacy counter.

Compounding

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Services, and the federal Food and Drug Administration.

Factors to Be Considered by Board of Pharmacy Inspectors

The following factors will be considered by the board inspectors as suggesting that a pharmacy which claims to be compounding is actually engaged in manufacturing which is beyond the scope of its pharmacy permit:

1. A professional relationship does not exist among the prescriber, patient and pharmacist who compounds and dispenses the drug product.

2. The pharmacy solicits or advertises for business from any practitioner or other entity for specific products which the pharmacy compounds.

3. The pharmacy is compounding products which are essentially generic copies of FDA approved products which are commercially available.

4. The pharmacy is receiving and using drug substances or components without obtaining and retaining appropriate evidence of source or method of preparation.

5. The pharmacy is compounding drugs in anticipation of receiving prescriptions, as opposed to in response to individual prescriptions. The volume of such drugs compounded by the pharmacy is high when compared to the volume of prescriptions actually received for such drugs.

6. A significant amount of compounded drugs is distributed to patients or customers outside the pharmacy's normal trade area or across state lines.

7. Drugs are compounded by one pharmacy and dispensed by another pharmacy.

8. The pharmacy is not in general compliance with state or federal requirements for the production, preparation and maintenance of safe and effective drug products (for example B & P. Code §4009; H. & S. Code §§26000 et seq.).

This list is not exhaustive; other factors may be considered on a case-by-case basis. The Board of Pharmacy, DHS, and FDA do exchange referrals and otherwise cooperate in investigation and follow-up of complaints and other cases.

As to over-the-counter drug products, except where a prescription is involved, the board generally has no jurisdiction over them; the Department of Health Services and the federal Food and Drug Administration do have direct jurisdiction over OTC drug products, including through the Drug Efficacy Study Implementation (DESI) Program (see 21 C.F.R. §§211, 330.10 and 330.12).

And every pharmacy should keep in mind that these guidelines reflect the position of the Board of Pharmacy; as mentioned at the beginning of this article, pharmacies and pharmacists must also be aware of and in compliance with FDA and DHS statutes and regulations. Although those statutes and regulations are briefly described here, they are detailed, and any pharmacist or pharmacy owner who is uncertain whether the drugs to be prepared require special equipment, space, training or a separate manufacturer's license or registration should seek the advice of a person familiar with those laws and regulations.

PAs

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tasks delegated to a PA, the supervising physician may limit the PA's authority to issue oral, electronic, or written transmittal orders as the supervising physician deems appropriate.

Prepackaged Medications

As under current law, a PA acting at the direction of a supervising physician may hand to a patient of the supervising physician a properly labeled prescription drug prepackaged by a physician, a manufacturer as defined in the California Pharmacy Law, or a pharmacist. Any prescription transmitted or carried out by a PA, whether by dispensing prepackaged drugs or with a transmittal order, is subject to a reasonable quantitative limitation consistent with customary medical practice in the supervising physician's practice.