



California State Board of Pharmacy
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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.

**June 9, 2004
1:30 p.m. – 4:00 p.m.**

**Hilton Burbank Airport & Convention Center
2500 Hollywood Way
Burbank, CA 91505-1019
(818) 843-6000**

This committee meeting is open to the public and is held in a barrier-free facility in accordance with the Americans with Disabilities Act. Any person with a disability who requires a disability-related modification or accommodation in order to participate in the public meeting may make a request for such modification or accommodation by contacting Candy Place at telephone number (916) 445-5014, at least 5 days prior to the meeting.

A. Call to Order 1:30 p.m.

B. Introductions and Meeting Format

C. Discussion of Compounding Issues

- Law
 - Manufacturing/Compounding*
 - Efficacy* *Label on "unit of use" containers*
 - Definition* *Central Fill*
 - Veterinary* *Anticipatory* *OTC*
- Quality Standards
 - Non-sterile (USP 795/1075)*
 - Equipment Quality/Process Validation*
- Sterile Compounding
 - USP797/Pending California Regulations*
 - Environmental Control*
 - Definition of inhalation drugs, otics, and ophthalmic*
 - Oils/suspensions*

D. Notice to Board of Pharmacy Regarding Compounding from Bulk Drugs and Letter in Response from APhA, IACP and NCPA

E. Next Meeting – September 22, 2004

Adjournment 4:00 p.m.

Meeting materials will be available on the board's Web site on June 2, 2004.

AGENDA ITEM C
LAW
MANUFACTURING/COMPOUNDING

California Board of Pharmacy Licensing Committee
Workgroup on Compounding
Subcommittee: Compounding vs. Manufacturing
3/29/04(a)

1. The subcommittee (Compounding vs. Manufacturing) met at McGuff Compounding Pharmacy Services, Inc. on 3/12/04.
2. Subcommittee members:
 - a. Dan Willis
 - b. Wayne Vega
 - c. Mike Koch
 - d. Bill Blair
 - e. Guest: Then Nguyen (4th year pharmacy student)
3. Business:
 - a. Charge: The subcommittee established a charge to itself based on the March 3, 2004 meeting of the Licensing Committee. The subcommittee determined that they were to establish a mechanism whereby a board inspector could determine whether a pharmacy was engaged in compounding or in manufacturing.
 - b. The subcommittee reviewed and considered several documents (These are available if requested):
 1. Pharmacy Compounding and the FDA
 2. CPGs issued in 2002
 3. Sample OTC Regulations
 4. IACP Hosts Discussion between Manufacturing and Compounding Practices
 5. As Druggists Mix Customized Brew, FDA Raises Alarm
 6. Missouri Rules
 7. The Virtual Line
 8. Overview of Pharmacy Laws Related to Compounding
 9. Policy for Determination of Quantity to Compound for Future Furnishing
 10. Licensing Committee Workgroup on Compounding, Meeting Materials
 11. FDAMA 503a
 - c. In 1995, the California Board of Pharmacy established guidelines for distinguishing compounding from manufacturing. The sc decided to use the same format and to modify and revise the factors in the guidelines to be considered by the board inspectors. The revised document will suggest that a pharmacy which claims to be compounding is actually engaged in manufacturing which is beyond the scope of its pharmacy permit.
 - d. The subcommittee is recommending the following changes highlighted in red:

Board of Pharmacy Guidelines for Distinguishing Compounding from Manufacturing, ~~summer 1995~~ spring 2004.

Definitions:

1. B&P Code 4033. Manufacturer

- (a) “Manufacturer” means and includes every person who prepares, derives, produces, compounds, or repackages any drug or device except a pharmacy that manufactures on the immediate premises, where the drug or device is sold to the ultimate consumer.**
- (b) Notwithstanding subdivision (a), manufacturer shall not mean a pharmacy compounding a drug for parenteral therapy, pursuant to a prescription, for delivery to another pharmacy for the purposes of delivering or administering the drug to the patient or patients named in the prescription provided that neither the components for the drug nor the drug are compounded, fabricated, packaged, or otherwise prepared prior to receipt of the prescription.**
- (c) Notwithstanding subdivision (a), manufacturer: shall not mean a pharmacy that, at a patient’s request, repackages a drug previously dispensed to the patient, or to the patient’s agent, pursuant to a prescription.**

2. B&P Code 4037. Pharmacy

- (a) “Pharmacy” means an area, place, or premise licensed by the board in which the profession of pharmacy is practiced and where prescriptions are compounded. “Pharmacy” includes but is not limited to, any area, place, or premise described in a license issued by the board wherein controlled substances, dangerous drugs, or dangerous devices are stored, possessed, prepared, manufactured, derived, compounded, or repackaged, and from which the controlled substance, dangerous drugs, or dangerous devices are furnished, sold, or dispensed at retail. “Pharmacy” shall not include any area in a facility licensed by the State department of Health Services where floor supplies, ward supplies, operating room supplies, or emergency room supplies of dangerous drugs or dangerous devices are stored or possessed solely for treatment of patients registered for treatment in the facility or for treatment of patients receiving emergency care in the facility.**

Factors to Be Considered by the 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. . When considering these factors “compounding” does not include mixing, reconstituting, or other such acts that are performed in accordance with directions contained in approved labeling provided by the product’s manufacturer and other manufacturer directions consistent with that labeling. Nor is compounding defined by quality, quantity, or when the compounding takes place in relationship to obtaining a prescription.

- 1. “A professional relationship does not exist among the prescriber, patient and pharmacist who compounds and dispenses the drug product.” A professional relationship is said to exist if a physician issues a prescription, issues an order for

Office Use. A professional relationship is not necessary if the pharmacy is in compliance with B&P Code 4123.

~~2. "The pharmacy solicits or advertises for business from any practitioner or other entity for specific products which the pharmacy compounds." DELETED: the U.S. Supreme Court has declared this factor unconstitutional.~~

2. "The pharmacy is compounding products the same as FDA approved products that are commercially available in dosage form, strength, concentration, route of administration, performance characteristics and intended use.

When a compounded drug is dispensed to a patient the prescriber must be notified. Filling a prescription for a drug or device where the prescriber specifically states "compounded" on the order is considered prescriber notification. . Prescriber notification is not necessary in cases where compounding is assumed (i.e. no commercial product is available).

Pharmacies may compound drugs that were previously available commercially but are not readily available in the market or have been removed from the market for reasons other than safety or efficacy. This includes both dangerous drugs and OTC drugs.

~~4. "The pharmacy is receiving and using drug substances or components without obtaining and retaining appropriate evidence of source or method of preparation DELETED: This factor will soon be unnecessary when all drug substances and components will be traceable with pending legislation (pedigree law).~~

~~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." Delete: Beyond-use date of products and historical prescribing practices should be the only limitation to anticipatory compounding. In addition, good business practices should naturally regulate anticipatory compounding and dictate the proper balance between efficiency and maintenance of minimum amount of stock. As anticipatory compounding is otherwise regulated, this factor should not be used to distinguish between compounding and manufacturing.~~

~~6.2. "A significant amount of compounded drugs is distributed to patients or customers outside the pharmacy's normal trade or across state lines." Replace with:~~

3. Failing to be licensed in those states where compounded products are delivered and failing to operate in conformance with applicable state law regulating the practice of pharmacy

~~7.3. "Drugs are compounded by one pharmacy and dispensed by another pharmacy."~~

4. 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 except as permitted by B&P Code 4123 and CCR 1716.1.

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.”~~

~~DELETE: This factor does not distinguish between compounding and manufacturing.~~

5. ~~Compounding drugs intended for human use that have been 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.~~

Compounding for Future Furnishing is lawful. Refer to CCR 1751.2 Record Requirements-Compounding for Future Furnishing. Beyond-use date of products and historical prescribing practices should be the only limitation to anticipatory compounding. In addition, good business practices should naturally regulate anticipatory compounding and dictate the proper balance between efficiency and maintenance of minimum amount of stock.

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 referral 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 the Drug Efficacy Study Implementation (DESI) Program (see C.F.R. 221, 330.10 and 330.12).

Appendix A

Sec. 216.24 **Drug** products withdrawn or removed from the market for reasons of safety or effectiveness.

The following **drug** products were withdrawn or removed from the market because such **drug** products or components of such **drug** products were found to be unsafe or not effective. The following **drug** products may not be compounded under the exemptions provided by section 503A(a) of the Federal **Food, Drug, and Cosmetic Act**:

Adenosine phosphate: All **drug** products containing adenosine phosphate.

Adrenal cortex: All **drug** products containing adrenal cortex.

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 preoperative skin preparation.

Chlormadinone acetate: All **drug** products containing chlormadinone acetate.

Chloroform: All **drug** products containing chloroform.

Cobalt: All **drug** products containing cobalt salts (except radioactive forms of cobalt and its salts and cobalamin and its derivatives).

Dexfenfluramine hydrochloride: All **drug** products containing dexfenfluramine hydrochloride.

Diamthazole dihydrochloride: All **drug** products containing diamthazole dihydrochloride.

Dibromsalan: All **drug** products containing dibromsalan.

Diethylstilbestrol: All oral and parenteral **drug** products containing 25 milligrams or more of diethylstilbestrol per unit dose.

Dihydrostreptomycin sulfate: All **drug** products containing dihydrostreptomycin sulfate.

Dipyrrone: All **drug** products containing dipyrrone.

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.

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 dermatologic 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.

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.

Dated: March 1, 1999.

William K. Hubbard,

Acting Deputy Commissioner for Policy.

[FR Doc. 99-5517 Filed 3-5-99; 8:45 am]

BILLING CODE 4160-01-F

Respectfully submitted,

William J. Blair, Pharm.D.

Secretary

AGENDA ITEM C

LAW

OTC – Nonprescription Compounding

Non-Prescription Compounding

Background:

As compounding becomes more prevalent, an area where the public could be served better needs to be addressed. That is the area of compounding non-prescription products. This area has not been addressed in the laws of the State of California except three situations. 1) Business and Professions Code (B&P) 4006 says that the Board may restrict the sale of a specific drug if they find it to be dangerous to the public. 2) B&P 4240 May allow for the restriction on the sale of poisons 3) And, B&P 4342 may regulate in cases of poor quality and/or strength. Otherwise, B&P 4057 states “as provided in Sections 4006, 4240, and 4342, this chapter does not apply to the retail sale of nonprescription drugs that are not subject to Section 4022 (emphasis added) and that are packaged or bottled in the manufacturer's or distributor's container and labeled in accordance with applicable federal and state drug labeling requirements.”

Some definitions may be in order at this point:

4022. "Dangerous drug" or "dangerous device" means any drug or device unsafe for self-use in humans or animals (emphasis added), and includes the following:

(a) Any drug that bears the legend: "Caution: federal law prohibits dispensing without prescription," "Rx only," or words of similar import.

(b) Any device that bears the statement: "Caution: federal law restricts this device to sale by or on the order of a _____, "Rx only," or words of similar import, the blank to be filled in with the designation of the practitioner licensed to use or order use of the device.

(c) Any other drug or device that by federal or state law can be lawfully dispensed only on prescription or furnished pursuant to Section 4006.

4025. "Drug" means any of the following:

(a) Articles recognized in the official United States Pharmacopoeia, official National Formulary or official Homeopathic Pharmacopoeia of the United States, or any supplement of any of them.

(b) Articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans or other animals.

(c) Articles (other than food) intended to affect the structure or any function of the body of humans or other animals.

(d) Articles intended for use as a component of any article specified in subdivision (a), (b), or (c).

4025.1. "Nonprescription drug" means a drug which may be sold without a prescription and which is labeled for use by the consumer in accordance with the requirements of the laws and rules of this state and the federal government

4033. (a) "Manufacturer" means and includes every person who prepares, derives, produces, compounds, or repackages any drug or device except a pharmacy that manufactures on the immediate premises where the drug or device is sold to the ultimate consumer.

Conclusion from State Law

As stated in B&P 4033 a pharmacy is not manufacturing if it makes the drug on the immediate premises where the drug is sold to the consumer. If that drug that is made is not a dangerous drug as defined in B&P 4022, then it may legally be sold without a prescription, unless that particular drug has been found to be dangerous to the public health as described in B&P Sections 4006, 4240, and 4342.

Federal Law

The FDA has a similar exemption for Pharmacies as the State does. When asked, a supervising inspector for the State Board also provided information on FDA regulations. His letter stated, "In response to your...wanting clarification of the manufacture of OTC products. I have included a copy of Chapter 5 FD&C Act Subchapter A Drug and Devices, §510 and I direct you to §510(g)."

(§510 (g): The foregoing subsections shall not apply to (1) pharmacies which maintain establishments in conformance with any applicable local laws regulating the practice of pharmacy and medicine and which are regularly engaged (emphasis added) in dispensing prescription drugs or devices, upon prescriptions of practitioners licensed to administer such drugs or devices 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.)

The letter continues, "Also, for your consideration is the following from *Pharmacy Law Digest*, 35th edition, page 64, "The FDA's authority for its position on manufacturing practices can be found in the Federal, Food, Drug, and Cosmetic Act. Section 501(a)(2)(B) of the Act [21 U.S.C. § 351 (a)(2)(B)] provides that a drug will be deemed adulterated if the methods used in or the facilities or controls used for its manufacture, procession, Packing, or holding do not conform to current good manufacturing practice. This section of the law can be made applicable to wholesalers, retailers, pharmacies, and hospitals as well as to drug manufacturers. However, the FDA states that the CGMP regulations only apply to organizations engaged in the preparation of a drug product and, therefore, do not apply to wholesalers, retailers, pharmacies, and hospitals engaged in activities that are traditional to them. Pharmacies are exempt from FDA manufacturer registration, but only if they do not manufacture, prepare, propagate, compound or process drugs for sale other than in the regular course of dispensing and selling drugs at retail [21 U.S.C. § 510 (g)(1).] The exemption from regular FDA factory inspection is given to pharmacies by 21 U.S.C. § 704 (a)(2)(A); again, the pharmacy may engage only in the regular business of dispensing and selling drugs at retail. Consequently, repackaging and re-labeling of drugs for off-premises (emphasis added) sale can be interpreted as out of the regular course of the pharmacy's business and, hence, nullify the exemptions in §§ 510(g) and 704(a) and the FDA exemption of the pharmacy from CGMP compliance."

This input is very much appreciated. § 510 (g) gives an exemption to pharmacies who are regularly engaged in filling prescriptions from registering as a manufacturer and from strict adherence to CGMP (thus eliminating the issue of adulteration). § 704 gives an exemption to pharmacies for inspection purposes as long as they are selling at their own premises. These are the two laws that are commonly used to show an exemption for over all compounding. However, none of these regulations prohibit the compounding of non-prescription drugs. In fact, the states of Alabama, Arkansas, Oklahoma and Kansas, specifically allow for non-prescription compounding under these federal regulations, and many other states allow it without a specific regulation.

So, while there has been question in the past as to the legality of compounding without a prescription, we can see here that based on California law there are exemptions allowing for the compounding of non-prescription drugs, and that the federal laws do not prohibit it.

There also exists a public need for some compounding of non-prescription products. The same reasons that exist for a need to compound prescription items also exist for non-prescription products. Some of these are: products that are no longer available due to non-profitability, or back orders, patient allergies to dyes and fillers, or the need of a non-available strength or form. In addition to this, many herbalists and nutritionists with no education can put together natural drugs, but currently, many pharmacists believe that even with their extended education and license, they might be prosecuted for the same act. A pharmacy license was never intended to stop a pharmacist from mixing remedies that the general public was allowed, but to show that the person holding the license is more qualified to actually do so, and to ensure that only those qualified could mix the dangerous drugs.

With this in mind it is essential for the state to develop guidelines specifically for the compounding of non-prescription products. This would help clear up any misunderstandings, and create a method of regulating for the safety of the public. We have come up with a set of guidelines that we feel would allow for compounding within the limits set forth in the exemptions, but would stop those who want to use a pharmacy license to become a manufacturer of OTC's.

Proposed:

A pharmacy may compound ingredients in a strength that would not normally require a prescription (over the counter strengths) if they are in compliance with non-prescription compounding guidelines. Otherwise, an inspector may conclude that the pharmacy may be conducting business more as a manufacturer and could be referred to the Department of Health Services, Food and Drug Branch.

Non-prescription Compounding versus Manufacturing Guidelines

- 1) Products will not be available in the front end of the store. They will be behind the counter and only be available upon request.
- 2) Products will only be furnished after consultation with a pharmacist.
- 3) Ingredients shall not be provided in a strength that has been concluded to be only available by prescription.
- 4) No product that was removed from the market for safety reasons will be furnished to the market from which it was removed. (Products removed from human use may still be used in animals if no such restriction for animal use was made and visa-versa.)
- 5) No products shall be furnished to a third party for resale.
- 6) All products shall be furnished within the pharmacies own retail establishment.
- 7) No products shall be made that are that are commercially available in dosage form, strength, concentration, route of administration, performance characteristics and intended use.
- 8) May be made in reasonable amounts in anticipation of estimated needs.

Submitted by: Dan Wills, Chairman, Subcommittee on Compounding v. Manufacturing

Sample OTC Regulations from other States

Alabama

(Adopted) H.B. 314/S.B. 53

Section 10. A pharmacy may prepare a compounded drug product to be sold over the counter without a prescription order. The product may be prepared from Prescription Only drugs, but shall not exceed recommended strengths and doses. The finished product must not be one for which a prescription is required. It must be properly labeled with the product's designated name, directions for use, list of active ingredients and any necessary warnings. A compounded product shall be sold directly to the consumer after professional interaction or consultation between the pharmacist and the consumer. The product may be prepared in advance in reasonable amounts in anticipation of estimated needs. The product shall be stored within the prescription department. The product may not be sold in bulk to other pharmacies or vendors for resale.

Arkansas

07-02-0002 Good Compounding Practices

B. 4. Pharmacy Generated Products (PGP): means a medical product that is prepared, packaged, and labeled in a pharmacy that can be sold by the pharmacy without a prescription.

K. Pharmacy Generated Product Requirements:

1. A Pharmacy Generated Product (PGP) may be prepared from legend drugs, not to exceed recommended strengths and doses.
2. PGP will be labeled properly and will be sold with the public's health and welfare in mind.
3. A PGP cannot be bulk compounded to sell to a second entity for resale. This would require a manufacturer's permit.

Oklahoma

Title 535, Subchapter 10 Good Compounding Practices

535:15-10-2. **Definitions**

"Pharmacy Generated Products" or "(PGP)" means a medical product that is prepared, packaged, and labeled in a pharmacy that can be sold by the pharmacy without a prescription.

535:15-10-11. **Pharmacy generated product requirements**

- (a) A Pharmacy Generated Product (PGP) may be prepared from RX Only drugs, not to exceed recommended strengths and doses.
- (b) PGP will be labeled properly and will be sold with the public's health and welfare in mind.
- (c) Compounded PGP's are to be sold directly to the consumer after professional interaction or consultation with the health care provider and the consumer.
- (d) A PGP cannot be bulk compounded to sell to a second entity for resale. This would require a manufacturer's permit.

Kansas

Proposed Article 13. Compounding

68-13-3. Definitions

(d) "Pharmacy Generated Products" ("PGP") means a medical product that is prepared, packaged, and labeled in a pharmacy that can be sold by the pharmacy without a prescription.

AGENDA ITEM C
STERILE
COMPOUNDING

USP 797/Pending CA Regulations

From: "Hank Rahe" <hrahe@mic4.com>
Subject: USP 797
Date: Sun, 28 Mar 2004 20:05:01 -0500
MIME-Version: 1.0

Hello Hello,

Have attached the information we discussed at the meeting on March 3rd in Oakland. Sorry I am so late but have had a difficult travel schedule.

Seems clear that USP 797 is a standard of practice that will be enforced by JCAHO and the USP and FDA supports the standard. The difficult issue is enforcement in areas not covered by the Board of Pharmacy such as physicians practices - I know that New Jersey had some problems with not enforcing pharmacy regulations across the board.

Let me know if you would like any additional clarification and I will send additional information as it becomes available. I will be doing a comparison of the proposed California regulations compared to USP 797 and can provide a summary if you wish.

References from USP 27 – NF22

Reference – Page 2350 - Introduction

The content of this chapter {(797) Pharmaceutical Compounding – Sterile Preparations } applies to health care institutions, pharmacies, physician practice facilities and other facilities in which CSP's are prepared, stored and dispensed.

Reference – page vii – Council of Experts

The Council of Experts is the *standards setting* body for USP

Reference – page ix - Legal Recognition

The USP-NF is recognized by law and custom in many countries throughout the world. In the United States, the Federal Food, drug and cosmetic Act (FD&C Act) uses the term “official compendium” to mean the official USP, The official NF, the official *Homeopathic Pharmacopeia* of the United States, or any supplement to them. FDA may enforce compliance with official standards in USP –NF under the adulteration and misbranding provisions of the FD&C Act.

Reference – page xii – Compounded Preparations

Compounded Preparations- Standards in USP-NF for compounded preparations may be enforced at both the Federal and State levels.

Reference – page xxxv – Pharmaceutical Compounding

This chapter, which was previously entitled *Sterile Drug Products for Home Use (1206) USP 26- NF 21* was revised based on the FDA Advisory Committee on Compounding recommended from it's July 13, 2002 meeting that this chapter be recognized as the **national standard** for compounded sterile preparation techniques and practices. In response, USP renumbered and renamed (1206) to provide enforceable guidance to qualified health professionals who compound sterile preparations.

Reference – page 2107

The USP describes in the section on “Physical Tests and Determinations a number of activities in which it defines facilities, equipment, containers and methods that are required to meet the standards defined in USP.

Presentation by Darryl Rich – Associate Director JCAHO (Joint
Commission Accreditation of Health Organizations)

Presented in Las Vegas March 4th, 2004

- Legal Implications – Federal
 1. The Federal Food, Drugs and Cosmetics Act recognizes the USP-NF as the official compendia of standards
 2. Chapter 1 through 999 is considered official monographs and standards of the USP-NF.
 3. If a drug product that appears in a monograph if the USP – NF fails to meet the standards of strength, quality purity packaging or labeling contained in the monograph – it may be deemed “misbranded or “ adulterated” under the Act.
Source – Legal Council, USP
 4. Although the law primarily relates to interstate commerce, any drug that is “adulterated” or “misbranded” or mislabeled that are sold, dispensed or distributed is a violation of the requirements of the Food, Drugs and Cosmetics Act. Source – Pharmacy Law Digest
 5. “Will go after compounded products that are supposed to be sterile but are contaminated, misbranded or adulterated based on compliant or incident”
Source: Jane Axelrad, FDA
 6. Legal Implications States
 - a. State act that permit enforcement
 1. DE, FL, MI, MN, NE, NJ OK
 - b. States with Food, Drug and Cosmetics Act the same as federal are:
AL, AR, DE, DC, FL
 - c. States that have Food, Drug and Cosmetic Act are:
All but AK,AZ,ME,MA,MS,NH,SD,UT,WV, WI
Source 2001-2003 NABP – survey of Pharmacy Law
 7. Legal Implications – Risk
Lawyers have successfully used the USP-NF as evidence of national standard of practice in lawsuits

8. Implications – JCAHO

1. compliance with USP chapter 797 is considered as part of a federal law and regulation (FDC Act).
2. Even though not proactively enforced by the responsible enforcement agency (FDA), JCAHO still expects compliance by accredited organizations.

Suggestions:

Based on the above and the fact that California does have Food, Drug and Cosmetics Act it may be wise to review the California Law as to compliance to federal requirements contained in the federal Food, Drug and Cosmetics Act. USP 797 is clearly a standard of practice and as such is enforceable in federal law.

California Department of Justice faces a dilemma on how to enforce the this beyond the Board of Pharmacy that does not have jurisdiction for locations such as physician practice facilities and other facilities in which CSP's are prepared, stored and dispensed.

The review of current proposed California regulations compared to USP 797 will take me an additional two weeks.

Hank Rahe

WASHINGTON PHARMACY LAW: A USER'S GUIDE

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Revised 3/23/04

Chapter 4 (Part 2). Extemporaneously Compounded Products

1. Extemporaneous compounding of medications is a long-standing aspect of the practice of pharmacy. When the FDCA was adopted in 1938, manufacturers were required to register with the FDA.
 - a. § 510(b) requires annual registration by every person engaging in the “manufacture, preparation, propagation, compounding, or processing of drug[s] ...”
 - b. However, § 510(g) exempts from registration “pharmacies ... regularly engaged in dispensing drugs and devices ... and which do not ... compound ... drugs other than in the regular course of their dispensing or selling drugs at retail ...”
 - c. Until the 1980s, the FDA and most commentators believed that pharmacists could compound any medication ordered by a physician without violating the FDCA. Some pharmacies began to expand their compounding business greatly, and a few used the excuse that they were compounding drugs to shield them from regulation for some potentially or actually harmful practices.
 - i. For example, the Seven Freedoms Pharmacy in Florida compounded a product called “GH-8,” and shipped the product around the United States via the mail. GH-8 consisted of a formulation of lidocaine, and it was alleged to retard aging reduce or eliminate many of the symptoms of aging. GH-8 was the only product compounded or sold by Seven Freedoms Pharmacy, and the “patients” joined Club Sene-X to receive prescriptions for GH-8, or to receive instructions for their own physician to prescribe GH-8. In a landmark lawsuit, [*United States v Sene-X Eleemosynary Corp.* \(479 F.Supp. 970, 1979\)](#), the US Court of Appeals ruled that Seven Freedoms Pharmacy was not engaged in the bona fide practice of pharmacy, that GH-8 was a new drug that had not been approved by the FDA, and that its distribution violated the FDCA.
 - ii. Injuries from poorly compounded prescriptions included overdoses of pediatric medications, blindness from non-sterile compounded eye drops, and deaths due to meningitis caused by non-sterile betamethasone injection. [Recent FDA surveys](#) have discovered several problems in a random selection of compounded products.
2. In response to these events, the FDA reexamined its position that compounding was exempt from FDA oversight. It determined that, although pharmacies do not need to register, §510(g) does not exempt pharmacies from the new drug requirements of the Act, which include the following three sections:
 - a. § 501(a)(2)(b) – A drug is adulterated if it is not manufactured in accordance with Current Good Manufacturing Practices (GMPs).
 - b. § 502(f)(1) – A drug is misbranded if it lacks adequate directions for use.
 - c. § 505 – An approved New Drug Application is required before a new drug can be marketed or introduced into the stream of commerce.Thus, the FDA determined, compounded products are new drugs, which come under its jurisdiction.
3. The FDA indicated that it had long recognized the role of compounding, and would exercise discretion in enforcing the FDCA against compounding pharmacists. Agencies, and prosecuting attorneys, are generally allowed discretion in enforcing laws and rules under their jurisdiction, if for no other reason that most agencies lack the resources to enforce every minor (*de minimis*)

violation. Thus, they are allowed to prioritize their use of resources. With regard to compounding by pharmacists, the FDA issued an Compliance Policy Guide which would be followed by FDA and its agents in determining when to act against pharmacies who are compounding medications. The Compliance Policy Guide indicated that pharmacies would not be charged with a violation of the FDCA if they met all of the following criteria.

- a. The pharmacies compounded products only upon receipt of prescriptions for individual patients, issued by an authorized prescriber, in the context of a *bona fide* (“good faith”) physician-pharmacist-patient relationship.
 - b. Pharmacists did not compound an inordinate supply of the product in advance of receiving prescriptions for the product.
 - c. Pharmacists did not use large-scale or commercial equipment.
 - d. Pharmacists did not use commercial-grade testing equipment
 - e. Products were prepared only from FDA-approved drug products.
 - f. Pharmacists did not compound products that were essentially copies of existing marketed dosage forms.
 - g. Pharmacists did not compound for resale to other practitioners, but only for sale to the end user of the product.
 - h. Pharmacists did not advertise or promote specific drugs, classes of drugs, or dosage forms, but could advise practitioners that they were capable of compounding drugs.
4. A group of pharmacists and consumers filed suit in Texas against the FDA’s development and use of the Compliance Guide. They argued, among other things, that the FDA failed to hold proper hearings before making what was, in essence, a rule regulating compounding. The federal court ruled that the FDA’s use of Compliance Guides was a legitimate internal policy making activity that did not require a formal rule-making process as is required to modify the Code of Federal Regulations. The court also ruled that because it was a guide only, the plaintiffs did not have standing to sue the FDA until or unless the FDA took actual action against an individual plaintiff.
5. Several national pharmacy organizations joined to persuade Congress to amend the FDCA to clearly indicate that compounding by pharmacists does not create a new drug covered by the FDCA. Congress enacted such a provision as part of the Food and Drug Administration Modernization Act of 1997 (FDAMA). FDAMA added a new section, §503A, which excluded compounded products from the definition of new drugs. The amendment stated that
- a. §§ 501(a)(2)(b), 502(f)(1), and 505 do not apply to drugs that are compounded ... for an individual identified patient, based on the unsolicited receipt of a valid prescription by a licensed pharmacist or physician
 - b. Limited quantities may be compounded prior to receiving a prescription, based on a history of the pharmacist receiving valid orders within an established relationship between the pharmacist, physician, and patient.
 - c. Components and methods used to compound the product
 - i. Must comply with USP or NF monographs, if they exist, and the USP Chapter on Pharmacy Compounding.
 - ii. If no monographs exist, the products must be made from components of approved drugs, or
 - iii. Must be components that appear on a bulk ingredients list developed by FDA [Proposed rule published 1/7/99].
 - iv. Must be manufactured in an FDA registered facility
 - d. Pharmacists are prohibited from compounding certain products:
 - i. May not compound products that are listed by FDA as having been removed from market due to lack of safety or efficacy [Final Rule published 3/8/99].
 - ii. May not compound “regularly or in an inordinate amount” products that are essentially copies of commercially available drug products.
 - iii. May not compound products that are listed by FDA as having demonstrable

difficulties in compounding [list to be developed].

- e. As with the Compliance Guide, the new section prohibited pharmacists from promoting a particular drug, a particular class of drugs, or a particular type of drug. Pharmacists were allowed to promote the fact that they had a compounding service.

5. Pharmacists in Nevada filed suit in federal court that challenged the prohibition of promotion of compounded products, arguing that the Act violated the free speech rights guaranteed under the First Amendment of the US Constitution.

- a. In general, speech may not be restricted by the government unless it meets the following three tests:
 - i. The restriction of commercial speech must fulfill a compelling government interest.
 - ii. The restriction must be reasonably related to the achievement of the government interest.
 - iii. The restriction must be the least intrusive option available to achieve the government interest.
- b. Political speech, in which individuals express their opinions to others, can only be restricted in extreme conditions, such as when the speech presents a “clear and present danger” to the safety of others. For example, in the landmark case of *Schenck v United States* (249 US 47, 1919) the Supreme Court said that a person does not have a right to falsely shout “Fire” in a crowded theater and cause a panic.
- c. Commercial speech, although still protected, may be more easily restricted, since the government has a compelling interest under the Commerce Clause of the Constitution to regulate interstate commerce, in part, by preventing false speech, among other things. The tests for regulating commercial speech were specified by the US Supreme Court in the case of *Central Hudson Gas & Electric v. Public Service Commission* (447 US 557, 1980). Under these “Central Hudson Tests,” government restriction of commercial speech is subject to a “four-prong test”:
 - i. Is the speech false or related to unlawful activity?
 - ii. Does the government assert a “substantial interest” in restricting the speech?
 - iii. Does the restriction directly advance the government interest?
 - iv. Is the restriction not more extensive than necessary to achieve the asserted government interest?
- d. The US District Court found that FDAMA was an unconstitutional restriction on commercial speech, in that it sought to prohibit promotion of a legal product, and commercial speech that was not demonstrated to be false. The court ruled that the government failed to demonstrate a substantial interest in preventing the spread of compounding, which would be the basis for restricting advertising. The court also ruled that the anti-promotion provisions of the Act could be invalidated without affecting the status of the other portions of §503A, or, in other words, that the offending provisions were “severable” from the rest of the Act.
- e. The government appealed, arguing in part that the anti-promotion provisions were a condition that Congress placed into the Act as part of an overall scheme, and were not severable. The government also argued again that the restrictions met a compelling government interest and met the Central Hudson tests. The 9th Circuit Court of Appeals affirmed the district court’s ruling that §503A’s prohibition of promotion of compounded drugs was unconstitutional, but reversed the district court’s ruling that these provisions were severable from the rest of §503A, and invalidated all of §503A. ([Western States Medical Center v. Shalala, 238 F.3d 1090, 9th Cir. 2001](#)).
 - i. Upon appeal to the Supreme Court, the 9th Circuit’s affirmation of the invalidation of §503A was allowed to stand, and the Supreme Court did not take

up the issue of severability. Thus, §503A was declared invalid, and has no current force in law.

- f. The FDA has subsequently reissued its Compliance Policy Guide, absent the restrictions on promotion. The current provisions of the Guide are as follows:

...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. ...
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.

- ii. The full text of the Compliance Policy Guide on Pharmacy Compounding is available on the [FDA webpage](#).

7. The USP has developed two chapters related to compounding. The first, chapter <795> of USP 27, relates to compounding of nonsterile products, and covers most compounding activities of community pharmacies. The second monograph, chapter <797> of USP 27, details good practices for compounding of sterile products, which includes home IV admixtures, eye drops, and similar products. The standards in these chapters were incorporated by reference in §503A prior to its invalidation, and remain as elements of the FDA's Enforcement Compliance Guide.

- a. The USP 27 chapter <795> provides the following standards for compounding of nonsterile formulations .
 - i. "Appropriate stability evaluation is performed or determined from the literature for establishing reliable beyond-use dating." (27 USP 2346)
 - ii. "... Beyond-use dates are to be assigned conservatively." (27 USP 2347)

- iii. Clean clothing and appropriate protective apparel are required.
- iv. Compounding areas are limited to personnel involved in compounding, and the pharmacist shall exclude persons with lesions or other illnesses that may compromise the product.
- g. Requirements for facilities used in compounding are specified in WAC 246-878-040:
 - i. There shall be adequate space and facilities, and non-sterile compounding shall be separate from sterile compounding facilities.
 - ii. Bulk containers shall be properly stored, including under refrigeration if necessary.
 - iii. Adequate water and other supplies must be available for compounding and cleaning.
 - iv. Facilities must be maintained in clean and sanitary condition.
- h. Compounding of sterile products must conform with WAC 246-871.
- i. The Washington regulation does NOT incorporate by reference the standards of USP chapters <795> or <797>. However, these standards are widely regarded as best practices, and should be followed wherever applicable.



House of Delegates Session—2004

Board of Directors report on the Council on Legal and Public Affairs

The Council on Legal and Public Affairs is concerned with (a) laws and government administrative regulations, (b) proposed laws and regulations, and (c) pharmacy ethics.

William H. Puckett, Board Liaison

Council members

Ronald M. Barnes, Chair (Georgia)
Roxanne H. Homar, Vice Chair (Wyoming)
Ernest R. Anderson, Jr. (Massachusetts)
Helen M. Calmes (Louisiana)
Alan K. Knudsen (Florida)
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Robert M. Patti (Pennsylvania)
Marc H. Stranz (Colorado)
Deborah J. Tapley (South Carolina)
Sylvia M. Thomley, Student Member (Wisconsin)
Brian M. Meyer, Secretary

Policy recommendations

A. Medicare Prescription Drug Benefit

To strongly advocate a fully funded prescription drug program for eligible Medicare beneficiaries that maintains the continuity of patient care and ensures the best use of medications; further,

To recommend that the program should at a minimum contain the following: (1) appropriate product reimbursement based on transparency of drug costs, (2) payment for indirect costs and practice expenses related to the provision of pharmacy services, based on a study of those costs, (3) appropriate coverage and payment for patient care services provided by pharmacists, and (4) open access to the pharmacy provider of the patient's choice.

(Note: *Fully funded* means the federal government will make adequate funds available to fully cover the Medicare program's share of prescription drug program costs; *eligible* means the federal government may establish criteria by which Medicare beneficiaries qualify for the prescription drug program.)

(Note: This proposed policy would supersede ASHP policy 0317.)

Background

The Council reviewed policy 0317 in response to delegate Recommendations to review the description of "fully funded" by the federal government, the meaning of "any willing provider" as contained in the policy, and the practice of different copays between

local and mail service pharmacies. The Council believed, and the Board concurred, that "fully funded" was accurately defined by the parenthetical statement in the policy to mean that the government must fully commit funds to the extent of the benefit and that this clause did not limit the Society to supporting only a comprehensive benefit for all Medicare beneficiaries. With respect to the phrase "any willing provider," Council members and the Board agreed with the delegate Recommendation that it has a specific meaning when used in state law, and this wording was changed to more clearly reflect the Council's intent of preserving existing relationships with pharmacy providers that best meet patients' needs. Concerning the different copays between community and mail service pharmacies, the Council and Board believed economic disparities would be addressed by replacing "any willing provider" with language referring to the patient's choice rather than to a business decision by a pharmacy to participate in a network. The emphasis is now on the patient's choice, as opposed to the choice by a pharmacy to accept a health plan's terms and conditions for inclusion in a particular pharmacy network.

The Board noted that with passage of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) (the outpatient Medicare drug benefit), this policy will be particularly important as ASHP works with the Centers for Medicare and Medicaid Services (CMS) in crafting regulations to implement this new Part D benefit. In addition, this policy will continue to be used in advocacy if Congress considers future changes to the law.

The Council also discussed various payment policies of the Centers for Medicare and Medicaid Services for different health-system practice settings. The Council noted the pervasive use of average wholesale price as a benchmark in the payment formulas in all settings. Members observed that studies by government agencies (the General Accounting Office [GAO] and the Inspector General [IG] of the Department of Health and Human Services) attempt to calculate a provider's acquisition price for a prescription drug product by estimating it from the average wholesale price less discounts and

other price concessions. Policy proposals based on these studies use an extreme example of high margin between acquisition cost and actual reimbursement and presume that is applicable for most or all products.

Members believed transparency of a provider's acquisition cost would enable accurate reimbursement for the acquisition cost of the drug. Transparency about a provider's cost of a prescription drug would not force price reductions by any entity throughout the supply chain, but it would enable CMS to obtain acquisition prices directly from a pharmacy. The Council also noted the need to explicitly reimburse pharmacy providers for all costs associated with providing beneficiaries with the product in a safe and appropriate manner, including payment for indirect costs and practice expenses related to the provision of pharmacy services. These costs are not currently well documented by the profession; therefore, further study is needed to ensure proper reimbursement. Subsequently, with the passage of MMA, studies and market surveys by the GAO and IG will begin to identify these costs in order to achieve transparency of a provider's acquisition cost.

Finally, the Council felt that with enactment of an outpatient prescription drug benefit for Medicare, CMS could develop options for electronic adjudication of claims for covered medications and related pharmacist services similar to those of state Medicaid programs.

Policy 0317, Medicare Prescription Drug Benefit, reads:

To strongly advocate a fully funded prescription drug program for eligible Medicare beneficiaries that maintains the continuity of patient care and ensures the best use of medications (*fully funded* means the federal government will make adequate funds available to fully cover the Medicare program's share of prescription drug program costs; *eligible* means that the federal government may establish criteria by which Medicare beneficiaries qualify for the prescription drug program); further,

To recommend that the program should at a minimum contain the following: (1) appropriate product reimbursement, (2) appropriate coverage and payment for patient care services provided by pharmacists, and (3) open access that allows any willing provider to participate.

B. Compounding by Health Professionals

To advocate the adoption, in all applicable state laws and regulations governing health care practice, of the intent of the requirements and the outcomes for patient safety as described in *United States Pharmacopeia* Chapter 797 ("Pharmaceutical Compounding—Sterile Preparations").

Background

The Council discussed portions of a delegate Recommendation concerning the practice of compounding in general and compounding of sterile preparations in particular. The Council's discussion included a review of the new *United States Pharmacopeia* (USP) Chapter 797, "Pharmaceutical Compounding—Sterile Preparations" (effective January 1, 2004). The Council also reviewed the Food and Drug Administration's (FDA) compliance policy guides (CPGs) dealing with compounding in hospitals (CPG 460.100) and pharmacy compounding in general (CPG 460.200).

In addition, the Council received a status report on the depth of regulation by state boards of pharmacy and noted that 15 states refer to USP standards in their regulations. However, recent activity by state boards is leading to a patchwork of regulation at the state level. A lack of consistency among states with respect to the USP standards or ASHP guidelines was noted. The Council noted and the Board agreed that compounding is an inherent part of the practice of pharmacy and should remain a state-regulated activity, but that recent incidents leading to death and injury require the adoption of a uniform national standard by state boards of pharmacy, including assertive oversight. In addition, the Council underscored and the Board concurred with the need for state boards to have

adequate resources and properly trained inspectors to protect the public health with respect to compounded preparations.

It is important to note that the Council and Board wanted compounding, particularly of sterile preparations, to be consistently and uniformly regulated by the states in accordance with the intent of USP Chapter 797 across all health professions and practice settings. The Council and Board particularly wanted the practice of compounding sterile preparations in patient care areas and physician offices covered by this chapter as referenced in applicable state regulations. In addition, the Council suggested that ASHP work with the National Association of Boards of Pharmacy (NABP) to incorporate a reference to the chapter in its model pharmacy practice act.

The Council also discussed preliminary planning of possible initiatives by the profession to accredit pharmacies that engage in compounding, certify pharmacists who compound preparations, and verify the ingredients used in compounding. The Council also requested that ASHP seek clarification from the FDA concerning the treatment of investigational new drug protocols as they relate to current agency guidance on compounding.

C. Uniform State Laws and Regulations Regarding Pharmacy Technicians

To advocate that pharmacy move toward the following model with respect to technicians as the optimal approach to protecting public health and safety: (1) development and adoption of uniform state laws and regulations regarding pharmacy technicians, (2) mandatory completion of a nationally accredited standardized program of education and training as a prerequisite to pharmacy technician certification, and (3) mandatory certification by the Pharmacy Technician Certification Board (or another comparable nationally validated, psychometrically sound certification program approved by the state board of pharmacy) as a prerequisite to the state board of pharmacy granting the technician permission to engage in the full scope of responsibilities authorized by the state; further,

To advocate registration of pharmacy technicians by state boards of pharmacy; further,

To advocate, with respect to certification, as an interim measure until the optimal model is fully implemented, that individuals be required either (1) to have completed a nationally accredited standardized program of education and training or (2) to have at least one year of full-time equivalent experience as pharmacy technicians before they are eligible to become certified; further,

To advocate that licensed pharmacists be held accountable for the quality of pharmacy services provided and the actions of pharmacy technicians under their charge.

(Note: *Certification* is the process by which a nongovernmental agency or association grants recognition to an individual who has met certain predetermined qualifications specified by that agency or association. *Registration* is the process of making a list or being enrolled in an existing list; registration should be used to help safeguard the public through interstate and intrastate tracking of the technician work force and preventing individuals with documented problems from serving as pharmacy technicians.)

(Note: This proposed policy would supersede ASHP policy 0322).

Background

In their consideration of work force issues, the Council on Educational Affairs (COEA) and the Council on Legal and Public Affairs (COLPA) discussed requirements for certification of technicians and the regulatory role of state boards of pharmacy. The COEA proposed a policy addressing the requirements for a pharmacy technician to be eligible to sit for the PTCB exam. Those requirements were either completion of an accredited program of education and experiential training or one year of full-time experience as a pharmacy technician. The Board decided to include this point in the revision of policy 0322 presented here.

The Council on Legal and Public Affairs reviewed policy 0322 in light of state legislative proposals that require a pharmacy technician to be certified by passing the Pharmacy Technician Certification Board (PTCB) exam or an exam approved by the state board of pharmacy. Policy 0322 advocates that state governments mandate certification by PTCB of all pharmacy technicians. Council members observed that a requirement for the PTCB exam exclusively would be rejected by state boards, since boards would always want the option to approve other exams, similar to their option to use the North American Pharmacist Licensure Examination (NAPLEX) or another board-approved exam for pharmacist licensure. Council members held differing opinions on whether to approve a nationally recognized certification program other than that administered by PTCB. The Council believed standards-based training is needed before certification to ensure that technicians are adequately prepared to practice in all settings. The Council had much discussion and a close vote on the revision of policy 0322. Members noted that it was likely that states would adopt the PTCB exam out of practicality, since more than 150,000 technicians are already certified through the PTCB process.

The Board also considered ASHP's comments to the Accreditation Council for Pharmacy Education (ACPE) on "The Need for Uniform National Standards for the Education and Training of Pharmacy Technicians," which proposed a logical relationship among several steps that should be taken to formalize the occupation of pharmacy technicians. That relationship is captured in the first clause of the policy proposal. The three-part model described here addresses uniform state laws and regulations, mandatory education and training, and mandatory certification. The second clause continues existing ASHP policy that advocates registration of pharmacy technicians by boards of pharmacy to track the work force and prevent an individual with documented problems from serving as a technician in another state. The third clause captures the recommendation of the Council on Educational Affairs regarding eligibility for certification. The fourth clause continues existing policy that advocates accountability by a licensed pharmacist.

Policy 0322, Regulation of Pharmacy Technicians, reads:

To advocate and support registration of pharmacy technicians by state boards of pharmacy (*registration* is the process of making a list or being enrolled in an existing list; registration should be used to help safeguard the public through interstate and intrastate tracking of the technician work force and preventing individuals with documented problems from serving as pharmacy technicians); further,

To advocate that state governments mandate certification by the Pharmacy Technician Certification Board (PTCB) of all pharmacy technicians (*certification* is the process by which a nongovernmental agency or association grants recognition to an individual who has met certain predetermined qualifications specified by that agency or association); further,

To advocate the adoption of uniform standards for the education and training of all pharmacy technicians to ensure competence and the protection of public health and safety; further,

To advocate that licensed pharmacists should be held accountable for the quality of pharmacy services provided and the actions of pharmacy technicians under their charge.

D. Importation of Pharmaceuticals

To oppose importation of pharmaceuticals except in cases in which the Food and Drug Administration determines it would be necessary for the health and welfare of United States citizens.

(Note: This proposed policy would supersede ASHP policy 0320.)

Background

The Council discussed the illegal importation (currently described by some in Congress as re-importation) of prescription drug products from a variety of countries. Council and Board members noted that the terms "re-importation" and "importation" were often used interchangeably. They further noted that although legal importation by manufacturers is allowed by the FDA, importation by individuals is considered illegal. Moreover, the Council and Board noted that the issue of the safety of the drug supply is being obscured by the issue of allowing individual citizens to purchase prescription drugs from overseas locations in an attempt to purchase medications at lower prices. Council members continued to believe and the Board concurred that the integrity of the drug supply is paramount and that options other than importation, including adequate prescription drug coverage for seniors and other uninsured individuals, would permit access to medications from locations in the United States, with the benefit of oversight by the FDA and state boards of pharmacy. To maintain clarity and avoid confusing terms in policy 0320, adopted by the House of Delegates last year, the Council suggested deleting the term re-importation and replacing it with importation.

Policy 0320, Re-importation of Pharmaceuticals, reads:

To oppose re-importation of pharmaceuticals except in cases where the Food and Drug Administration determines it would be necessary for the health and welfare of United States citizens.

E. Home Intravenous Therapy Benefit

To support the continuation of a home intravenous therapy benefit under federal and private health insurance plans, and expand the home infusion benefit under Medicare Part B at an appropriate level of reimbursement for the associated pharmaceutical services, supplies, and equipment.

(Note: This proposed policy would supersede ASHP policy 9004.)

Background

Policy 9004 was reviewed as part of sunset review. The Council believed and the Board concurred that it is important to have a policy on home intravenous and related services. The Council revised the policy to reflect the profession's experience with the benefit since it was adopted by Medicare. The policy was revised to support continuation and expansion of the benefit and appropriate reimbursement. The Council also incorporated the sense of policy 8212, Home Health Care, which was proposed for discontinuation.

Policy 9004, Home Intravenous Therapy, reads:

To support the implementation of a home intravenous therapy benefit under federal and private medical plans, along with an appropriate level of reimbursement for the pharmaceutical services, supplies, and equipment associated with this type of health care.

F. Home Health Care

To discontinue ASHP policy 8212, Home Health Care, which reads:

To support, based on the following principles, the extension of home health services under Medicare and Medicaid as alternatives to institutionalization:

1. Pharmaceutical services should be covered specifically in any legislation.
2. Pharmaceutical services should be a required provision of all home health programs.
3. The responsibility for financial control and quality of services should be assumed through a centralized provider entity.

Background

In sunset review of this policy, the Council believed and the Board concurred that the policy's purposes had been achieved and that the sense of the policy was sufficiently covered in the proposed policy that revises and supersedes policy 9004.

G. NABP Model Pharmacy Practice Act Language

To discontinue ASHP policy 9409, NABP Model Pharmacy Practice Act Language on the Responsibility of the Pharmacist for Overall Medication Distribution Systems, which reads:

ASHP should work with the National Association of Boards of Pharmacy to clarify language in the Model Pharmacy Practice Act concerning the responsibility of the pharmacist for the overall medication distribution system and to eliminate specific task requirements, allowing practitioners to focus on improving drug therapy through formulation of a therapeutic plan and detection, prevention, and resolution of medication-related problems.

Background

The policy was reviewed as part of sunset review, and the Council and Board believed NABP's model act now reflects the policy's intent.

H. Generic Pharmaceutical Testing

To discontinue ASHP policy 9010, Generic Pharmaceutical Testing, which reads:

To support and foster legislative and regulatory initiatives designed to improve and restore public and professional confidence in the drug approval and regulatory process in which all relevant data are subject to public scrutiny.

Background

The policy was reviewed as part of sunset review, and the Council and Board believed that the public's confidence in generics had been restored and there were no current concerns in this area.

Board actions

Task analysis of technician practice. The Council recommended and the Board voted

To request that the Pharmacy Technician Certification Board conduct a new task analysis to assess new levels of practice by technicians.

The Council strongly encouraged ASHP to request that the Pharmacy Technician Certification Board conduct a new task analysis to assess current levels of practice in all settings by technicians. Council members were concerned that the entry level for pharmacy technician certification may not reflect the level of skills technicians need to perform certain tasks in all areas of practice while still protecting the public health. Members noted that technicians' practice has evolved since the PTCB program was established and that a new task analysis was needed to determine standards for the exam and qualifications for taking the exam. In addition, such a task analysis would serve as a basis for considering additional testing and qualifications for technician practice.

Health-system centralized repackaging. The Council recommended and the Board voted

To seek clarification from the Food and Drug Administration concerning the ability of a health system to repackage patient-specific and non-patient-specific medication doses for use within the system.

As part of its discussion concerning counterfeit pharmaceuticals, the Council also discussed a delegate Recommendation concerning regulation of repackaging operations by health systems for medications used by patients of a particular system. There are reports that health-system centralized repackaging of patient-specific and non-patient-specific doses is being disallowed by FDA inspectors. However, members report that state board inspectors allow such repackaging for hospitals and health systems that are under the common control of a health care entity.

Sunset review of ASHP professional policies. As part of sunset review of existing ASHP policies, the following were reviewed by the Council and Board and found to be still appropriate. (No action by the House of Delegates is needed to continue these policies.)

- ASHP Position on Assisted Suicide (9915)
- ASHP Statement on Pharmacist's Decision-making on Assisted Suicide (9916)
- Reporting Medication Errors and Adverse Drug Reactions (9918)
- Management of Blood Products and Derivatives (9919)
- Drug Nomenclature (9011)
- Therapeutic Interchange (8708)

Other Council activity

Medication therapy management services and provider status under Medicare. The Council received an update on legislation that would provide a prescription drug benefit for Medicare beneficiaries. Specifically, it would create a new Part D benefit for beneficiaries who choose to pay a monthly premium for this coverage. The benefit would be provided by health plans that contract to provide the services, which would include medication therapy management services (MTMS). Council members noted that MTMS is a step toward full provider status under Part B of the Medicare program.

Council members urged ASHP to consider educational programming for the membership and increasing public awareness about MTMS under the Part D benefit and other provisions of the new law. The Council also believed ASHP should develop communication materials that pharmacists can use to convince administrators about providing these services. Publication of such material should be targeted to periodicals and journals that reach administrators.

Counterfeit medications. The Council discussed the current situation concerning counterfeit drugs and the effectiveness of federal and state laws to prevent those products from entering the supply chain. Members reviewed the status of regulations to implement the Prescription Drug Marketing Act of 1987 and noted that the effective date had been postponed five times. In addition, the Council discussed a new law and regulations in Florida and noted the requirement for a seller to provide a certified and authenticated sales history of the product throughout the supply chain, originating with the source manufacturer. Council members observed that although the new Florida law and regulations are an important first step, changes in technology need to be accommodated in any reformed regulatory scheme. For example, techniques used by the U.S. Treasury in protecting the nation's currency should be adapted for the pharmaceutical supply chain. Council members noted the need for uniformity of state regulation or a national process in order to hold drug wholesalers (authorized and secondary) to the same standard, thereby maintaining the integrity of the drug supply. Any changes in federal law and regulation should be consistent with recent changes made in Florida. The council reviewed policy 0321 and believed it was appropriate and adequate to address this issue. The Council also believed that because of the interstate nature of the supply chain, FDA should be the lead regulator with respect to transactions by wholesalers and others that involve interstate commerce. The Council believed there is still a role for state government in regulating the activities of wholesalers as in-state business entities (e.g., tax collection, employment law).

The Council also briefly discussed products that are in short supply in relation to the issue of counterfeiting and the sudden availability of these products from secondary wholesalers and other suppliers. The Council noted the need for ASHP to collect promotional materials (facsimile and other solicitations) from these suppliers and provide them to FDA and other appropriate agencies for verification of the source of the product.

Patient safety. The Council reviewed the current status of FDA's proposed rule concerning machine-readable codes (bar coding) on prescription drug products. It noted that a final regulation was expected by the end of 2003 or early 2004. (A final rule was issued on February 26, 2004.) Council members believed current policy 0308 concerning machine-readable coding and related technology, developed by the Council on Administrative Affairs, was adequate for advocacy with FDA and others on this issue.

The Council also reviewed a proposal for a unique identifier for products that would include the lot number. It would combine the National Drug Code number and four more digits to allow for 9999 lots of a given product. The Council believed the proposal was a worthy idea but noted that other parts of the proposal involving tax credits to fund it were outside the jurisdiction of the FDA.

The Council reviewed current legislation that would provide for confidentiality and protection for individuals who voluntarily report medical or medication errors to patient safety organizations

(PSOs). Council members noted that the legislation would create a nonpunitive environment in which to learn from errors. They were pleased that existing PSOs that receive reports (e.g., the Institute for Safe Medication Practices) would be of the type protected from legal discovery in administrative and civil proceedings. Legislative language remains to be completed with respect to coverage for criminal proceedings.

Direct-to-consumer marketing. The Council discussed recent action by the FDA to review research on consumer-directed promotion of prescription drugs through print, broadcast, and other types of media. It noted that guidance published by the FDA in 1999 indicated the agency would review experience with the guidance to determine whether it would withdraw, continue, or modify the guidance. The Council believed there was no need to revise ASHP policy 9701, which opposes direct-to-consumer advertising of specific prescription drug products.

Comparative effectiveness studies. The Council discussed legislative proposals to require comparative effectiveness studies by the Agency for Healthcare Research and Quality prior to marketing. Council members acknowledged the need for unbiased head-to-head comparison of competing products, but they noted that it would be important for the data to be used appropriately so as not to restrict patients' access to medications that best meet their individual needs.

Regulation of dietary supplements. The Council was updated on recent dialogue with groups representing manufacturers of nonprescription drug products and dietary supplements. Council members noted that a statement on dietary supplements is currently being drafted to express ASHP's views on regulation of these products. Input from these groups has been solicited, and any comments received will be acknowledged in the final statement.

Public funding of residency programs and work force capacity building. The Council was updated on the current status of funding for pharmacy residency programs. It applauded the retention of funding for general pharmacy practice residencies for the 2004 fiscal year beginning October 1, 2003. The Council voted to seek clarification from the Centers for Medicare and Medicaid Services regarding funding for specialized residencies. Council members believed current ASHP policy 0325 was adequate for advocacy on the issue of finding ways to fund specialized residency programs. The Council also reviewed "The Case for Public Funding of Residency Programs," published by ASHP, and noted the need to pursue all five recommendations outlined in the paper, with particular emphasis on establishing dedicated funding for certain practice areas (geriatrics and primary care) and underserved locations. The Council also reviewed proposed legislation to create a Commission on the Healthcare Workforce and a recently initiated demonstration project for pharmacists by the National Health Service Corps.

Conscientious objection by pharmacists. The Council reviewed policy 9802 with respect to state legislation providing for emergency contraception. Members found the policy to be adequate in supporting a pharmacist's individual right to refuse to dispense a prescription while providing the right for the patient to receive the legally prescribed treatment.

Outcomes approach to state regulation. The Council also discussed a report by a task force of the National Association of Boards of Pharmacy on shifting the focus of pharmacy regulation from the dispensing process to regulating for outcomes. Council members described the situation in their own states and concluded that the concept was still evolving and that it warranted ongoing review by ASHP.

Emergency preparedness update. The Council reviewed emergency preparedness at the state and local levels. Council members reviewed advocacy material distributed to attendees at the an-

nual National Conference of State Legislators. It reinforces the need for federal, state, and local agencies to include pharmacy in planning and training for all types of hazards and emergency preparedness activities. A significant gap in coordination still exists between hospitals and state health departments as well as federal agencies. Council members observed that pharmacists are often not included in the first or primary level of communication about training and planning. This lack of inclusion leads to a gap in preparedness as it relates to the use of medications as part of a community's first response to a natural or manmade disaster. Council members acknowledged that progress had been made since September 11, 2001, but urged ASHP to continue to advocate a role for pharmacists in this critical area.

Health-System Pharmacy 2015. The Council discussed the goals and objectives of ASHP's Health-System Pharmacy 2015 initiative. In relation to the Council's purview dealing with laws and regulations as well as pharmacy ethics, members noted that access to health care, understandable communications, and an adequate public health infrastructure are key to meeting the 2015 goals. Council members also noted that some goals may be set too low or that they may already be standards for accreditation by the Joint Commission on Accreditation of Healthcare Organizations (in the case of goal 2.3) or mandated by the Centers for Medicare and Medicaid Services for skilled-nursing facilities. Members acknowledged that, overall, the goals and objectives are ambitious but that much progress can be achieved over the 2015 initiative's life span of 12 years.

AGENDA ITEM D



RECEIVED BY CALIF
BOARD OF PHARMACY
2004 APR 13 11:57
Food and Drug Administration
Rockville MD 20857

APR 2 2004

- NOTICE TO BOARD OF PHARMACY - -

Dear Executive Director/Administrator:

In recent years, availability of "compounded" veterinary drug products has increased steadily. While some compounded drugs may have a place in veterinary practice, compounding of drugs for use in animals, except in limited circumstances, is not permitted under federal law.

The compounding of new animal drugs is only permitted if conducted in accordance with the Animal Medical Drug Use Clarification Act (AMDUCA) and its implementing regulations at Title 21, Code of Federal Regulations (21CFR), Part 530. Neither AMDUCA nor these regulations permit compounding from bulk drugs. Further, they required that compounding be done by or on the order of a licensed veterinarian, within the context of a valid veterinarian/client/patient relationship, and from approved human or veterinary drugs. Some approved drugs, however, are prohibited from extralabel use, including compounding, in food-producing animals, 21 CFR 530.41. On July 14, 2003, the Food and Drug Administration (FDA), Center for Veterinary Medicine (CVM) issued a revised Compliance Policy Guide that updated the Agency's policy on the enforcement of illegal compounded veterinary drug products.

In an effort to determine the extent of illegal veterinary compounding activities, CVM is issuing inspection assignments to FDA field offices to inspect certain pharmacies. These pharmacies were selected after evaluating trade complaints and promotional materials submitted to CVM over the last few years. Only twenty pharmacies were selected at this time due to limited resources.

The purpose of this letter is to request your Board's assistance and participation on these inspections. By your participation, the State and the FDA will learn the regulations pertaining to veterinary drug compounding that each enforces. If you are contacted by an FDA investigator, we hope that your Board will participate in this important initiative. While these initial inspections may not include a pharmacy from your State, we still wanted to inform you of FDA's position on compounded veterinary drugs and to request your participation in future assignments.

Thank you in advance for your time and efforts. Hopefully, together we can achieve a foundation for the safe and legal compounding of veterinary drugs. If you have any questions regarding this letter, please contact Compliance Officer William Bargo at 301-827-6605.

Sincerely yours,

A handwritten signature in cursive script that reads "Gloria J. Dunnavan". The signature is written in black ink and is positioned above the printed name and title.

Gloria J. Dunnavan

Director

Office of Compliance

Center of Veterinary Medicine



NCPA



APhA

American Pharmacists Association
Improving medication use. Advancing patient care.



**International Academy of
Compounding Pharmacists**

April 16, 2004

Gloria J. Dunnavan
Director
Office of Compliance
Center for Veterinary Medicine
Food and Drug Administration
7519 Standish Place
Rockville, MD 20855

RE: FDA Notice on Compounded Veterinary Medications

Dear Ms. Dunnavan:

The pharmacy organizations listed below have become aware of a notice (dated April 2, 2004) from the Food and Drug Administration's (FDA) Center for Veterinary Medicine (CVM) to the state boards of pharmacy regarding FDA's interpretation of a federal regulation, 21 CFR 530.13, to ban compounding from bulk drug substances for animal patients. We are writing to express our serious concern with this letter and the sudden change in FDA enforcement policy it indicates. We urge the Agency to retract this letter.

According to the April 2nd letter, the CVM's actions against "illegal" compounded veterinary products are based upon the Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA) and its implementing regulations at 21 CFR 530.13. We question FDA's interpretation of 21 CFR 530.13. Adopted in 1996, 21 CFR 530.13 addresses the "compounding of a product from approved animal or human drugs by a veterinarian or a pharmacist on the order of a veterinarian within the practice of veterinary medicine." While these regulations do not explicitly state that compounding from bulk drug substances is acceptable, 21 CFR 530.13 also does not explicitly prohibit the use of bulk drug substances to compound medications for animals, a traditional part of the practice of pharmacy. In fact, after the regulation's adoption, the Agency continued to allow veterinary compounding from bulk drug substances until now. We must question the basis for this apparent change in interpretation eight years later.

Congress and FDA have repeatedly recognized the importance of compounding from bulk drug substances for humans. Congress specified in Section 503A of the Food and Drug Administration Modernization Act of 1997 (FDAMA) that pharmacists may compound from bulk drug substances that:

1. comply with the standards of an applicable United States Pharmacopeia or National Formulary monograph, if a monograph exists, and the United States Pharmacopeia chapter on pharmacy compounding; or,
2. are drug substances that are components of drugs approved by the FDA; or
3. are drug substances that appear on a list developed, by the FDA.

After FDAMA Section 503A was struck down by the Supreme Court (not because the Court found compounding to be unsafe or illegal, but due to advertising restrictions found to violate

first amendment rights of freedom of speech), FDA issued a compliance policy guide for compounding for humans that clearly allows compounding from bulk drug substances. The FDA has given NO indication why compounding from bulk drugs for humans is acceptable but compounding from bulk drug substances for non-food-producing animals is unacceptable.

Perhaps most concerning about the Agency's sudden change in interpretation and enforcement of 21 CFR 530.13, is the lack of prior communication with the pharmacy and veterinary professions and state regulatory agencies. It is our understanding that the April 2nd letter is the first communication with state boards of pharmacy regarding the Agency's current intent to investigate veterinary compounding within their states – an area that has historically, and continues to be, within the state's authority.

This sudden and drastic change appears to stem from a July 2003 compliance policy guide (CPG) Sec. 608.400 - Compounding of Drugs for Use in Animals (CPG 7125.40) issued without allowing public input or collaboration with the pharmacy profession or state regulatory agencies. The new CPG differs dramatically from the Agency's prior CPG, issued in 1996, which stated that compounding from bulk drugs for non-food producing animals would not ordinarily be considered for regulatory action. The new CPG makes no distinction between food producing and non-food producing animals and incorrectly states the compounding for both populations is prohibited.

As the Agency is aware, there has been substantial controversy since the release of the new CPG. We believe that the FDA overstepped its authority in issuing the CPG and incorrectly includes the use of bulk drug ingredients as an indication of manufacturing. The form of compounded drug product ingredients should have no bearing on efforts to distinguish manufacturing, regulated by the FDA, from traditional compounding, regulated by the states. We also believe that FDA violated its own regulation by not allowing prior public input and that the refusal to have comment cannot be excused on the basis of a court decision issued 14 months earlier.

Until the controversy is resolved, we strongly urge the Agency to retract the letter to state boards of pharmacy. Any enforcement of the Agency's new interpretation of 21 CFR 530.13 by state boards of pharmacy or FDA would threaten the health and safety of thousands of animal patients. Veterinary compounding, including compounding with bulk drug substances, remains a vital element of many animals' medication therapies. Veterinary compounding serves a unique population that simply cannot always be treated using commercially available medications.

There are many circumstances that may require pharmacists to compound medications for veterinary patients from bulk drug substances. Situations that require compounding of such products may include:

- 1) Discontinued Products: commercial products that have been discontinued from the market, not for reasons of safety or effectiveness;
- 2) Product Purity: using finished dosage forms to compound sterile dosage forms may add unnecessary excipients to the compound and increase the risk of pyrogen contamination;
- 3) No Alternative Therapy: There is no commercial alternative to treat the disease state or condition remedied by the compounded product;
- 4) Patient Compliance: a compounded dosage form often improves therapeutic outcomes in animal patients by improving patient compliance.

The reality is that, if pharmacists are limited to using FDA-approved, commercially available drugs to compound products for animals, many animals would die, go untreated, or suffer needlessly.

Our organizations collectively have thousands of compounding pharmacist members committed to helping animals obtain the best medical result. The industry standard of practice is consistent with allowing the use of bulk drug substances in compounding for non-food producing animals. Pharmacists must be allowed access to bulk drug substances to meet veterinarian and animal patient needs, especially in non-food producing, companion, and exotic animals.

In summary, we request that the Agency retract its letter to state boards of pharmacy dated April 2, 2004. The sudden and dramatic change in interpretation of 21 CFR 530.13 appears unwarranted. The FDA has not provided any rationale for the change in interpretation of a regulation eight years after its adoption. We recommend an open dialogue between the FDA, the pharmacy and veterinary professions, state regulatory agencies, and other key stakeholders to ensure that pharmacists can continue to provide veterinarians and their animal patients with needed medications.

Sincerely,



John A. Gans, Executive Vice President
American Pharmacists Association (APhA)



L.D. King, Executive Director
International Academy of Compounding Pharmacists (IACP)



Bruce Roberts, Executive Vice President
National Community Pharmacists Association (NCPA)

cc: State Boards of Pharmacy
Lester Crawford, FDA Commissioner