COMMONWEALTH OF VIRGINIA

Meeting of the Board of Pharmacy

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Agenda of Meeting
Ad hoc Committee on Compounding

May 13, 2013

1pm-5pm

TOPIC	PAGE(S)

Call to Order: Jody H. Allen, Committee Chairman

- Welcome & Introductions
- Reading of Emergency Evacuation Script
- Approval of Agenda

Call for Public Comment: The Board will not receive comment on any regulation process for which a public comment period has closed or any pending disciplinary matters. The Board will receive comments on specific topics on this agenda at the time the matter is taken up by the Board.

Committee Objectives: To identify common areas of confusion and non-compliance with compounding requirements and recommend consensus language to the board for its consideration when adopting guidance to address the identified areas.

Overview of Compounding Requirements: Caroline Juran, Executive Director; Eric Kastango, Principal-CEO, Clinical IQ, LLC

- Va. Code §54.1-3410.2 (within HB2312), Regulation 18VAC110-20-321, and Guidance Document 110-36 — 1-10
- USP-NF requirements for sterile compounding — 11-14

Discuss 13 areas of confusion/non-compliance identified by staff & develop consensus language for providing guidance — 15

Review 17 draft FAQs suggested by staff — 16-18

Identify other possible areas of concern/non-compliance & develop consensus language for providing guidance

Adjournment

*****The committee will have a working lunch at 1pm; lunch will be provided for committee participants.**

VIRGINIA ACTS OF ASSEMBLY -- 2013 RECONVENED SESSION

CHAPTER 765

An Act to amend and reenact §§ 54.1-2408.1, 54.1-3401, 54.1-3410.2, 54.1-3434.1, and 54.1-3434.2 of the Code of Virginia, relating to compounding pharmacies.

[H 2312]

Approved April 3, 2013

Be it enacted by the General Assembly of Virginia:

1. That §§ 54.1-2408.1, 54.1-3401, 54.1-3410.2, 54.1-3434.1, and 54.1-3434.2 of the Code of Virginia are amended and reenacted as follows:

§ 54.1-2408.1. Summary action against licenses, certificates, registrations, or multistate licensure privilege; allegations to be in writing.

A. Any health regulatory board may suspend the license, certificate, registration, *permit,* or multistate licensure privilege of any person holding a license, certificate, registration, *permit,* or licensure privilege issued by it without a hearing simultaneously with the institution of proceedings for a hearing, if the relevant board finds that there is a substantial danger to the public health or safety which warrants this action. A board may meet by telephone conference call when summarily suspending a license, certificate, registration, *permit,* or licensure privilege if a good faith effort to assemble a quorum of the board has failed and, in the judgment of a majority of the members of the board, the continued practice by the individual constitutes a substantial danger to the public health or safety. Institution of proceedings for a hearing shall be provided simultaneously with the summary suspension. The hearing shall be scheduled within a reasonable time of the date of the summary suspension.

B. Any health regulatory board may restrict the license, certificate, registration, *permit,* or multistate licensure privilege of any person holding a license, certificate, registration, *permit,* or licensure privilege issued by it without proceeding simultaneously with notification of an informal conference pursuant to §§ 2.2-4019 and 54.1-2400, if the relevant board finds that there is a substantial danger to the public health or safety that warrants this action. A board may meet by telephone conference call when summarily restricting a license, certificate, registration, *permit,* or licensure privilege if a good faith effort to assemble a quorum of the board has failed and, in the judgment of a majority of the members of the board, the continued practice by the individual constitutes a substantial danger to the public health or safety. The informal conference shall be scheduled within a reasonable time of the date of the summary restriction.

C. Allegations of violations of this title shall be made in writing to the relevant health regulatory board.

§ 54.1-3401. Definitions.

As used in this chapter, unless the context requires a different meaning:

"Administer" means the direct application of a controlled substance, whether by injection, inhalation, ingestion or any other means, to the body of a patient or research subject by (i) a practitioner or by his authorized agent and under his direction or (ii) the patient or research subject at the direction and in the presence of the practitioner.

"Advertisement" means all representations disseminated in any manner or by any means, other than by labeling, for the purpose of inducing, or which are likely to induce, directly or indirectly, the purchase of drugs or devices.

"Agent" means an authorized person who acts on behalf of or at the direction of a manufacturer, distributor, or dispenser. It does not include a common or contract carrier, public warehouseman, or employee of the carrier or warehouseman.

"Anabolic steroid" means any drug or hormonal substance, chemically and pharmacologically related to testosterone, other than estrogens, progestins, corticosteroids, and dehydroepiandrosterone.

"Animal" means any nonhuman animate being endowed with the power of voluntary action.

"Automated drug dispensing system" means a mechanical or electronic system that performs operations or activities, other than compounding or administration, relating to pharmacy services, including the storage, dispensing, or distribution of drugs and the collection, control, and maintenance of all transaction information, to provide security and accountability for such drugs.

"Board" means the Board of Pharmacy.

"Bulk drug substance" means any substance that is represented for use, and that, when used in the compounding, manufacturing, processing, or packaging of a drug, becomes an active ingredient or a finished dosage form of the drug; however, "bulk drug substance" shall not include intermediates that are used in the synthesis of such substances.

"Change of ownership" of an existing entity permitted, registered or licensed by the Board means (i) the sale or transfer of all or substantially all of the assets of the entity or of any corporation that owns

or controls the entity; (ii) the creation of a partnership by a sole proprietor, the dissolution of a partnership, or change in partnership composition; (iii) the acquisition or disposal of 50 percent or more of the outstanding shares of voting stock of a corporation owning the entity or of the parent corporation of a wholly owned subsidiary owning the entity, except that this shall not apply to any corporation the voting stock of which is actively traded on any securities exchange or in any over-the-counter market; (iv) the merger of a corporation owning the entity or of the parent corporation of a wholly-owned subsidiary owning the entity with another business or corporation; or (v) the expiration or forfeiture of a corporation's charter.

"Compounding" means the combining of two or more ingredients to fabricate such ingredients into a single preparation and includes the mixing, assembling, packaging, or labeling of a drug or device (i) by a pharmacist, or within a permitted pharmacy, pursuant to a valid prescription issued for a medicinal or therapeutic purpose in the context of a bona fide practitioner-patient-pharmacist relationship, or in expectation of receiving a valid prescription based on observed *historical patterns of* prescribing ~~patterns~~ *and dispensing*; (ii) by ~~or~~ ~~for~~ a practitioner of medicine, osteopathy, podiatry, dentistry, or veterinary medicine as an incident to his administering or dispensing, if authorized to dispense, a controlled substance in the course of his professional practice; or (iii) for the purpose of, or as incident to, research, teaching, or chemical analysis and not for sale or for dispensing. The mixing, diluting, or reconstituting of a manufacturer's product drugs for the purpose of administration to a patient, when performed by a practitioner of medicine or osteopathy licensed under Chapter 29 (§ 54.1-2900 et seq.), a person supervised by such practitioner pursuant to subdivision A 6 or A 19 of § 54.1-2901, or a person supervised by such practitioner or a licensed nurse practitioner or physician assistant pursuant to subdivision A 4 of § 54.1-2901 shall not be considered compounding.

"Controlled substance" means a drug, substance or immediate precursor in Schedules I through VI of this chapter. The term shall not include distilled spirits, wine, malt beverages, or tobacco as those terms are defined or used in Title 3.2 or Title 4.1.

"DEA" means the Drug Enforcement Administration, United States Department of Justice, or its successor agency.

"Deliver" or "delivery" means the actual, constructive, or attempted transfer of any item regulated by this chapter, whether or not there exists an agency relationship.

"Device" means instruments, apparatus, and contrivances, including their components, parts and accessories, intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or animals or to affect the structure or any function of the body of man or animals.

"Dialysis care technician" or "dialysis patient care technician" means an individual who is certified by an organization approved by the Board of Health Professions pursuant to Chapter 27.01 (§ 54.1-2729.1 et seq.) and who, under the supervision of a licensed physician, nurse practitioner, physician assistant or a registered nurse, assists in the care of patients undergoing renal dialysis treatments in a Medicare-certified renal dialysis facility.

"Dialysis solution" means either the commercially available, unopened, sterile solutions whose purpose is to be instilled into the peritoneal cavity during the medical procedure known as peritoneal dialysis, or commercially available solutions whose purpose is to be used in the performance of hemodialysis not to include any solutions administered to the patient intravenously.

"Dispense" means to deliver a drug to an ultimate user or research subject by or pursuant to the lawful order of a practitioner, including the prescribing and administering, packaging, labeling or compounding necessary to prepare the substance for that delivery. However, dispensing shall not include the transportation of drugs mixed, diluted, or reconstituted in accordance with this chapter to other sites operated by such practitioner or that practitioner's medical practice for the purpose of administration of such drugs to patients of the practitioner or that practitioner's medical practice at such other sites. For practitioners of medicine or osteopathy, "dispense" shall only include the provision of drugs by a practitioner to patients to take with them away from the practitioner's place of practice.

"Dispenser" means a practitioner who dispenses.

"Distribute" means to deliver other than by administering or dispensing a controlled substance.

"Distributor" means a person who distributes.

"Drug" means (i) articles or substances recognized in the official United States Pharmacopoeia National Formulary or official Homeopathic Pharmacopoeia of the United States, or any supplement to any of them; (ii) articles or substances intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in man or animals; (iii) articles or substances, other than food, intended to affect the structure or any function of the body of man or animals; or (iv) articles or substances intended for use as a component of any article specified in clause (i), (ii), or (iii). "Drug" does not include devices or their components, parts or accessories.

"Drug product" means a specific drug in dosage form from a known source of manufacture, whether by brand or therapeutically equivalent drug product name.

"Electronic transmission prescription" means any prescription, other than an oral or written prescription or a prescription transmitted by facsimile machine, that is electronically transmitted directly to a pharmacy without interception or intervention from a third party from a practitioner authorized to

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prescribe or from one pharmacy to another pharmacy.

"Facsimile (FAX) prescription" means a written prescription or order, which is transmitted by an electronic device over telephone lines that sends the exact image to the receiving pharmacy in hard copy form.

"FDA" means the United States Food and Drug Administration.

"Hashish oil" means any oily extract containing one or more cannabinoids, but shall not include any such extract with a tetrahydrocannabinol content of less than 12 percent by weight.

"Immediate precursor" means a substance which the Board of Pharmacy has found to be and by regulation designates as being the principal compound commonly used or produced primarily for use, and which is an immediate chemical intermediary used or likely to be used in the manufacture of a controlled substance, the control of which is necessary to prevent, curtail, or limit manufacture.

"Label" means a display of written, printed or graphic matter upon the immediate container of any article. A requirement made by or under authority of this chapter that any word, statement or other information appear on the label shall not be considered to be complied with unless such word, statement or other information also appears on the outside container or wrapper, if any, of the retail package of such article, or is easily legible through the outside container or wrapper.

"Labeling" means all labels and other written, printed or graphic matter on an article or any of its containers or wrappers, or accompanying such article.

"Manufacture" means the production, preparation, propagation, conversion or processing of any item regulated by this chapter, either directly or indirectly by extraction from substances of natural origin, or independently by means of chemical synthesis, or by a combination of extraction and chemical synthesis, and includes any packaging or repackaging of the substance or labeling or relabeling of its container. This term does not include compounding.

"Manufacturer" means every person who manufactures.

"Marijuana" means any part of a plant of the genus Cannabis whether growing or not, its seeds or resin; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds, or its resin. Marijuana shall not include any oily extract containing one or more cannabinoids unless such extract contains less than 12 percent of tetrahydrocannabinol by weight, nor shall marijuana include the mature stalks of such plant, fiber produced from such stalk, oil or cake made from the seeds of such plant, unless such stalks, fiber, oil or cake is combined with other parts of plants of the genus Cannabis.

"Medical equipment supplier" means any person, as defined in § 1-230, engaged in the delivery to the ultimate consumer, pursuant to the lawful order of a practitioner, of hypodermic syringes and needles, medicinal oxygen, Schedule VI controlled devices, those Schedule VI controlled substances with no medicinal properties which are used for the operation and cleaning of medical equipment and solutions for peritoneal dialysis.

"Narcotic drug" means any of the following, whether produced directly or indirectly by extraction from substances of vegetable origin, or independently by means of chemical synthesis, or by a combination of extraction and chemical synthesis: (i) opium, opiates, and any salt, compound, derivative, or preparation of opium or opiates; (ii) any salt, compound, isomer, derivative, or preparation thereof which is chemically equivalent or identical with any of the substances referred to in clause (i), but not including the isoquinoline alkaloids of opium; (iii) opium poppy and poppy straw; (iv) coca leaves and any salt, compound, derivative, or preparation of coca leaves, and any salt, compound, isomer, derivative, or preparation thereof which is chemically equivalent or identical with any of these substances, but not including decocainized coca leaves or extraction of coca leaves which do not contain cocaine or ecgonine.

"New drug" means: (i) any drug, except a new animal drug or an animal feed bearing or containing a new animal drug, the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling, except that such a drug not so recognized shall not be deemed to be a "new drug" if at any time prior to the enactment of this chapter it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use; or (ii) any drug, except a new animal drug or an animal feed bearing or containing a new animal drug, the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions.

"Nuclear medicine technologist" means an individual who holds a current certification with the American Registry of Radiological Technologists or the Nuclear Medicine Technology Certification Board.

"Official compendium" means the official United States Pharmacopoeia National Formulary, official Homeopathic Pharmacopoeia of the United States, or any supplement to any of them.

"Official written order" means an order written on a form provided for that purpose by the United States Drug Enforcement Administration, under any laws of the United States making provision therefor,

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if such order forms are authorized and required by federal law, and if no such order form is provided then on an official form provided for that purpose by the Board of Pharmacy.

"Opiate" means any substance having an addiction-forming or addiction-sustaining liability similar to morphine or being capable of conversion into a drug having such addiction-forming or addiction-sustaining liability. It does not include, unless specifically designated as controlled under Article 4 (§ 54.1-3437 et seq.), the dextrorotatory isomer of 3-methoxy-n-methylmorphinan and its salts (dextromethorphan). It does include its racemic and levorotatory forms.

"Opium poppy" means the plant of the species Papaver somniferum L., except the seeds thereof.

"Original package" means the unbroken container or wrapping in which any drug or medicine is enclosed together with label and labeling, put up by or for the manufacturer, wholesaler, or distributor for use in the delivery or display of such article.

"Person" means both the plural and singular, as the case demands, and includes an individual, partnership, corporation, association, governmental agency, trust, or other institution or entity.

"Pharmacist-in-charge" means the person who, being licensed as a pharmacist, signs the application for a pharmacy permit and assumes full legal responsibility for the operation of the relevant pharmacy in a manner complying with the laws and regulations for the practice of pharmacy and the sale and dispensing of controlled substances; the "pharmacist-in-charge" shall personally supervise the pharmacy and the pharmacy's personnel as required by § 54.1-3432.

"Poppy straw" means all parts, except the seeds, of the opium poppy, after mowing.

"Practitioner" means a physician, dentist, licensed nurse practitioner pursuant to § 54.1-2957.01, licensed physician assistant pursuant to § 54.1-2952.1, pharmacist pursuant to § 54.1-3300, TPA-certified optometrist pursuant to Article 5 (§ 54.1-3222 et seq.) of Chapter 32, veterinarian, scientific investigator, or other person licensed, registered or otherwise permitted to distribute, dispense, prescribe and administer, or conduct research with respect to, a controlled substance in the course of professional practice or research in the Commonwealth.

"Prescriber" means a practitioner who is authorized pursuant to §§ 54.1-3303 and 54.1-3408 to issue a prescription.

"Prescription" means an order for drugs or medical supplies, written or signed or transmitted by word of mouth, telephone, telegraph or other means of communication to a pharmacist by a duly licensed physician, dentist, veterinarian or other practitioner, authorized by law to prescribe and administer such drugs or medical supplies.

"Prescription drug" means any drug required by federal law or regulation to be dispensed only pursuant to a prescription, including finished dosage forms and active ingredients subject to § 503 (b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 353 (b)).

"Production" or "produce" includes the manufacture, planting, cultivation, growing or harvesting of a controlled substance or marijuana.

"Proprietary medicine" means a completely compounded nonprescription drug in its unbroken, original package which does not contain any controlled substance or marijuana as defined in this chapter and is not in itself poisonous, and which is sold, offered, promoted or advertised directly to the general public by or under the authority of the manufacturer or primary distributor, under a trademark, trade name or other trade symbol privately owned, and the labeling of which conforms to the requirements of this chapter and applicable federal law. However, this definition shall not include a drug which is only advertised or promoted professionally to licensed practitioners, a narcotic or drug containing a narcotic, a drug which may be dispensed only upon prescription or the label of which bears substantially the statement "Warning - may be habit-forming," or a drug intended for injection.

"Radiopharmaceutical" means any drug that exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons and includes any non-radioactive reagent kit or radionuclide generator that is intended to be used in the preparation of any such substance, but does not include drugs such as carbon-containing compounds or potassium-containing salts that include trace quantities of naturally occurring radionuclides. The term also includes any biological product that is labeled with a radionuclide or intended solely to be labeled with a radionuclide.

"Sale" includes barter, exchange, or gift, or offer therefor, and each such transaction made by any person, whether as an individual, proprietor, agent, servant or employee.

"Therapeutically equivalent drug products" means drug products that contain the same active ingredients and are identical in strength or concentration, dosage form, and route of administration and that are classified as being therapeutically equivalent by the United States Food and Drug Administration pursuant to the definition of "therapeutically equivalent drug products" set forth in the most recent edition of the Approved Drug Products with Therapeutic Equivalence Evaluations, otherwise known as the "Orange Book."

"USP-NF" means the current edition of the United States Pharmacopeia-National Formulary.

"Warehouser" means any person, other than a wholesale distributor, engaged in the business of selling or otherwise distributing prescription drugs or devices to any person who is not the ultimate user or consumer. No person shall be subject to any state or local tax by reason of this definition.

"Wholesale distribution" means distribution of prescription drugs to persons other than consumers or

patients, subject to the exceptions set forth in § 54.1-3401.1.

"Wholesale distributor" means any person engaged in wholesale distribution of prescription drugs including, but not limited to, manufacturers; repackers; own-label distributors; private-label distributors; jobbers; brokers; warehouses, including manufacturers' and distributors' warehouses, chain drug warehouses conducting wholesale distributions, and wholesale drug warehouses; independent wholesale drug traders; and retail pharmacies conducting wholesale distributions. No person shall be subject to any state or local tax as a wholesale merchant by reason of this definition.

The words "drugs" and "devices" as used in Chapter 33 (§ 54.1-3300 et seq.) and in this chapter shall not include surgical or dental instruments, physical therapy equipment, X-ray apparatus or glasses or lenses for the eyes.

The terms "pharmacist," "pharmacy" and "practice of pharmacy" as used in this chapter shall be defined as provided in Chapter 33 (§ 54.1-3300 et seq.) unless the context requires a different meaning.

§ 54.1-3410.2. Compounding; pharmacists' authority to compound under certain conditions; labeling and record maintenance requirements.

A. A pharmacist may engage in compounding of drug products when the dispensing of such compounded products is (i) pursuant to valid prescriptions for specific patients and (ii) consistent with the provisions of § 54.1-3303 relating to the issuance of prescriptions and the dispensing of drugs.

Pharmacists shall label all compounded drug products that are dispensed pursuant to a prescription in accordance with this chapter and the Board's regulations, and shall include on the labeling an appropriate beyond-use date as determined by the pharmacist in compliance with USP-NF standards for pharmacy compounding.

B. A pharmacist may also engage in compounding of drug products in anticipation of receipt of prescriptions based on a routine, regularly observed prescribing pattern.

Pharmacists shall label all products compounded prior to dispensing with (i) the name and strength of the compounded medication or a list of the active ingredients and strengths; (ii) the pharmacy's assigned control number that corresponds with the compounding record; (iii) an appropriate beyond-use date as determined by the pharmacist in compliance with USP-NF standards for pharmacy compounding; and (iv) the quantity.

C. In accordance with the conditions set forth in subsections A and B, pharmacists shall not distribute compounded drug products for subsequent distribution or sale to other persons or to commercial entities, including distribution to pharmacies or other entities under common ownership or control with the facility in which such compounding takes place.

A pharmacist may, however, deliver compounded products dispensed pursuant to valid prescriptions to alternate delivery locations pursuant to § 54.1-3420.2.

A pharmacist may also provide compounded products to practitioners of medicine, osteopathy, podiatry, dentistry, or veterinary medicine to administer to their patients in the course of their professional practice, either personally or under their direct and immediate supervision.

Pharmacists shall label all compounded products distributed to practitioners for administration to their patients with (i) the statement "For Administering in Prescriber Practice Location Only"; (ii) the name and strength of the compounded medication or list of the active ingredients and strengths; (iii) the facility's control number; (iv) an appropriate beyond-use date as determined by the pharmacist in compliance with USP-NF standards for pharmacy compounding; and (v) quantity.

D. Pharmacists shall personally perform or personally supervise the compounding process, which shall include a final check for accuracy and conformity to the formula of the product being prepared, correct ingredients and calculations, accurate and precise measurements, appropriate conditions and procedures, and appearance of the final product.

E. Pharmacists shall ensure compliance with USP-NF standards for both sterile and non-sterile compounding.

F. Pharmacists may use bulk drug substances in compounding when such bulk drug substances:

1. Comply with the standards of an applicable United States Pharmacopoeia or National Formulary monograph, if such monograph exists, and the United States Pharmacopoeia chapter on pharmacy compounding; or are drug substances that are components of drugs approved by the FDA for use in the United States; or are otherwise approved by the FDA;

2. Are manufactured by an establishment that is registered by the FDA; or

3. Are distributed by a licensed wholesale distributor or registered nonresident wholesale distributor, or are distributed by a supplier otherwise approved by the FDA to distribute bulk drug substances if the pharmacist can establish purity and safety by reasonable means, such as lot analysis, manufacturer reputation, or reliability of the source.

G. Pharmacists may compound using ingredients that are not considered drug products in accordance with the USP-NF standards and guidance on pharmacy compounding.

H. Pharmacists shall not engage in the following:

1. The compounding for human use of a drug product that has been withdrawn or removed from the market by the FDA because such drug product or a component of such drug product has been found to be unsafe. However, this prohibition shall be limited to the scope of the FDA withdrawal; ~~or~~

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2. The regular compounding or the compounding of inordinate amounts of any drug products that are essentially copies of commercially available drug products. However, this prohibition shall not include (i) the compounding of any commercially available product when there is a change in the product ordered by the prescriber for an individual patient, (ii) the compounding of a commercially manufactured drug only during times when the product is not available from the manufacturer or supplier, (iii) the compounding of a commercially manufactured drug whose manufacturer has notified the FDA that the drug is unavailable due to a current drug shortage, (iv) the compounding of a commercially manufactured drug when the prescriber has indicated in the oral or written prescription for an individual patient that there is an emergent need for a drug that is not readily available within the time medically necessary, or (v) the mixing of two or more commercially available products regardless of whether the end product is a commercially available product; *or*

3. The compounding of inordinate amounts of any preparation in cases in which there is no observed historical pattern of prescriptions and dispensing to support an expectation of receiving a valid prescription for the preparation. The compounding of an inordinate amount of a preparation in such cases shall constitute manufacturing of drugs.

I. Pharmacists shall maintain records of all compounded drug products as part of the prescription, formula record, formula book, or other log or record. Records may be maintained electronically, manually, in a combination of both, or by any other readily retrievable method.

1. In addition to other requirements for prescription records, records for products compounded pursuant to a prescription order for a single patient where only manufacturers' finished products are used as components shall include the name and quantity of all components, the date of compounding and dispensing, the prescription number or other identifier of the prescription order, the total quantity of finished product, the signature or initials of the pharmacist or pharmacy technician performing the compounding, and the signature or initials of the pharmacist responsible for supervising the pharmacy technician and verifying the accuracy and integrity of compounded products.

2. In addition to the requirements of subdivision I 1, records for products compounded in bulk or batch in advance of dispensing or when bulk drug substances are used shall include: the generic name and the name of the manufacturer of each component or the brand name of each component; the manufacturer's lot number and expiration date for each component or when the original manufacturer's lot number and expiration date are unknown, the source of acquisition of the component; the assigned lot number if subdivided, the unit or package size and the number of units or packages prepared; and the beyond-use date. The criteria for establishing the beyond-use date shall be available for inspection by the Board.

3. A complete compounding formula listing all procedures, necessary equipment, necessary environmental considerations, and other factors in detail shall be maintained where such instructions are necessary to replicate a compounded product or where the compounding is difficult or complex and must be done by a certain process in order to ensure the integrity of the finished product.

4. A formal written quality assurance plan shall be maintained that describes specific monitoring and evaluation of compounding activities in accordance with USP-NF standards. Records shall be maintained showing compliance with monitoring and evaluation requirements of the plan to include training and initial and periodic competence assessment of personnel involved in compounding, monitoring of environmental controls and equipment calibration, and any end-product testing, if applicable.

J. Practitioners who may lawfully compound drugs for administering or dispensing to their own patients pursuant to §§ 54.1-3301, 54.1-3304, and 54.1-3304.1 shall comply with all provisions of this section and the relevant Board regulations.

K. Every pharmacist-in-charge or owner of a permitted pharmacy or a registered nonresident pharmacy engaging in sterile compounding shall notify the Board of its intention to dispense or otherwise deliver a sterile compounded drug product into the Commonwealth. Upon renewal of its permit or registration, a pharmacy or nonresident pharmacy shall notify the Board of its intention to continue dispensing or otherwise delivering sterile compounded drug products into the Commonwealth. Failure to provide notification to the Board shall constitute a violation of Chapter 33 (§ 54.1-3300 et seq.) or Chapter 34 (§ 54.1-3400 et seq.). The Board shall maintain this information in a manner that will allow the production of a list identifying all such sterile compounding pharmacies.

§ 54.1-3434.1. Nonresident pharmacies to register with Board.

A. Any pharmacy located outside the Commonwealth that ships, mails, or delivers, in any manner, Schedule II through VI drugs or devices pursuant to a prescription into the Commonwealth shall be considered a nonresident pharmacy, shall be registered with the Board, shall designate a pharmacist in charge who is licensed as a pharmacist in Virginia and is responsible for the pharmacy's compliance with this chapter, and shall disclose to the Board all of the following:

1. The location, names, and titles of all principal corporate officers and the name and Virginia license number of the designated pharmacist in charge, if applicable. A report containing this information shall be made on an annual basis and within 30 days after any change of office, corporate officer, or pharmacist in charge.

2. That it maintains, at all times, a current unrestricted license, permit, certificate, or registration to

conduct the pharmacy in compliance with the laws of the jurisdiction, within the United States or within another jurisdiction that may lawfully deliver prescription drugs directly or indirectly to consumers within the United States, in which it is a resident. The pharmacy shall also certify that it complies with all lawful directions and requests for information from the regulatory or licensing agency of the jurisdiction in which it is licensed as well as with all requests for information made by the Board pursuant to this section.

3. As a prerequisite to registering *or renewing a registration* with the Board, the nonresident pharmacy shall submit a copy of ~~the most recent~~ *a current* inspection report resulting from an inspection conducted by the regulatory or licensing agency of the jurisdiction in which it is located *that indicates compliance with the requirements of this chapter, including compliance with USP-NF standards for pharmacies performing sterile and non-sterile compounding.* The inspection report shall be deemed current *for the purpose of this subdivision* if the inspection was conducted ~~within the past five years~~ *(i) no more than six months prior to the date of submission of an application for registration with the Board or (ii) no more than two years prior to the date of submission of an application for renewal of a registration with the Board.* However, if the nonresident pharmacy has not been inspected by the regulatory or licensing agency of the jurisdiction in which it is licensed within the ~~past five years~~ *required period*, the Board may accept an inspection report or other documentation from another entity that is satisfactory to the Board or the Board may cause an inspection to be conducted by its duly authorized agent and may charge an inspection fee in an amount sufficient to cover the costs of the inspection.

4. For a nonresident pharmacy that dispenses more than 50 percent of its total prescription volume pursuant to an original prescription order received as a result of solicitation on the Internet, including the solicitation by electronic mail, that it is credentialed and has been inspected and that it has received certification from the National Association of Boards of Pharmacy that it is a Verified Internet Pharmacy Practice Site, or has received certification from a substantially similar program approved by the Board. The Board may, in its discretion, waive the requirements of this subdivision for a nonresident pharmacy that only does business within the Commonwealth in limited transactions.

5. That it maintains its records of prescription drugs or dangerous drugs or devices dispensed to patients in the Commonwealth so that the records are readily retrievable from the records of other drugs dispensed and provides a copy or report of such dispensing records to the Board, its authorized agents, or any agent designated by the Superintendent of the Department of State Police upon request within seven days of receipt of a request.

6. That its pharmacists do not knowingly fill or dispense a prescription for a patient in Virginia in violation of § 54.1-3303 and that it has informed its pharmacists that a pharmacist who dispenses a prescription that he knows or should have known was not written pursuant to a bona fide practitioner-patient relationship is guilty of unlawful distribution of a controlled substance in violation of § 18.2-248.

7. That it maintains a continuous quality improvement program as required of resident pharmacies, pursuant to § 54.1-3434.03.

The requirement that a nonresident pharmacy have a Virginia licensed pharmacist in charge shall not apply to a registered nonresident pharmacy that provides services as a pharmacy benefits administrator.

B. Any pharmacy subject to this section shall, during its regular hours of operation, but not less than six days per week, and for a minimum of 40 hours per week, provide a toll-free telephone service to facilitate communication between patients in the Commonwealth and a pharmacist at the pharmacy who has access to the patient's records. This toll-free number shall be disclosed on a label affixed to each container of drugs dispensed to patients in the Commonwealth.

C. Pharmacies subject to this section shall comply with the reporting requirements of the Prescription Monitoring Program as set forth in § 54.1-2521.

D. The registration fee shall be the fee specified for pharmacies within Virginia.

E. A nonresident pharmacy shall only deliver controlled substances that are dispensed pursuant to a prescription, directly to the consumer or his designated agent, or directly to a pharmacy located in Virginia pursuant to regulations of the Board.

§ 54.1-3434.2. Permit to be issued.

The Board shall only register nonresident pharmacies that maintain a current unrestricted license, certificate, permit, or registration as a pharmacy in a jurisdiction within the United States, or within another jurisdiction that may lawfully deliver prescription drugs directly or indirectly to consumers within the United States.

Applications for a nonresident pharmacy registration, under this section, shall be made on a form furnished by the Board. The Board may require such information as it deems is necessary to carry out the purpose of the section.

The permit or nonresident pharmacy registration shall be renewed annually on a date determined by the Board in regulation. Renewal is contingent upon the nonresident pharmacy providing documentation of *a current inspection report in accordance with subdivision A 3 of § 54.1-3434.1;* continuing current, unrestricted licensure in the resident jurisdiction; and continuing certification if required in subdivision

A 4 of § 54.1-3434.1.

from *Regulations Governing the Practice of Pharmacy*

18VAC110-20-321. Compounding.

The compounding of both sterile and non-sterile drug products shall be performed in accordance with USP-NF compounding standards and §54.1-3410.2 of the Code of Virginia.

Virginia Board of Pharmacy

COMPLIANCE WITH USP STANDARDS FOR COMPOUNDING

§54.1-3410.2 requires pharmacies performing sterile or non-sterile compounding to comply with USP Standards. USP standards for sterile and non-sterile compounding may be found in the current editions of the USP-NF. In accordance with 18VAC110-20-170, the Board requires a pharmacy to maintain references consistent with the pharmacy's scope of practice and with public safety.

USP Chapter 795 lists the requirements for non-sterile compounding including information about the compounding environment, equipment, stability criteria and beyond-use dating and records. USP Chapter 797 lists requirements for policies and procedures, training and evaluation of personnel performing sterile compounding, determining risk levels and the physical standards for the sterile compounding area. The Board expects that the requirements of Chapters 795 and 797 will be found in compliance at time of inspection.

The terms "annually" and "semiannually" as used in USP Chapters 795 and 797 are defined to mean every 12 months and every 6 months, respectively. Records associated with annual and semiannual requirements shall be maintained in accordance with USP standards. Such records may be maintained as an electronic image that provides an exact image of the document that is clearly legible provided such electronic image is retrievable and made available at the time of inspection or audit by the Board or an authorized agent.

Compounding Pharmacy Requirements & Practices: Safety and Quality of Compounding Medications

Eric S. Kastango, MBA, RPh, FASHP
Clinical IQ, LLC

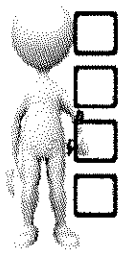
Disclaimer

"Although I am an USP Expert Consultant, I am speaking today in my individual capacity and not as a member of the Committee or as a USP representative.

The views and opinions presented are entirely my own. They do not necessarily reflect the views of USP, nor should they be construed as an official explanation or interpretation of <797>."

USP Chapter <797>

- The intent of the chapter was:
  - "to prevent patient harm and fatality from microbial contamination (nonsterility), excessive bacterial endotoxins, large content errors in the strength of correct ingredients, and incorrect ingredients in CSPs."
- Became effective January 1, 2004
- Revised December 2007
- Revisions official June 1, 2008
- Currently undergoing another revision (2010-2015)



USP Chapter <797>

- The chapter applies to ***all practice settings*** where CSPs are prepared and stored
  - health care institutions
  - Pharmacies
  - physician practice
  - other facilities
- Since it is numbered <1000, it is an ***enforceable standard***

USP <797>

5

- The intent of the chapter is "to prevent patient harm and fatality from microbial contamination (nonsterility), excessive bacterial endotoxins, large content errors in the strength of correct ingredients, and incorrect ingredients in CSPs."
- Effective January 1, 2004
  - Revised December 2007
  - Official June 1, 2008
- Scope of chapter:
  - Applies to all practice settings where CSP's are prepared and stored (Health care institutions, pharmacies, physician practices and other facilities)

As A Reminder....

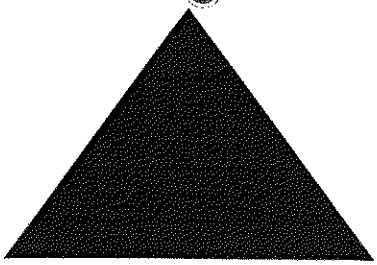
- Chapters <797> are the U.S. Standards for quality in sterile compounding respectively by act of Congress
- USP <797> applies to pre-administration manipulations of compounded sterile preparations including compounding, transportation, and storage.
- USP <797> applies to all compounding personnel without distinction as to site or profession – all patients deserve to be protected from medication errors and contamination

USP <797> Elements

- There are three broad areas that contribute to meeting the objectives of USP <797>

Contamination Control	Training and Documentation	CSP Checks and Tests
• Address particulate contamination, personnel, products, process • Create a clean environment where aseptic manipulations will take place	• Competency for personnel and others allowed in cleanroom • Theoretical training for proficiency • Written policies, procedures • Document training	• Reduce occurrence of contamination • Verify the process (validated aseptic CSPs) • Use the same process each time • If contamination or error happens, detect it and take action

Underlying USP <797> Philosophy: A risk based approach to CSPs



Source: CliniRPJ, LLC; USP-NF2010, Chapter <797>, and Fortenge, ES. Blueprint for implementing USP Chapter <797> for compounding sterile preparations. *Am J Health-Syst Pharm*. 2005; 62:1271-88.

Chapter<797> Beyond-Use Dating (BUD) Paradigm

- Recognizes the possibility that the CSP was inadvertently contaminated during compounding process
- For patient safety, BUD based on two factors:
  - Drug's chemical stability in conjunction with microbiological limits,
- Concern that microbial over-colonization of solutions would occur over time.
  - pH of solution is a consideration
    - Neutral (pH 6-8) favorable for microbial colonization
- BUD will always be whichever is shorter

Microbiological BUD

Risk Category	Room Temp	Refrigerator	Freezer (≤-10 °C)
Immediate Use	1 hour	1 hour	N/A
Low	48 hours	14 days	45 days
Low w/ 12-hr BUD	12 hours or less	12 hours or less	N/A
Medium	30 hours	9 days	45 days
High	24 hours	3 days	45 days

Hazardous Drugs as CSPs

- NIOSH Guidelines consulted for guidance
- Use of a ventilated cabinet
  - BSC or CACI required
- Hazardous drug storage and preparation in separate negative pressure ISO 7 with ISO 7 ante area
- Personnel protection specified
- Use of closed-system transfer devices must be within BSC or CACI
- Disposal according to state and federal regulations

Hand Hygiene

- Hand washing is defined as the vigorous, brief (30 seconds) rubbing together of all surfaces of lathered hands, followed by rinsing under a stream of water.
- Hand washing suspends microorganisms and mechanically removes them by rinsing with water.
- Single most important way to reduce the risks of transmitting germs
- Even after using anti-microbial soap, there is still about 20,000 microbes per sq. mm

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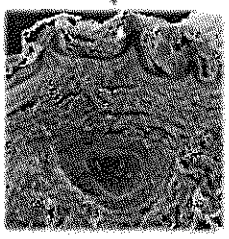
Compounding Personnel

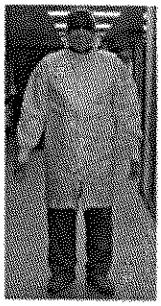
Stratum Corneum: surface of skin composed of dead skin cells



- People are "particle generators". Even though we can't "see" it, we shed over **one million** skin cells per hour! And, those cells contain microorganisms
- The human body harbors an average of 150-200 different classes of bacteria
- The body sheds 5 grams of skin fragments each day along with shedding 1 layer of skin every 5 days (size range 10 to 300 micron – 1000th of a mm)
- "Our greatest asset and also our biggest liability!"

Compounding Personnel

- Hair net
- Beard cover and face mask
- Gown
  - Nonsterile
- Gloves
  - Sterile
- Shoe covers



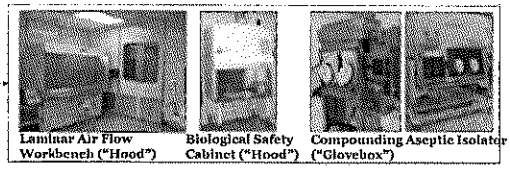
Environmental Controls

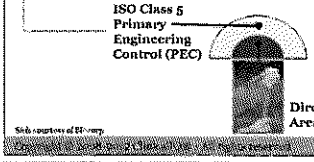
- Aimed at creating ISO 5, 7, and 8 environments
- ISO 5 – LAFW, BSC, CAI, CACI are "Primary Engineering Controls"
- Must maintain ISO 5 during dynamic (in use) working conditions
- Unidirectional airflow required

Environmental Controls

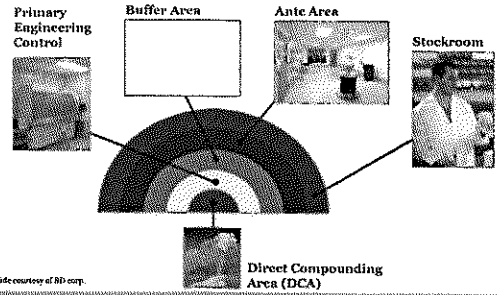
- ISO 7 buffer area and ISO 8 ante area – are "Secondary engineering controls"
- Must maintain ISO 7 or 8 during dynamic (in use) working conditions
- Airflow and balance testing required at the installation site
- Only personnel and materials essential for compounding and cleaning are permitted

Primary Engineering Controls





Surround the DCA with layers of protection



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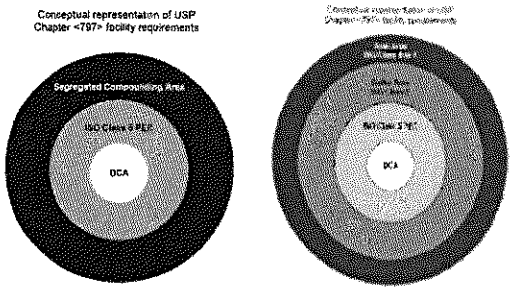
ISO Class 5 Sources, Buffer Areas, and Ante Areas



Environmental Sampling

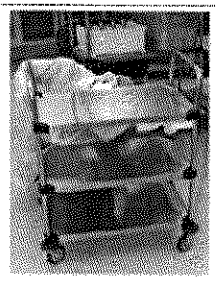
- Environmental Sampling section has been separated into a facility-related performance metric and a personnel –related performance metric
- Facility-related Environmental Sampling
  - Viable air sampling via volumetric method (impaction) to occur at least every 6 months
- Personnel-related Environmental Sampling
  - Personnel fingertip sampling during initial training, with media fills and as a competency assessment tool
  - Surface sampling for viable microorganisms

Environmental Sampling

- Designed to demonstrate that the primary and secondary engineering controls, disinfecting procedures, and work practices result in a suitable environment for aseptic compounding
- Utilizes several approaches to assess and evaluate:
  - Total particle counts
  - Air viable organism cfu
  - Surface viable organism cfu
  - Finger touch plates

Cleaning and Disinfection

- Routine cleaning & disinfection decreases the overall *bioburden* in the compounding area therefore reducing the risk of contamination to *CSPs*.
- It is one part of an overall quality management plan. Other components include:
  - Design/function of *primary* and *secondary engineering controls*
  - Material/component handling procedures
  - Personnel hand hygiene and garbing
  - Environmental sampling/testing



Images courtesy CleanIQ™, LLC.

Standard Operating Procedures

- Requires formalized policies, processes and procedures used in preparing CSPs
- One element of quality that may not be routinely performed in pharmacies is documentation, or written "proof" that compounding occurring properly

Remember the Patient

- Even though you may not see the patient, always remember that real people, the patients, receive CSPs made at your pharmacy.
- Patients who receive CSPs are mothers and fathers, brothers and sisters. They are loved ones who need to receive our best efforts.

14

Background:
To facilitate discussion, staff has identified 13 areas of confusion/non-compliance for which the committee may consider providing guidance. Additionally, staff drafted 17 FAQs below for the committee's consideration and approval as a means of providing guidance.

Areas of concern/non-compliance identified by staff for which the committee may choose to provide guidance:

1. How to perform appropriate sterility testing & areas to consider when evaluating quality of an outside testing company
   a. Method suitability
   b. Membrane filtration vs. direct inoculation
   c. The use of two media (TSB and FTM)
   d. Best practices for associated recordkeeping
2. Compounding in batches and when sterility testing must be performed
3. How to extend BUD
4. Use of 0.22 micron filters and filter integrity testing (aka bubble point)
5. Employee aseptic media fills and gloved fingertip sampling; best practices for associated recordkeeping
6. Air and surface sampling
7. Certification of cleanrooms and primary engineering controls; areas to consider when evaluating quality of a certification company; clarification that certifications must be performed under dynamic conditions and indicate ISO standard, not simply whether room "passed"
8. When must a CSP be placed in an autoclave
9. Clarification regarding multidose meeting USP 51; preservative not sufficient, must do testing to determine appropriate multi-dose vial
10. Recommended BUDs referenced in Chapter <795> for non-sterile compounds and whether pharmacists may exceed these recommended BUDs
11. Under what conditions may a glovebox be used to perform sterile compounding; room conditions; risk levels which may be performed
12. May hazardous drugs be made in the same hood as nonhazardous drugs
13. Under what conditions may hazardous drugs be made in a positive air pressure room

Other areas of concern/non-compliance for which staff drafted FAQs for the committee's consideration and approval:

1. ***Where may information regarding USP-NF standards for compounding be located?***
   A subscription to the current version of "USP on Compounding: A Guide for the Compounding Practitioner" may be purchased at http://www.usp.org/store/products-services/usp-compounding This guide provides access to all compounding-related General Chapters from the USP-NF and is updated with the release of each new USP-NF edition and supplement. The latest edition, USP 36- NF 31, published on November 1, 2012 becomes official May 1, 2013.

2. ***Does the law require compliance only with Chapter 797?***
   No, the law requires compliance with all applicable chapters within USP-NF. Regarding sterile compounding, pharmacists should pay particularly close attention to General Chapters: <1> Injections, <51> Antimicrobial Effectiveness Testing, <71> Sterility Testing, <85> Bacterial Endotoxin Testing, and <797> Pharmaceutical Compounding-Sterile Preparations.

3. ***In the absence of sterility testing, what beyond use dates (BUDs) must be used?***
   When sterility testing has not been performed, the assigned BUD must not exceed the following allowances:

	Controlled Room Temperature	Refrigerator	Freezer
Low-risk	48 hours	14 days	45 days
Medium-risk	30 hours	9 days	45 days
High-risk	24 hours	3 days	45 days

4. ***Is it appropriate to assign a BUD of 90 days in the absence of sterility testing if there is literature indicating the stability of the drug is assured for 90 days?***
   No, it is inappropriate and a violation of law to assign a BUD which exceeds the USP default BUDs in the absence of sterility testing. Drug stability should not be confused with drug sterility.

5. ***What is skip lot testing and may skip lot testing be used to perform sterility testing of compounded sterile products?***
   Skip lot testing is a process that only tests a fraction of the drugs compounded. It is NOT appropriate for sterility testing. It may only be used for ensuring consistency and drug strength (potency). Because skip lot testing is complex and requires a robust program, it may not be possible for a pharmacy to properly implement. Information regarding skip lot testing may be accessed at
   http://www.itl.nist.gov/div898/handbook/pmc/section2/pmc27.htm

6. ***How may a hospital pharmacy "batch-producing" limited quantity of CSPs for IN-HOUSE use extend the BUD past the default dating in Chapter <797> (referenced in question 3)?***

EACH BATCH must undergo sterility testing in accordance with USP Chapter <71> in order to extend the BUD past the default dating in Chapter <797> and the appropriate documentation must be kept on file for presentation upon inspection.

7. ***How often must the primary engineering control, e.g., laminar airflow workbench and secondary engineering control, e.g., ante and buffer rooms be certified?***
Certification of the primary and secondary engineering controls shall be performed no less than every six months and whenever the device or room is relocated, altered, or major service to the facility is performed. The certification must be performed no later than *the last day of the sixth month*, following the previous certification.
***Note- this guidance reflects a change to Major Deficiencies 22 and 23 in Guidance Document 110-9 which was amended at the March 2013 full board meeting.

8. ***Must pharmacists, who only verify the accuracy of the CSP and do not directly prepare the CSP, perform media-fill testing?***
Yes, pharmacists that verify the accuracy of a CSP must have also performed and passed a media fill test prior to performing this function.

9. ***Must compounding personnel who work in multiple pharmacies, to include pharmacy interns on rotations, pass a media-fill test at each pharmacy where they will prepare CSPs?***
Yes, all compounding personnel working in multiple pharmacies, to include pharmacy interns on rotations, must pass a media-fill test at each pharmacy prior to performing sterile compounding.

10. ***How often must media-fill testing be performed?***
Media-fill testing of all compounding personnel shall be performed initially prior to beginning sterile compounding and at least annually thereafter for low and medium-risk compounding, and semiannually for high-risk level compounding. ***Note - the terms "annually" and "semi-annually" are defined within Guidance Document 110-36 to mean every 12 months and every 6 months, respectively.

11. ***If compounding personnel fail a media-fill test, may they continue preparing compounded sterile products?***
No, compounding personnel who failed a media-fill test may not be allowed to prepare compounded sterile products (low, medium, or high-risk) prior to retraining and receipt of a passing media-fill test. ***Note- this guidance reflects a change to Major Deficiency 26a in Guidance Document 110-9 which was amended at the March 2013 full board meeting.

12. ***Do batches less than 25 require sterility testing to be performed?***
No, however, the batches may not be assigned a BUD which exceeds the default BUDs referenced in question #3.

13. ***Because batches less than 25 do not require sterility testing to be performed, may the CSP which may have been autoclaved be assigned an extended BUD based on stability data?***
No, in the absence of sterility testing the batch may not be assigned a BUD which exceeds the default BUDs (referenced in question #3) even if the CSP underwent autoclaving.

14. ***Does USP-NF address how long a CSP may hang for infusion?***
No, USP-NF does not address how long a CSP may hang for infusion. Refer to facility policy on this issue. USP-NF, however, does require the administration of CSPs to begin prior to the assigned BUD.

15. ***May a pharmacist repackage Avastin for office administration (not pursuant to a patient-specific prescription)?***
No. Pharmacies supply physicians with Avastin for an off-label use involves repackaging the manufactured drug product into smaller volume syringes. It does not constitute compounding as defined in Va Code §54.1-3401. While pharmacists may repackage a drug product when dispensing a drug pursuant to an individual prescription, a pharmacist may not repackage drug solely for distribution purposes. The board has historically interpreted the repackaging of a drug for distribution purposes as an act restricted to a manufacturer, defined in Va Code §54.1-3401. This interpretation appears consistent with recent warning letters from the US Food and Drug Administration (FDA).

16. ***May a pharmacist repackage Avastin pursuant to a patient-specific prescription?***
Yes, the law does not prohibit a pharmacist from repackaging a drug as part of the dispensing process pursuant to a patient-specific prescription.

17. ***May a prescriber or patient obtain a compounded sterile product from an out-of-state pharmacy that is not registered by the Virginia Board of Pharmacy as a nonresident pharmacy?***
No, only nonresident pharmacies registered by the Virginia Board of Pharmacy may ship compounded sterile products into Virginia. Verification of registration may be determined at https://secure01.virginiainteractive.org/dhp/cgi-bin/search_publicdb.cgi by searching the business name and choosing the occupation of "non-resident pharmacy".