Virginia Regulatory Town Hall

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Emergency Regulation and Notice of Intended Regulatory Action (NOIRA) Agency Background Document

Agency name	Board of Medicine, Department of Health Professions
Virginia Administrative Code (VAC) citation	18VAC85-20
Regulation title	Regulations Governing the Practice of Medicine, Osteopathic Medicine, Podiatry and Chiropractic
Action title	Rules for mixing, diluting and reconstituting
Document preparation date	9/28/05

This form is used when an agency wishes to promulgate an emergency regulation (to be effective for up to one year), as well as publish a Notice of Intended Regulatory Action (NOIRA) to begin the process of promulgating a permanent replacement regulation.

This information is required for executive branch review and the Virginia Registrar of Regulations, pursuant to the Virginia Administrative Process Act (APA), Executive Orders 21 (2002) and 58 (1999), and the *Virginia Register Form, Style, and Procedure Manual.*

Preamble

The APA (Code of Virginia § 2.2-4011) states that an "emergency situation" is: (i) a situation involving an imminent threat to public health or safety; or (ii) a situation in which Virginia statutory law, the Virginia appropriation act, or federal law requires that a regulation shall be effective in 280 days or less from its enactment, or in which federal regulation requires a regulation to take effect no later than 280 days from its effective date.

1) Please explain why this is an "emergency situation" as described above.
2) Summarize the key provisions of the new regulation or substantive changes to an existing regulation.

The adoption of an "emergency" regulation by the Board of Medicine is required to comply with amendments to the Drug Control Act (§ 54.1-3400 et seq.), exempting doctors of medicine or osteopathic medicine who mix, dilute or reconstitute drugs from the definition of compounding. The second enactment clause in Chapter 475 of the 2005 Acts of the Assembly states:

2. That notwithstanding the provisions of Chapter 33 (§ 54.1-3300 et seq.) of Title 54.1, the Board of Medicine shall, within 280 days of the enactment of this act, promulgate regulations establishing standards for the mixing, diluting, or reconstituting of a manufacturer's product drugs for the purpose of administration to a patient by a practitioner of medicine or osteopathy or a person supervised by such person, and the transportation of these drugs. The Board of Medicine shall also promulgate regulations establishing standards for facilities in which mixing, diluting, or reconstituting of a manufacturer's product drugs for the purpose of administration to a patient by a practitioner of medicine or osteopathy or a person supervised by such person occurs, including a regular inspection program.

The key provisions of the new regulation include the definition and requirements for "immediate-use" sterile mixing, diluting or reconstituting, requirements for low, medium or high risk mixing, diluting or reconstituting and the responsibilities of the supervising doctor.

Legal basis

Other than the emergency authority described above, please identify the state and/or federal legal authority to promulgate this proposed regulation, including: 1) the most relevant law and/or regulation, including Code of Virginia citation and General Assembly chapter number(s), if applicable, and 2) promulgating entity, i.e., agency, board, or person. Describe the legal authority and the extent to which the authority is mandatory or discretionary.

Regulations are promulgated under the general authority of Chapter 24 of Title 54.1 of the Code of Virginia. Section 54.1-2400, which provides the Board of Medicine the authority to promulgate regulations to administer the regulatory system:

§ 54.1-2400 -General powers and duties of health regulatory boards
The general powers and duties of health regulatory boards shall be:
…
6. To promulgate regulations in accordance with the Administrative Process Act (§ 9-6.14:1 et seq.) which are reasonable and necessary to administer effectively the regulatory system. Such regulations shall not conflict with the purposes and intent of this chapter or of Chapter 1 (§ 54.1-100 et seq.) and Chapter 25 (§ 54.1-2500 et seq.) of this title. …

The changes to the Drug Control Act necessitates the adoption of regulations by the Board of Medicine are found in:

§ 54.1-3401. Definitions.

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

"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 prescribing patterns; (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.) or a person supervised by such practitioner pursuant to subdivisions 4, 6, or 19 of § 54.1-2901, shall not be considered compounding. …

"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.

Purpose

Please describe the subject matter and intent of the planned regulatory action. Also include a brief explanation of the need for and the goals of the new or amended regulation.

The purpose of the regulatory action is compliance with a statutory mandate for regulations establishing standards for mixing, diluting or reconstituting of sterile drug products by doctors or personnel under their supervision to be administered to patients. In addition, the law requires establishment of standards for facilities in which the mixing, diluting or reconstituting of sterile drug products occurs and for the transportation of such drugs.

Substance

Please detail any changes that are proposed. Please outline new substantive provisions, all substantive changes to existing sections, or both where appropriate. Set forth the specific reasons why the regulation is essential to protect the health, safety, or welfare of Virginians. Delineate any potential issues that may need to be addressed as a permanent final regulation is developed.

Current section number	Proposed new section number	Current requirement	Proposed change and rationale
n/a	400	n/a	**Requirements for immediate-use sterile mixing, diluting or reconstituting.** A. For the purposes of this chapter, the mixing, diluting, or reconstituting of sterile manufactured drug products, when

			there is no direct contact contamination and administration begins within eight hours of the completion time of preparation shall be considered immediate-use. If manufacturers' instructions or any other accepted standard specifies or indicates an appropriate time between preparation and administration of less than eight hours, the mixing, diluting or reconstituting shall be in accordance with the lesser time. No direct contact contamination means that there is no contamination from touch, gloves, bare skin or secretions from the mouth or nose. Emergency drugs used in the practice of anesthesiology and administration of allergens may exceed eight hours after completion of the preparation, provided there is compliance with all other requirements of this section. *The committee first reviewed the standards for compounding drug products found in Chapter 797 of the U. S. Pharmacopeia, which is recognized as the official compendia of drug standards. The intent of Chapter 797 is to "prevent harm and fatality to patients that could result from microbial contamination (nonsterility)…" Currently, there are three levels of compounding under USP – Low, Medium and High Risk. Compounding must be performed in an ISO Class 5 laminar airflow workbench (hood) which is located in an ISO Class 8 buffer room with an ante area.* *New definitions and standards have been proposed for USP Chapter 797 that would create an exemption from the ISO Class 5 requirement for "immediate-use" compounded products, defined as three or fewer sterile products when there is no direct contact contamination, and administration begins within one hour and is completed within 12 hours of preparation. The immediate-use exemption became the starting point for regulations governing mixing, diluting and reconstituting by doctors, but it became apparent that the limitation of three or fewer products and the beginning of administration within one hour would be too burdensome on a number of doctors' practice and the patients they serve. Therefore, the committee concluded that immediate-use could entail the preparation of any number of products with administration to begin within 8 hours, the equivalent of a day of office hours. Exceptions were made for: 1) products for which the manufacturer or another accepted standard specifies an appropriate time of less than 8 hours; 2) emergency drugs that are used in anesthesiology, since it is common practice to mix up those drugs at the beginning of the day and have them available on the cart for emergency administration at any time during procedures requiring anesthesia, which often extends beyond 8 hours; and 3) administration of allergens to exceed the eight hours after preparation, since*

			many of them are prepared and sent home with the patient to administer over a periods of days or weeks. The product must be mixed, diluted or reconstituted with no direct contact contamination in accordance with standards set in subsection B. B. Doctors of medicine or osteopathic medicine who engage in immediate-use mixing, diluting or reconstituting shall: 1. Ensure that all personnel under their supervision who are involved in immediate-use mixing, diluting or reconstituting are appropriately and properly trained in and utilize the practices and principles of sanitization techniques, aseptic manipulations and solution compatibility. Evidence of such training by a doctor of medicine or osteopathic medicine shall be documented and maintained in personnel files. *(Initially, the committee considered a proposal to require personnel who prepare such products to pass a media fill test of aseptic manipulative skills for initial approval and at least once a year thereafter, at a cost of approximately $35. The committee concluded that such a test was burdensome and that individual practitioners could train persons under their supervision in immediate-use mixing, diluting or reconstituting as required for their practices. Since the Board has statutory authority to inspect such practices, the committee recommended that evidence of training be documented and maintained in personnel files.)* For the purposes of this chapter, aseptic manipulations shall mean to: a. Design a specific site, such as a countertop, in an area of the practice facility where personnel traffic is restricted and activities that may contribute to microbial contamination (eg., eating, food preparation, placement of used diagnostic devices and materials and soiled linens) are prohibited. b. Sanitize the preparation area with 70% isopropanol in water that does not contain added ingredients, such as dyes and glycerin. c. Thoroughly wash hands to wrists with detergent or soap and potable water. Substitution of hand washing by treatment with sanitizing agents containing alcohol and/or 70% isopropanol in water is acceptable. d. Don clean gloves that do not contain powdered lubricants, without touching non-sterile materials. *The Ad Hoc Committee initially recommended that sterile gloves be used in mixing, diluting and reconstituting but the Board determined that it was not practical to keep the gloves sterile and it was too costly. Sterile gloves cost $.44 a pair, but 100 clean gloves can be purchased for $5.00.*

			e. Sanitize necks of ampuls to be opened and stoppers of vials to be needle-punctured with isopropanol. f. Avoid direct contact contamination of sterile needles, syringes, and other drug administration devices and sites on containers of manufactured sterile drug products from which drugs are administered. Sources of direct contact contamination include, but are not limited to, touch by personnel and non-sterile objects, human secretions, blood, and exposure to other non-sterile materials. *The component requirements for aseptic manipulations were developed and recommended by the committee chair, an infectious disease specialist and the member who advises USP on standards for compounding. The specificity in regulation is essential because discussions revealed that aseptic manipulation is not always a common practice in many physician offices in the mixing, diluting or reconstituting of sterile drug products.* 2. Establish procedures for verification of the accuracy of the product that has been mixed, diluted, or reconstituted to include a second check performed by a doctor of medicine or osteopathic medicine or a pharmacist or by a physician assistant or a licensed nurse who has been specifically trained pursuant to subdivision B 1 of this subsection in immediate-use mixing, diluting or reconstituting, unless such mixing, diluting or reconstituting is performed by a doctor of medicine or osteopathic medicine, a pharmacist or a certified registered nurse anesthetist. *Since mixing, diluting and reconstituting can be performed by unlicensed persons or by licensees for whom compounding sterile drug products is not typically within their scope of training and education, it is necessary to have a second check of the procedure and solution performed by a person who has compounding within their scope of practice or by a licensee who has been specifically trained in immediate-use mixing, diluting or reconstituting.* 3. Provide a designated, sanitary work space and equipment appropriate for aseptic manipulations. *While the Board stopped short of requiring a laminar hood for immediate-use mixing, diluting or reconstituting, it was agreed that space and equipment set aside for aseptic manipulation was essential to ensure sterility and safety.* 4. Document or ensure that personnel under his supervision documents in the patient record or other readily-retrievable record that identifies the patient and the following: the

			names of drugs mixed, diluted or reconstituted, the date of preparation, and the date of administration as evidence that the mixing, diluting or reconstituting was immediate-use. *When there is an inspection of a physician office or investigation of a complaint, a physician must be able to document that the mixing, diluting or reconstituting being performed qualified for the definition of "immediate-use." The elements required to be placed in the patient record are consistent with standard practice for most physicians.* 5. Develop and maintain a policy and procedure manual for the procedures to be followed in mixing, diluting or reconstituting of sterile products and for the training of personnel pursuant to subdivision B 1 of this subsection. *A policy and procedure manual is necessary for consistency in a practice and for a physician to be able to provide evidence of training personnel and demonstrate that established practices are compliant with regulations.* C. Any mixing, diluting or reconstituting of drug products that are hazardous to personnel shall be performed consistent with requirements of all applicable federal and state laws and regulations for safety and air quality, to include but not be limited to those of the Occupational Safety and Health Administration (OSHA). For the purposes of this chapter, Appendix A of the National Institute for Occupational Safety and Health publication, *Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings* will serve as the reference list of hazardous drug products. *Although certain drugs, such as chemotherapy, may qualify for immediate-use mixing, diluting or reconstituting, their toxicity to personnel requires an additional level of protection and sterility. Those hazardous drug products are currently listed in Appendix A of an OSHA publication and mixing, diluting or reconstituting of those products requires compliance with applicable federal and state laws for safety and air quality.*
n/a	410	n/a	**Requirements for low, medium- or high-risk sterile mixing, diluting or reconstituting.** A. Any mixing, diluting or reconstituting of sterile products that does not meet the criteria for immediate-use as set forth in 18VAC85-20-400 A shall be defined as low-, medium-, or high-risk compounding under the definitions of Chapter 797 of the U. S. Pharmacopeia (USP). *If the mixing, diluting or reconstituting being performed does not meet the Board's liberal definition of immediate-*

			use, the compounding then falls under the requirements of Chapter 797 as the standard for sterility and safety. B. Until July 1, 2007, all low-, medium-, or high-risk mixing, diluting or reconstituting of sterile products shall comply with the standards for immediate-use mixing, diluting or reconstituting as specified in 18VAC85-20-400. Beginning July 1, 2007, doctors of medicine or osteopathic medicine who engage in low-, medium-, or high-risk mixing, diluting or reconstituting of sterile products shall comply with all applicable requirements of USP Chapter 797. Subsequent changes to the USP Chapter 797 shall apply within one year of the official announcement by USP. C. A current copy, in any published format, of USP Chapter 797 shall be maintained at the location where low-, medium- or high-risk mixing, diluting or reconstituting of sterile products is performed. *With the changes proposed to USP Chapter 797, all pharmacies and other entities that engage in sterile compounding will have until July 1, 2007 for compliance with requirements for buffer zones and clean rooms for compounding. Therefore, the Board granted the same timeframe for compliance, but until such time, anyone who engages in low-, medium-, or high-risk mixing, diluting or reconstituting of sterile products must comply with Board requirements for immediate-use.*
n/a	420	n/a	**Responsibilities of doctors who mix, dilute or reconstitute drugs in their practices.** A. Doctors of medicine or osteopathic medicine who delegate the mixing, diluting or reconstituting of sterile drug products for administration retain responsibility for patient care and shall monitor and document any adverse responses to the drugs. *The ultimate responsibility for mixing, diluting or reconstituting of sterile drug products remains with the doctor who has delegated such procedures to persons under his supervision. The rule reiterates that responsibility and the obligation to monitor and document any adverse responses.* B. Doctors who engage in the mixing, diluting or reconstituting of sterile drug products in their practices shall disclose this information to the board in a manner prescribed by the board, and are subject to unannounced inspections by the board or its agents. *Disclosure of mixing, diluting or reconstituting of sterile drug products in their practices will likely take the form of a check box on the biennial renewal form. There is no*

			additional application or form to submit to comply with this requirement.

Alternatives

Please describe all viable alternatives to the proposed regulatory action that have been or will be considered to meet the essential purpose of the action.

There were no viable options to the adoption of regulations; it was mandated by Chapter 475 of the 2005 Acts of the Assembly. Given the scope of the regulated activity and potential impact of requirements on mixing, diluting and reconstituting drug products by doctors or persons under their supervision, the Board decided to constitute an ad hoc committee and task it with developing recommendations for emergency regulations. Chaired by John Armstrong, MD, a specialist in infectious disease, the committee was comprised of doctors with expertise in specialties where mixing, diluting and reconstituting drug products commonly occurs and doctors from practices in urban and rural Virginia. Member of the committee included James T. May, MD, hematologist/oncologist; Richard Ingram, MD, hematologist/oncologist; James Bowles, MD, rural family practice; Burt Sundin, MD, plastic surgery; Hugh Bryan, MD, orthopedic surgeon; and Thomas Leecost, DPM, podiatrist and President of the Board. In addition, the committee included two pharmacists who have expertise in compounding - David Newton, Professor of Pharmacy at Shenandoah University and the Chair of the 2000-2005 Sterile Compounding Committee of the Council of Experts for the United States Pharmacopeia, and Lea Ann Hansen, hematology/oncology at MCV School of Pharmacy. The committee held four public meetings in which all parties were encouraged to participate, and members worked individually on language for the group's consideration. Throughout the course of discussion and development of regulatory language, members of the committee communicated with colleagues in their specialties and in other specialties.

In the process of negotiated rule-making, there was a wide range of opinion, hours of discussion, and numerous drafts and redrafts. The regulation recommended to the Board was a consensus document that did not satisfy all the interested parties in its entirety but was adopted to achieve a balance of public safety and impact on practice.

Family impact

Please assess the impact of the emergency regulatory action on the institution of the family and family stability.

There is no impact on the institution of the family and family stability.