Clearinghouse Rule 22-007

STATE OF WISCONSIN
PHARMACY EXAMINING BOARD

IN THE MATTER OF RULEMAKING	:	PROPOSED ORDER OF THE
PROCEEDINGS BEFORE THE	:	PHARMACY EXAMINING BOARD
PHARMACY EXAMINING BOARD	:	ADOPTING RULES
	:	(CLEARINGHOUSE RULE)

PROPOSED ORDER

An order of the Pharmacy Examining Board to amend Phar 15.33 (10) and 15.37 (1); create Phar 15.30 (10m), (14g) and (14r), and 15.37 (5), (6), and (7); and repeal and recreate Phar 15.34, relating to compounding pharmaceuticals.

Analysis prepared by the Department of Safety and Professional Services.

ANALYSIS

Statutes interpreted: ss. 450.01 (16)

Statutory authority: ss. 15.08 (5) (b), and 450.02 (3) (d) and (e), Stats.

Explanation of agency authority:

The Board shall promulgate rules for its own guidance and for the guidance of the trade or profession to which it pertains and define and enforce professional conduct and unethical practices not inconsistent with the law relating to the particular trade or profession. [s. 15.08 (5) (b), Stats.]

The board may promulgate rules necessary for the administration and enforcement of this chapter and ch. 961 and establish minimum standards for the practice of pharmacy. [s. 450.02 (3) (d) and (e), Stats.]

Related statute or rule: N/A

Plain language analysis:

The objective of the rule is to review the updated United States Pharmacopeia (USP) 795 and 797 standards, which originally had a publication date of June 1, 2019 with an anticipated official date of December 1, 2019. However, due to appeals filed, the 2019 revisions of the USP are currently on hold. The 2008 USP 795 and 797 are the current standard for pharmacy compounding until those 2019 standards are published and effective.

Even though the Board will not be moving forward with the 2019 revisions at this time, there are still updates that need to be made to Phar 15 to align it with the 2008 USP 795 and 797 chapters that are currently in effect. It is the Board's intent to amend Phar 15 without creating an unnecessary burden on Wisconsin pharmacies, while still aligning it with the current USP chapters. When new updated standards are available, the Board will consider opening a new scope statement to address any further changes if applicable.

Summary of, and comparison with, existing or proposed federal regulation:

The states are primarily responsible for the oversight of compounding in pharmacies. Pursuant to the Drug Quality and Security Act, the federal government is responsible for outsourcing facilities, which by definition are not pharmacies, and are subject to current good manufacturing practice requirements, labeling requirements and may distribute compounded drugs in response to an order that is not patient specific.

The Food, Drug and Cosmetic Act requires drugs to be prepared, packed or held under sanitary conditions.

Summary of public comments received on statement of scope and a description of how and to what extent those comments and feedback were taken into account in drafting the proposed rule: N/A

Comparison with rules in adjacent states:

Illinois: For patient-specific prescriptions, sterile and unsterile pharmaceutical compounding is governed by the USP 42-NF 37 from the 2019 USP Compounding Compendium, except for USP Chapter 800. Additionally, all pharmacies that compound drugs must maintain a set of minimum standards and equipment. These requirements include a specific area for compounding materials, accurate scales or measuring equipment, a separate area for compounding, a record keeping system for tracking compounded drugs, drug distribution procedures, and labelling. For non-patient specific or "office use" of non-sterile compounded drugs, additional requirements apply. Among them, retrievable records must be maintained for at least 5 years and specific labelling requirements for office use. Additional requirements for sterile compounding include current reference materials, pharmacist availability at all times to answer patient and health care professional questions, and emergency medications for adverse drug reactions to compounded sterile drugs. [Illinois Administrative Code s. 1330.640]

Iowa: Iowa requires compliance with the current revisions of USP Chapters 795 and 797. In addition, an FDA registered outsourcing facility must be licensed as a pharmacy in Iowa. [Iowa Administrative Code ss. 657.20.3, 657.20.4, and 657.20.6]

Michigan: Michigan requires a pharmacy that provides compounding services to be licensed as a pharmacy and authorized to provide compounding services. The pharmacy

must be accredited through a national accrediting organization and be in compliance with USP standards. [Michigan Compiled Laws s. 333.17748]

Minnesota: Minnesota requires pharmacies compounding nonsterile drug preparations to follow USP chapter 795 standards. Pharmacies compounding sterile drug preparations are required to follow USP chapter 797 standards. [Minnesota Administrative Rules s.6800.3300]

Summary of factual data and analytical methodologies:

The Pharmacy Examining Board primarily utilized United States Pharmacopeia chapters 795 and 797 which are the recognized pharmacopeia standards.

Analysis and supporting documents used to determine effect on small business or in preparation of economic impact analysis:
The proposed rules were posted for a period of 30 days to solicit public comment on economic impact, including how the proposed rules may affect businesses, local government units, and individuals. No economic impact comments were received.

Fiscal Estimate and Economic Impact Analysis:

The Fiscal Estimate and Economic Impact Analysis are attached.

Effect on small business:

These proposed rules do have an economic impact on small businesses, as defined in s. 227.114 (1), Stats. and were submitted to the Small Business Regulatory Review Board for a determination on whether the rules will have a significant economic impact on a substantial number of small businesses. The Department's Regulatory Review Coordinator may be contacted by email at Daniel.Hereth@wisconsin.gov, or by calling (608) 267-2435.

Agency contact person:

Nilajah Hardin, Administrative Rules Coordinator, Department of Safety and Professional Services, Division of Policy Development, 4822 Madison Yards Way, P.O. Box 8366, Madison, Wisconsin 53708; telephone 608-267-7139; email at DSPSAdminRules@wisconsin.gov.

Place where comments are to be submitted and deadline for submission:

Comments may be submitted to Nilajah Hardin, Administrative Rules Coordinator, Department of Safety and Professional Services, Division of Policy Development, 4822 Madison Yards Way, P.O. Box 8366, Madison, WI 53708-8366, or by email to DSPSAdminRules@wisconsin.gov. Comments must be received on or before the public hearing on February 14, 2022 at 11:00 a.m., to be included in the record of rule-making proceedings.

TEXT OF RULE

SECTION 1 Phar 15.30 (10m), (14g), and (14r) are created to read:

Phar 15.30 (10m) "High-risk level compounded sterile preparations" means preparations compounded from non-sterile ingredients or from ingredients that are incorporated using non-sterile equipment before terminal sterilization, or from commercially manufactured sterile products that lack effective antimicrobial preservatives and whose preparation, transfer, sterilization, and packaging is performed in air quality worse than ISO class 5 for more than one hour. Water containing preparations that are stored for more than six hours before terminal sterilization are also classified as high-risk level compounded sterile preparations.

(14g) "Low-risk level compounded sterile preparations" means preparations compounded with aseptic manipulations entirely within ISO class 5 or better air quality using only sterile ingredients, products, components, and devices. The compounding process involves only transfer, measuring, and mixing, using no more than three commercially manufactured sterile products, and not more than two entries into one sterile container or package to make the compounded sterile preparations. The compounding process is limited to aseptically opening ampules, penetrating sterile stoppers on vials with sterile needles and syringes, and transferring sterile liquids in sterile syringes to sterile administration devices, package containers of other sterile products, and containers for storage and dispensing.

(14r) "Medium-risk level compounded sterile preparations" means preparations compounded under low-risk level conditions but which require multiple individual or small doses of sterile products to be combined or pooled to prepare compounded sterile preparations that will be administered either to multiple patients or to one patient on multiple occasions. The compounding process includes complex aseptic manipulations other than single volume transfer, and requires an unusually long duration, such as that required to complete dissolution or homogeneous mixing.

SECTION 2 Phar 15.33 (10) is amended to read:

Phar 15.33 (10) Entry points on bags and vials shall be wiped with small sterile 70% isopropyl alcohol swabs or comparable method for disinfecting, allowing the isopropyl alcohol to dry before piercing stoppers with sterile needles and breaking necks of ~~ampuls~~ ampules. The surface of the sterile 70% isopropyl alcohol swabs used for disinfecting entry points of sterile package and devices may not contact any other object before contacting the surface of the entry point. Particle generating material may not be used to disinfect the sterile entry points of packages and devices.

SECTION 3 Phar 15.34 is repealed and recreated to read:

Phar 15.34 Immediate use compounded sterile preparations. Immediate-use compounded sterile preparations are exempt from the requirements described for low-risk level, Category 1, and Category 2 compounding sterile preparations only when all the following criteria are met:

(1) The compounding process involves simple transfer of not more than three commercially manufactured packages of sterile nonhazardous products or diagnostic radiopharmaceutical products from the manufacturers' original containers and not more than two entries into any one container or package of sterile infusion solution or administration container or device.

(2) Unless required for the preparation, the compounding procedure is a continuous process not to exceed 1 hour.

(3) During preparation, aseptic technique is followed and, if not immediately administered, the finished compound sterile preparation is under continuous supervision to minimize the potential for contact with nonsterile surfaces, introduction of particulate matter or biological fluids, mix-ups with other compound sterile preparations, and direct contact of outside surfaces.

(4) Administration begins not later than 4 hours following the start of the preparation.

(5) Unless immediately and completely administered by the person who prepared it or immediate and complete administration is witnessed by the preparer, the compounded sterile preparation shall bear a label listing patient identification information, the names and amounts of all ingredients, the name or initials of the person who prepared it, and the exact 4-hour BUD and time.

(6) If administration of the compounded sterile preparation has not begun within 4 hours following the start of preparation, it shall be promptly, properly, and safely discarded.

SECTION 4 Phar 15.37 (1) is amended to read:

Phar 15.37 (1) Sterility and stability considerations shall be taken into account when establishing a BUD. Either Category 1 and 2, or low, medium, and high risk compounding preparation standards may be used, but not a combination of the two within the same pharmacy. The following dates and times for storage and initiation of administration of the compounded sterile preparations shall apply:

(a) For compounded sterile preparations including components from conventionally manufactured products, the BUD shall not exceed the shortest expiration of any of the starting components. If the compounded sterile preparation includes non-conventionally manufactured products, the BUD may not exceed the shortest BUD of any of the starting components.

(b) For Category 1 compounded sterile preparations, one of the following:

1. May not exceed 12 hours when the preparation is stored at controlled room temperature.

2. May not exceed 24 hours when the preparation is stored in a refrigerator.

(c) For aseptically processed Category 2 ~~compounded~~ processed sterile preparations, one of the following:

1. No sterility testing performed or sterility testing not passed, and ~~Prepared~~ prepared with one or more nonsterile ~~ingredients~~ starting components, ~~which are sterilized with a validated sterilization procedure prior to compounding no preservative added and no sterility testing performed~~ one of the following:

a. Within 14 days when the preparation is stored at controlled room temperature.

b. Within ~~7~~ 4 days when the preparation is stored in a refrigerator.

c. Within 45 days when the preparation is stored in a freezer.

2. ~~Prepared only with sterile ingredients, no preservative added and no~~ No sterility testing performed or sterility testing not passed, and prepared with only sterile starting components, one of the following:

a. Within ~~6~~ 4 days when the preparation is stored at controlled room temperature.

b. Within ~~9~~ 10 days when the preparation is stored in a refrigerator.

c. Within 45 days when the preparation is stored in a freezer.

3. ~~Prepared only with sterile ingredients, preservative added and no sterility~~ Sterility testing performed and passed, one of the following:

a. Within ~~28~~ 30 days when the preparation is stored at controlled room temperature.

b. Within ~~42~~ 45 days when the preparation is stored in a refrigerator.

c. Within ~~45~~ 60 days when the preparation is stored in a freezer.

~~4. Prepared only with sterile ingredients, no preservative added and sterility testing, one of the following:~~

~~a. Within 28 days when the preparation is stored at controlled room temperature.~~

~~b. Within 42 days when the preparation is stored in a refrigerator.~~

~~c. Within 45 days when the preparation is stored in a freezer.~~

~~5. Prepared only with sterile ingredients, preservative added and sterility testing, one of the following:~~

~~a. Within 42 days when the preparation is stored at controlled room temperature.~~

~~b. Within 42 days when the preparation is stored in a refrigerator.~~

~~c. Within 45 days when the preparation is stored in a freezer.~~

(d) For Category 2 compounded sterile preparations, terminally sterilized by a validated procedure, one of the following:

1. ~~Prepared with no preservative and no~~ No sterility testing performed or sterility testing not passed, one of the following:

a. Within 14 days when the preparation is stored at controlled room temperature.

b. Within 28 days when the preparation is stored in a refrigerator.

c. Within 45 days when the preparation is stored in a freezer.

2. ~~Prepared with no preservative added and sterility~~ Sterility testing performed and passed, one of the following:

a. Within ~~28~~ 45 days when the preparation is stored at controlled room temperature.

b. Within ~~42~~ 60 days when the preparation is stored in a refrigerator.

c. Within ~~45~~ 90 days when the preparation is stored in a freezer.

~~3. Prepared with preservative added and no sterility testing performed, one of the following:~~

~~a. Within 28 days when the preparation is stored at controlled room temperature.~~

~~b. Within 42 days when the preparation is stored in a refrigerator.~~

~~c. Within 45 days when the preparation is stored in a freezer.~~

~~4. Prepared with preservative added and sterility testing performed, one of the following:~~

~~a. Within 42 days when the preparation is stored at controlled room temperature.~~

~~b. Within 42 days when the preparation is stored in a refrigerator.~~

~~c. Within 45 days when the preparation is stored in a freezer.~~

SECTION 5 Phar 15.37 (5), (6), and (7) are created to read:

Phar 15.37 (5) For low-risk level compounded sterile preparations, in the absence of passing a sterility test:

(a) Within 48 hours when the preparation is stored at controlled room temperature.

(b) Within 14 days when the preparation is stored at cold temperatures between 2 and 8 degrees Celsius.

(c) Within 45 days when the preparation is stored in a solid frozen state at -20 degrees Celsius.

(d) For products prepared in an airflow workbench not located in a buffer area, administration shall begin within 12 hours or less of preparation.

(6) For medium-risk level compounded sterile preparations, in the absence of passing a sterility test:

(a) within 30 hours when the preparation is stored at controlled room temperature.

(b) within nine days when the preparation is stored at cold temperatures between 2 and 8 degrees Celsius.

(c) within 45 days when the preparation is stored in a solid frozen state at -20 degrees Celsius.

(7) For high-risk level compounded sterile preparations, in the absence of passing a sterility test:

(a) Within 24 hours when the preparation is stored at controlled room temperature.

(b) Within three days when the preparation is stored at cold temperatures.

(c) Within 45 days when the preparation is stored in a solid frozen state.

SECTION 6 EFFECTIVE DATE. The rules adopted in this order shall take effect on the first day of the month following publication in the Wisconsin Administrative Register, pursuant to s. 227.22 (2) (intro.), Stats.

(END OF TEXT OF RULE)
