TITLE 22. EXAMINING BOARDS
Part 15. Texas State Board of Pharmacy
Chapter 291. Pharmacies
Subchapter A. All Classes of Pharmacy

22 TAC §291.25

The Texas State Board of Pharmacy proposes new §291.25 concerning Pharmacies Compounding Non-Sterile Pharmaceuticals. The new section, if adopted, will outline operating standards for pharmacies that compound non-sterile pharmaceuticals and will implement the recommendations of the Board appointed Task Force on Compounding.

Gay Dodson, R.Ph., Executive Director/Secretary, has determined that, for the first five-year period the rule is in effect, there will be no fiscal implications for state government as a result of enforcing or administering the rule. There are no anticipated fiscal implications for local government.

Ms. Dodson has determined that, for each year of the first five-year period the rule will be in effect, the public benefit anticipated as a result of enforcing the rule will be the establishing of standards for the compounding of non-sterile pharmaceuticals by pharmacies. There is no fiscal impact anticipated for small or large businesses or to other entities who are required to comply with this section.

A public hearing to receive comments on the proposed new rule will be held at 9:00 a.m. on Tuesday, November 18, 2003, at the Health Professions Council Board Room, 333 Guadalupe Street, Tower II, Room 2-225, Austin, Texas 78701. Persons planning to present comments to the Board are asked to provide a written copy of their comments prior to the hearing or bring 20 copies to the hearing. Written comments on the new rule may be submitted to Allison Benz, R.Ph., M.S., Director of Professional Services, 333 Guadalupe Street, Suite 3-600, Austin, Texas, 78701, FAX: 512/305-8082, E-mail: allison.benz@tsbp.state.tx.us. Comments must be received by 5 p.m., November 12, 2003.

The new rule is proposed under sections 551.002 and 554.051 of the Texas Pharmacy Act (Chapters 551-566 and 568-569, Texas Occupations Code). The Board interprets section 551.002 as authorizing the agency to protect the public through the effective control and regulation of the practice of pharmacy. The Board interprets section 554.051(a) as authorizing the agency to adopt rules for the proper administration and enforcement of the Act. The Board interprets section 554.051(b) as authorizing the agency to make a rule concerning the operation of a licensed pharmacy located in this state applicable to a pharmacy licensed by the board that is located in another state, if the board determines the rule is necessary to protect the health and welfare of the citizens of this state.

The statutes affected by this rule: Chapters 551-566 and 568-569, Texas Occupations Code.

The agency hereby certifies that the proposed new rule has been reviewed by legal counsel and found to be a valid exercise of the agency's authority.

§291.25. Pharmacies Compounding Non-Sterile Pharmaceuticals
(a) Purpose. The purpose of this section is to provide standards for the compounding of non-sterile pharmaceuticals in Class A (Community), Class B (Nuclear), Class C (Institutional) and Class E (Non-resident) pharmacies. Pharmacies compounding non-sterile pharmaceuticals shall comply with the requirements of this section in addition to all provisions for their specific license classification.
(b) Definitions. In addition to the definitions for specific license classifications, the following words and terms, when used in this section, shall have the following meanings, unless the

context clearly indicates otherwise.

(1) Beyond-use date - The date after which a compounded preparation should not be used and is determined from the date the preparation was compounded.

(2) Component - Any ingredient intended for use in the compounding of a drug product, including those that may not appear in such product.

(3) Compounding - The preparation, mixing, assembling, packaging, or labeling of a drug or device:

(A) as the result of a practitioner's prescription drug or medication order, or an initiative based on the practitioner-patient-pharmacist relationship in the course of professional practice;

(B) in anticipation of prescription drug or medication orders based on routine, regularly observed prescribing patterns; or

(C) for the purpose of or as an incident to research, teaching, or chemical analysis and not for sale or dispensing.

(4) Manufacturing -The production, preparation, propagation, conversion, or processing of a drug or device, either directly or indirectly, by extraction from substances of natural origin or independently by means of chemical or biological synthesis and includes any packaging or repackaging of the substances or labeling or relabeling of the container and the promotion and marketing of such drugs or devices. Manufacturing also includes the preparation and promotion of commercially available products from bulk compounds for resale by pharmacies, practitioners, or other persons but does not include compounding.

(5) SOPs - Standard operating procedures.

(6) USP/NF - the United States Pharmacopeia/National Formulary

(c) Personnel.

(1) Pharmacist-in-charge. In addition to the responsibilities for the specific class of pharmacy, the pharmacist-in-charge shall have the responsibility for, at a minimum, the following concerning non-sterile compounding:

(A) determining that all personnel involved in non-sterile compounding possess the education, training, and proficiency necessary to properly and safely perform compounding duties undertaken or supervised;

(B) determining that all personnel involved in non-sterile compounding obtain continuing education appropriate for the type of compounding done by the personnel;

(C) assuring that the equipment used in compounding is properly maintained;

(D) maintaining an appropriate environment in areas where non-sterile compounding occurs; and

(E) assuring that effective quality control procedures are developed and followed.

(2) Pharmacists. Special requirements for non-sterile compounding.

(A) All pharmacists engaged in compounding shall:

(i) possess the education, training, and proficiency necessary to properly and safely perform compounding duties undertaken or supervised; and

(ii) obtain continuing education appropriate for the type of compounding done by the pharmacist.

(B) A pharmacist shall inspect and approve all components, drug product containers, closures, labeling, and any other materials involved in the compounding process.

(C) A pharmacist shall review all compounding records for accuracy and conduct in-process and final checks to assure that errors have not occurred in the compounding process.

(D) A pharmacist is responsible for the proper maintenance, cleanliness, and use of all equipment used in the compounding process.

(3) Pharmacy technicians. All technicians engaged in compounding shall:

(A) possess the education, training, and proficiency necessary to properly and safely perform compounding duties undertaken;

(B) obtain continuing education appropriate for the type of compounding done by the pharmacy technician: and

(C) perform compounding duties under the direct supervision of and responsible to a pharmacist.

(4) Training.

(A) All training activities shall be documented and covered by appropriate SOPs as outlined in subsection (d)(7)(A) of this section.

(B) All personnel involved in non-sterile compounding shall be well trained and must participate in continuing relevant training programs.

(d) Operational Standards.

(1) General requirements.

(A) Non-sterile drug products may be compounded in licensed pharmacies:

(i) upon presentation of a practitioner's prescription drug or medication order, or an initiative based on a valid pharmacist/patient/prescriber relationship; or

(ii) in anticipation of future prescription drug or medication orders based on routine, regularly observed prescribing patterns.

(B) Non-sterile compounding in anticipation of future prescription drug or medication orders must be based upon a history of receiving valid prescriptions issued within an established pharmacist/patient/prescriber relationship, provided that in the pharmacist's professional judgment the quantity prepared is stable for the anticipated shelf time.

(i) The pharmacist's professional judgment shall be based on the criteria used to determine a beyond-use date outlined in paragraph (4)(C) of this subsection.

(ii) Documentation of the criteria used to determine the stability for the anticipated shelf time must be maintained with the non-sterile compounding record.

(iii) Any product compounded in anticipation of future prescription drug or medication orders shall be labeled. Such label shall contain:

(I) name and strength of the compounded medication or list of the active ingredients and strengths;

(II) facility's lot number;

(III) beyond-use date as determined by the pharmacist using appropriate documented criteria as outlined in clause (i) of this subparagraph; and

(IV) quantity or amount in the container.

(C) Commercially available products may be compounded for dispensing or administration to individual patients or for distribution to practitioners provided the following conditions are met:

(i) the commercial product is not reasonably available from normal distribution channels in a timely manner to meet patient's needs; and

(ii) the prescribing practitioner has requested that the drug be compounded.

(D) Pharmaceuticals must be compounded for the exclusive use of the pharmacy where the products are compounded. Compounded pharmaceuticals may not be distributed for resale, including distribution to pharmacies under common ownership or control. This restriction does not apply to distributions of compounded pharmaceuticals to a practitioner under the following conditions.

(i) The practitioner requests the compounded pharmaceutical for administration, but not dispensing, to the practitioner's patients.

(ii) The quantity of all compounded pharmaceuticals distributed to all practitioners during the previous 12 months pursuant to this exception does not exceed 5% of all prescriptions compounded and dispensed during the previous 12 months. For the purpose of this exception, distributions to practitioners shall not be included in the 5% if the pharmacy receives and documents within 30 days of distribution, the name of the patient to whom the compounded pharmaceutical was administered.

(iii) Products compounded for physician administration to patients shall be labeled. Such label shall contain:

(I) the statement: "For Office Use Only";

(II) name and strength of the compounded medication or list of the active ingredients and strengths;

(III) facility's control number;

(IV) beyond-use date as determined by the pharmacist using appropriate documented criteria as outlined in paragraph (4)(C) of this subsection; and

(V) quantity or amount in the container.

(E) Compounding pharmacies/pharmacists may advertise and promote the fact that they provide non-sterile prescription compounding services, which may include specific drug products.

(2) Environment.

(A) Pharmacies regularly engaging in compounding shall have a designated and adequate area for the safe and orderly compounding of drug products, including the placement of equipment and materials. Pharmacies involved in occasional compounding shall prepare an area prior to each compounding activity which is adequate for safe and orderly compounding.

(B) Only personnel authorized by the responsible pharmacist shall be in the immediate vicinity of a drug compounding operation.

(C) A sink with hot and cold running water, exclusive of rest room facilities, shall be accessible to the compounding areas and be maintained in a sanitary condition. Supplies necessary for adequate washing shall be accessible in the immediate area of the sink and include:

(i) soap or detergent; and

(ii) air-driers or single-use towels.

(D) If drug products which require special precautions to prevent contamination, such as penicillin, are involved in a compounding operation, appropriate measures, including dedication of equipment for such operations or the meticulous cleaning of contaminated equipment prior to its use for the preparation of other drug products, must be used in order to prevent cross-contamination.

(3) Equipment and Supplies. The pharmacy shall:

(A) have a Class A prescription balance, or analytical balance and weights which shall be properly maintained and inspected at least every three years by the Texas State Board of Pharmacy; and

(B) have equipment and utensils necessary for the proper compounding of prescription drug or medication orders. Such equipment and utensils used in the compounding process shall be:

(i) of appropriate design and capacity, and be operated within designed operational limits;

(ii) of suitable composition so that surfaces that contact components, in-process material, or drug products shall not be reactive, additive, or absorptive so as to alter the safety, identity, strength, quality, or purity of the drug product beyond acceptable standards;

(iii) cleaned and sanitized immediately prior to each use; and

(iv) routinely inspected, calibrated (if necessary), or checked to ensure proper performance.

(4) Labeling. In addition to the labeling requirements of the pharmacy's specific license classification, the label dispensed or distributed pursuant to a prescription drug or medication order shall contain the following.

(A) The brand name, official name, or the principle active ingredients of the compounded pharmaceutical.

(B) A statement that the preparation has been compounded by the pharmacy.

(C) A beyond-use date after which the compounded pharmaceutical should not be used. The beyond-use date shall be determined as outlined in Chapter 795 of the USP concerning Pharmacy Compounding including the following.

(i) The pharmacist shall consider:

(I) physical and chemical properties of active ingredients;

(II) use of preservatives and/or stabilizing agents;

(III) dosage form;

(IV) storage containers and conditions; and

(V) scientific, laboratory, or reference data.

(ii) In the absence of stability information applicable for a specific drug or preparation, the following maximum beyond-use dates are to be used when the compounded pharmaceutical is packaged in tight, light-resistant containers and stored at controlled room temperatures.

(I) Nonaqueous liquids and solid formulations (Where the

manufactured drug product is the source of active ingredient): 25% of the time remaining until the product's expiration date or 6 months, whichever is earlier.

(II) Water-containing formulations (Prepared from ingredients in solid form): Not later than 14 days when refrigerated between 2 - 8 degrees Celsius (36 - 46 degrees Fahrenheit)

(III) All other formulations: Intended duration of therapy or 30 days, whichever is earlier.

(iii) Beyond-use date limits may be exceeded when supported by valid scientific stability information for the specific compounded pharmaceutical.

(5) Written drug information. Written information about the compounded drug or its major active ingredient(s) shall be given to the patient at the time of dispensing. A statement which indicates that the product was compounded by the pharmacy must be included in this written information. If there is no written information available, the patient should be advised in writing that the drug has been compounded and how to contact a pharmacist, and if appropriate the prescriber, concerning the drug.

(6) Drugs, components, and materials used in non-sterile compounding.

(A) Drugs used in non-sterile compounding shall preferably be a USP/NF grade substances manufactured in an FDA-registered facility.

(B) If USP/NF grade substances are not available shall be of a chemical grade in one of the following categories:

(i) Chemically Pure (CP);
(ii) Analytical Reagent (AR); or
(iii) American Chemical Society (ACS); or
(iv) Food Chemical Codex; or

(C) If a drug, component or material is not purchased from a FDA-registered facility, the pharmacist shall establish purity and stability by reasonable means, which may include lot analysis, manufacturer reputation, or reliability of source.

(D) All components shall be stored in properly labeled containers in a clean, dry area, under proper temperatures.

(E) Drug product containers and closures shall not be reactive, additive, or absorptive so as to alter the safety, identity, strength, quality, or purity of the compounded drug product beyond the desired result.

(F) Components, drug product containers, and closures shall be rotated so that the oldest stock is used first.

(G) Container closure systems shall provide adequate protection against foreseeable external factors in storage and use that can cause deterioration or contamination of the compounded drug product.

(H) A pharmacy may not compound a drug product which appears on an official federal Food and Drug Administration list of drug products withdrawn or removed from the market because they are found to be unsafe or not effective.

(7) Compounding process.

(A) All significant procedures performed in the compounding area shall be covered by written SOPs designed to ensure accountability, accuracy, quality, safety, an uniformity in the compounding process. At a minimum, SOPs shall be developed for:

(i) the facility;
(ii) equipment;
(iii) personnel;
(iv) actual compounding;
(v) product evaluation;
(vi) packaging; and
(vii) storage of compounded pharmaceuticals.

(B) Any compounded pharmaceutical with an official monograph in the USP/NF shall be compounded, labeled, and packaged in conformity with the USP/NF monograph for the drug.

(C) Any person with an apparent illness or open lesion that may adversely affect the safety or quality of a drug product being compounded shall be excluded from direct contact

with components, drug product containers, closures, any materials involved in the compounding process, and drug products until the condition is corrected.

(D) Personnel engaged in the compounding of drug products shall wear clean clothing appropriate to the operation being performed. Protective apparel, such as coats/jackets, aprons, hair nets, gowns, hand or arm coverings, or masks shall be worn as necessary to protect personnel from chemical exposure and drug products from contamination.

(E) At each step of the compounding process, the pharmacist shall assure that components used in compounding are accurately weighed, measured, or subdivided as appropriate to conform to the formula being prepared.

(8) Quality Control.

(A) The pharmacy shall follow established quality control procedures to monitor the output of compounded drug products for uniformity and consistency such as capsule weight variations, adequacy of mixing, clarity, or pH of solutions. When developing these procedures, pharmacy personnel shall consider the provisions of Chapter 795, concerning Pharmacy Compounding, Chapter 1075, concerning Good Compounding Practices, and Chapter 1160, concerning Pharmaceutical Calculations in Prescription Compounding contained in the current USP/NF. Such procedures shall be documented in the non-sterile compounding record.

(B) The pharmacy shall conduct and document end product evaluations appropriate for the preparation in accordance with written SOPs. End product evaluations for non-batch compounded pharmaceuticals may be performed on random samples. All batch compounded pharmaceuticals shall have end product evaluations.

(e) Records.

(1) Maintenance of records. Every record required by this section shall be kept by the pharmacy for at least two years.

(2) Compounding records.

(A) Compounding records for all compounded pharmaceuticals shall be maintained by the pharmacy electronically or manually as part of the prescription drug or medication order, formula record, formula book, or compounding log and shall include:

(i) the date of preparation;

(ii) a complete formula, including methodology and necessary equipment which includes the brand name(s) of the raw materials, or if no brand name, the generic name(s) and name(s) of the manufacturer(s) of the raw materials and the quantities of each;

(iii) signature or initials of the pharmacist or pharmacy technician performing the compounding;

(v) signature or initials of the pharmacist responsible for supervising pharmacy technicians and other supportive personnel and conducting in-process and final checks of compounded pharmaceuticals if pharmacy technicians perform the compounding function;

(vi) the quantity in units of finished products or grams of raw materials;

(vii) the package size and the number of units prepared;

(viii) the criteria used to determine the beyond-use date;

(ix) documentation of performance of quality control procedures. Documentation of the performance of quality control procedures is not required if the compounding process is done pursuant to a patient specific order and involves the mixing of two or more commercially available oral liquids or commercially available preparations when the final product is intended for external use; and

(B) Compounding records when batch compounding or compounding in anticipation of future prescription drug or medication orders.

(i) Master work sheet. A master work sheet shall be developed and approved by a pharmacist for each batch of pharmaceuticals to be prepared. Once approved, a duplicate of the master work sheet shall be used as the preparation work sheet from which each batch is prepared and on which all documentation for that batch occurs. The master work sheet shall contain at a minimum:

(I) the formula;

(II) the components;

(III) the compounding directions;

(IV) a sample label;

(V) evaluation and testing requirements;
(VI) specific equipment used during preparation; and
(VIII) storage requirements.

(ii) Preparation work sheet. The preparation work sheet for each batch of pharmaceuticals shall document the following:

(I) identity of all solutions and ingredients and their corresponding amounts, concentrations, or volumes;
(II) manufacturer lot number for each component;
(III) component manufacturer or suitable identifying number;
(IV) container specifications (e.g., syringe, pump cassette);
(V) unique lot or control number assigned to batch;
(VI) expiration date of batch-prepared products;
(VII) date of preparation;
(VIII) name, initials, or electronic signature of the person(s) involved in the preparation;
(IX) name, initials, or electronic signature of the responsible pharmacist;
(X) end-product evaluation and testing specifications, if applicable; and
(XI) comparison of actual yield to anticipated yield, when appropriate.