BOARDS AND COMMISSIONS

Board of Pharmacy

(Amendment)

201 KAR 2:320. Requirements for manufacturers and virtual manufacturers.

RELATES TO: KRS 315.010, 315.020(2), 315.036, 315.191(1)(a), 315.400, 315.404

STATUTORY AUTHORITY: KRS 315.020(2), 315.036, 315.191(1), 315.400

NECESSITY, FUNCTION, AND CONFORMITY: KRS 315.020, 315.036 and 315.191(1)(a) authorize the board to promulgate administrative regulations to regulate the manufacturers and virtual manufacturers of drugs and drug-related devices. This administrative regulation establishes the requirements for the regulation of manufacturers and virtual manufacturers.

Section 1. Definitions.

(1) "Component" means any raw material, ingredient, or article intended for use in the manufacture of a drug and drug-related device.

(2) "Drug sample" means a unit of a prescription drug that is not intended to be sold and is intended to promote the sale of the drug.

(3) "Illegitimate Product" is defined by KRS 315.400(11).

(4) "Manufacturer or virtual manufacturer" is defined by KRS 315.010(13).

(5) "Product" means a prescription drug in a finished dosage form for administration to a patient without substantial further manufacturing, such as capsules, tablets, and lyophilized products before reconstitution.

(6) "Relabeler" means:

(a) Any person who owns or operates an establishment that changes the content of the labeling from that supplied from the original manufacturer for distribution under the establishment's own name; and

(b) Does not include establishments that do not change the original labeling, but merely add their own name.

(7) "Repackager" is defined by KRS 315.400(16).

(8) "Suspect product" means a component, prescription drug, or drug-related device for which there is reason to believe that such component, prescription drug, or drug-related device:

(a) Is potentially counterfeit, diverted, or stolen;

(b) Is potentially intentionally adulterated such that the component, prescription drug, or drug-related device would result in serious adverse health consequences or death to humans or animals;

(c) Is potentially the subject of a fraudulent transaction; or

(d) Appears otherwise unfit for distribution such that the component, prescription drug, or drug-related device would result in serious adverse health consequences or death to humans or animals.

Section 2. Requirements.

(1) A manufacturer or virtual manufacturer engaging in manufacturing in the Commonwealth shall apply for a permit from the Board of Pharmacy in accordance with KRS 315.036 and this administrative regulation.

(2) A separate permit shall be required for each facility within the Commonwealth regardless of whether joint ownership or control exists.

(3) An agent or employee of a permit holder shall not be required to obtain a permit under this section when the agent or employee is acting in the usual course of business or employment.

(4) A permit shall not be issued or renewed unless the applicant demonstrates or continues to demonstrate acceptable operational procedures, including:

(a) Adequate operation, maintenance, and storage conditions to ensure proper lighting, ventilation, temperature and humidity control, sanitation, space, and security as per label requirements or official United States Pharmacopoeia (USP) compendium requirements, USP Chapter 659, Packaging and Storage Requirements as incorporated by reference in 201 KAR 2:105. Appropriate manual, electromechanical, or electronic temperature and humidity recording equipment, devices, or logs shall be utilized to document proper storage of components and drugs and drug-related devices;

(b) Separation and quarantine of deteriorated, damaged, outdated, misbranded, adulterated, or otherwise recalled components and drugs and drug-related devices until they are destroyed or returned;

(c) Providing accurate and precise records of all components and drugs and drug-related devices shipped or received including source and recipient, date, quantity, itemized description, and any other information pertinent to the receipt and distribution or disposition; and

(d) Providing proof of registration with the U.S. Food and Drug Administration (FDA), the U.S. Drug Enforcement Administration (DEA), and compliance with all federal, state, and local laws and regulations.

(5) Manufacturers and virtual manufacturers shall comply with all requirements as outlined in the Drug Supply Chain Security Act (DSCSA), 21 U.S.C. 360eee-360eee-4., if applicable.

(6) Manufacturers and virtual manufacturers shall establish a system to:

(a) Quarantine and investigate suspect product to determine if it is illegitimate; and

(b) Notify FDA, the Board of Pharmacy, and recipient(s) of illegitimate product, if illegitimate product is found.

(7) All virtual manufacturers shall be exempt from the requirements of subsection 2(4)(a) and (b) of this Section, and Section 5(1)(a) and (b) and (2)(a) and (b) of this administrative regulation.

Section 3. Qualifications for Permit.

(1) The Board of Pharmacy shall consider, at a minimum, the following factors in reviewing the qualifications of persons who engage in manufacture or virtual manufacture of drugs and drug-related devices within the Commonwealth:

(a) Any convictions of the officers of the applicant under any federal, state, or local laws relating to drugs, including drug samples and controlled substances;

(b) Any felony convictions of the applicant or its officers under federal, state, or local laws;

(c) The applicant's and its officers' past experience in the manufacture or virtual manufacture of drugs and drug-related devices, including drug samples and controlled substances;

(d) The furnishing by the applicant of false or fraudulent material in any application made in connection with drug manufacturing or virtual drug manufacturing;

(e) Suspension or revocation by federal, state, or local government of any license or permit currently or previously held by the applicant or its officers for the manufacture or virtual manufacture of any drugs and drug-related devices, including drug samples and controlled substances;

(f) Compliance with the requirements under any previously granted license or permit, if any; and

(g) Compliance with requirements to maintain or make available to the Board of Pharmacy or to federal, state, or local law enforcement officials those records required under this administrative regulation.

(2) The Board of Pharmacy shall have the right to deny a permit to an applicant if it determines that the granting of that permit would not be in the public interest based on health and safety considerations.

(3) A permit shall not be issued pursuant to this administrative regulation unless the applicant has furnished proof satisfactory to the Board of Pharmacy:

(a) That the applicant is in compliance with all applicable federal, state, and local laws and regulations relating to drugs and drug-related devices; and

(b) That the applicant is equipped as to land, buildings, and security to properly carry on the business described in the application.

(4) A permit issued pursuant to this administrative regulation may be disciplined, suspended, or revoked for failure to comply with the provisions of KRS 315.020, 315.036, 315.400, or this administrative regulation.

(5) No permit shall fail to designate a pharmacist-in-charge.

Section 4. Application, Fees, Renewals.

(1) An application for a permit shall be submitted to the Board of Pharmacy on the Application for a Permit to Operate as a Manufacturer or Virtual Manufacturer.

(2) An application shall be accompanied by the annual fee set forth in 201 KAR 2:050.

(3) An application shall include:

(a) The name, full business address, and telephone number of the applicant;

(b) All trade or business names used by the applicant;

(c) Addresses, telephone numbers, and the names of the persons for the facility used by the permit holder for the storage, handling, and manufacturing or virtual manufacturing of drugs and drug-related devices;

(d) The type of ownership or operation (i.e. partnership, corporation, or sole proprietorship);

(e) The name(s) of the owner and operator of the permit holder, including;

1. If a person, the name and Social Security number of the person;

2. If a partnership, the name and Social Security number of each partner, and the name of the partnership;

3. If a corporation, the name, Social Security number and title of each corporate officer and director, the corporate names, and the name of the state of incorporation; and

4. If a sole proprietorship, the full name and social security number of the sole proprietor and the name of the business entity; and

(f) A list of all licenses and permits issued to the applicant by any other state that authorizes the applicant to manufacture, virtual manufacture or possess drugs and drug-related devices.

(4) All permits shall:

(a) Expire on September 30 following the date of issuance; and

(b) Be:

1. Renewable annually thereafter upon completion of the Renewal Application to Operate as a Manufacturer or Virtual Manufacturer that is accompanied by the renewal fee set forth in 201 KAR 2:050; and

2. Nontransferable.

Section 5. Standards.

(1) Facilities.

(a) All facilities in which components and drugs and drug-related devices are labeled, relabeled, packaged, repackaged, stored, held, sold, offered for sale, exposed for sale, or kept for sale shall be of suitable size, construction, and location to facilitate cleaning, maintenance, and proper operations.

(b) All facilities shall meet all applicable federal, state, and local standards. The facility shall quarantine components and drugs and drug-related devices that are outdated, damaged, deteriorated, misbranded, recalled, or adulterated,

(c) A facility shall not be located in a residence.

(2) Security.

(a) A manufacturer shall be equipped with an alarm system to detect entry after hours.

(b) A manufacturer shall ensure that access from outside their premises is well-controlled and reduced to a minimum. This includes the installation of adequate lighting at the outside perimeter of the premises.

(c) Internal security policies shall be developed to provide reasonable protection against theft and diversion by limiting access to areas where components and drugs and drug-related devices are held to authorized personnel. These policies shall provide protection against tampering with computers or electronic records.

(d) A permit holder shall employ adequate personnel with the education and experience necessary to safely and lawfully engage in the manufacture or virtual manufacture of drugs and drug-related devices.

(e) Lists of officers, directors, managers and other persons in charge of manufacture or virtual manufacture, distribution or disposition, storage, and handling of components and drugs and drug-related devices, including a description of their duties and summary of their qualifications, shall be maintained for purpose of review.

(3) Recordkeeping requirements for companies handling prescription drugs and drug-related devices exempt from the DSCSA.

(a) Inventories and other records regarding the receipt and distribution or disposition of components and drugs and drug-related devices shall be maintained and readily available for inspection or photocopying by the Board of Pharmacy and authorized law enforcement officials for a period six (6) years. These records shall include:

1. The business name and address of the source of the components and drugs and drug-related devices including the seller or transferor and the address of the location from which the components and drugs and drug-related devices were shipped;

2. The business name and address to whom components and drugs and drug-related devices were shipped including the purchaser and the address of the location where the components and drugs and drug-related devices were shipped;

3. The identity and quantity of the components and drugs and drug-related devices received and distributed or disposed of; and

4. The dates of receipt and distribution or disposition of the components and drugs and drug-related devices.

(b) The manufacturer or virtual manufacturer shall keep production and process control records for a period of six (6) years following completion of manufacturing.

(c) Records described in this section that are kept at the inspection site or that can be readily retrievable within forty-eight (48) hours by computer or other electronic means shall be readily available for authorized inspection during the retention period. Records kept at a central location apart from the inspection site and not electronically retrievable shall be made available for inspection within two (2) working days of a request by the Board of Pharmacy or an authorized official of a federal, state, or local law enforcement agency.

(d) Manufacturers and virtual manufacturers shall maintain an ongoing list of verified persons and businesses with whom they do business.

(e) A permitted manufacturer and virtual manufacturer may sell or distribute drugs and drug-related devices only to the following:

1. A currently permitted manufacturer or virtual manufacturer;

2. A currently licensed third-party logistics provider;

3. A currently licensed wholesaler;

4. A currently permitted pharmacy;
5. A currently licensed outsourcing facility;
6. A currently licensed practitioner;
7. A currently permitted repackager or relabeler;
8. A currently licensed hospital, but only for use by or in that hospital pursuant to KRS 217.182(1);
9. A person in charge of a laboratory, but only for use in that laboratory for scientific and medical research purposes pursuant to KRS 217.182(1); or
10. Any other appropriately licensed or permitted facility in the jurisdiction in which it is located.

(f) Manufacturers and virtual manufacturers shall maintain a system for the mandatory reporting of any theft, suspected theft, diversion, or other significant loss of any component or drug or drug-related device to the Board of Pharmacy and if applicable the FDA and DEA.

(4) Written policies and procedures, requirements for companies handling prescription drugs and drug-related devices exempt from the DSCSA.

(a) A manufacturer or virtual manufacturer shall establish, maintain, and adhere to written policies and procedures for all operations including production, process controls, receipt, security, storage, inventory, and distribution or disposition of components and drugs and drug-related devices.

(b) There shall be written policies and procedures for identifying, recording, and reporting losses or thefts.

(c) There shall be written policies and procedures to assure that the manufacturer and virtual manufacturer prepares for, protects against, and handles crisis situations that affect the security, operation, and records of the permit holder. These crises shall include fires, floods, or other natural disasters, and situations of local, state, or national emergency.

(d) There shall be written policies and procedures for managing and correcting all errors or inaccuracies in inventories.

(e) There shall be written policies and procedures to assure that any outdated components or drugs or drug-related devices or any components or drugs or drug-related devices with an expiration date that, in the manufacturer's or virtual manufacturer's view, does not allow sufficient time for repacking or resale shall be segregated and shall be prepared for return or otherwise destroyed, and this shall be documented.

(f) There shall be written policies and procedures by which the manufacturer or virtual manufacturer exercises control over the shipping and receiving of all components and drugs and drug-related devices within the operation.

(g) There shall be written policies and procedures for investigating suspect product and reporting illegitimate product to the Board of Pharmacy, FDA, and recipient(s) of illegitimate product.

(5) Returned, damaged, and outdated drugs and drug-related devices. A manufacturer or virtual manufacturer shall maintain and follow a written procedure to assure the proper handling and disposal of returned components or drugs or drug-related devices. If conditions under which a drug or drug-related device has been returned cast doubt on the drug or drug-related device's safety, identity, strength, quality, or purity, then the drug or drug-related device shall be destroyed, or returned to the supplier, unless examination, testing, or other investigation proves that the drug or drug-related device meets appropriate standards of safety, identity, strength, quality, and purity. In determining whether the conditions under which a drug or drug-related device has been returned cast doubt on the drug or drug-related device's safety, identity, strength, quality, or purity, the manufacturer or virtual manufacturer shall consider, among other things, the conditions

under which the drug or drug-related device has been held, stored, or shipped before or during its return and the condition of the drug or drug-related device and its container, carton, or labeling, as a result of storage or shipping.

(6) Handling recalls. A manufacturer or virtual manufacturer shall adopt, maintain, and follow a written policy and procedure for handling recalls and withdrawals of components or drugs or drug-related devices. The policy shall cover all recalls and withdrawals due to:

(a) Any voluntary action on the part of the manufacturer or virtual manufacturer;

(b) The direction of the FDA, or any other federal, state, or local government agency; and

(c) Replacement, relabeling, or repackaging of existing component or drug or drug-related devices.

(7) Procedures.

(a) A visual examination of all materials received or shipped shall be made to guarantee product identity and to reasonably guard against acceptance or delivery of damaged, contaminated, tampered, or otherwise unfit stock.

(b) A manufacturer or virtual manufacturer shall be subject to the provisions of any applicable federal, state, or local laws or regulations that relate to drug product and drug-related devices salvaging or reprocessing.

Section 6. Pharmacist-in-charge. A manufacturer or virtual manufacturer shall designate a pharmacist-in-charge of the facility. The pharmacist-in-charge shall review security and records by conducting and documenting an on-site inspection not less than quarterly.

Section 7. Violations.

(1) A drug manufacturer or virtual manufacturer shall not distribute prescription drugs and drug-related devices directly to a consumer or a patient.

(2) A manufacturer or virtual manufacturer shall not operate in a manner that endangers the public health.

(3) Violation of any of these provisions shall be grounds for the discipline, suspension, or revocation of the permit.

Section 8. Incorporation by Reference.

(1) The following material is incorporated by reference:

(a) "Application for a Permit to Operate as a Manufacturer or Virtual Manufacturer", June 2023~~[May 2020]~~; and

(b) "Renewal Application to Operate as a Manufacturer or Virtual Manufacturer", June 2023~~[May 2020]~~.

(2) This material may be inspected, copied, or obtained, subject to applicable copyright law, at the Kentucky Board of Pharmacy, State Office Building Annex, Suite 300, 125 Holmes Street, Frankfort, Kentucky 40601-8024, Monday through Friday, 8 a.m. through 4:30 p.m. This material is also available on the board's Web site at https://pharmacy.ky.gov/Businesses/Pages/Manufacturers.aspx.

CHRISTOPHER HARLOW, Pharm.D., Executive Director

APPROVED BY AGENCY: June 7, 2023

FILED WITH LRC: June 7, 2023 at 1:45 p.m.

PUBLIC HEARING AND COMMENT PERIOD: A public hearing on this administrative regulation shall be held on August 30, 2023, at 10:00 a.m. Eastern Time via zoom. Individuals interested in being heard at this hearing shall notify this agency in writing by five workdays prior to the hearing, of their intent to attend. If no notification of intent to attend the hearing is received by that date, the hearing may be canceled. This hearing is

open to the public. Any person who wishes to be heard will be given an opportunity to comment on the proposed administrative regulation. A transcript of the public hearing will not be made unless a written request for a transcript is made. If you do not wish to be heard at the public hearing, you may submit written comments on the proposed administrative regulation. Written comments shall be accepted through August 31, 2023. Send written notification of intent to be heard at the public hearing or written comments on the proposed administrative regulation to the contact person.

CONTACT PERSON: Christopher Harlow, Executive Director, Kentucky Board of Pharmacy, 125 Holmes Street, Suite 300, State Office Building Annex, Frankfort, Kentucky 40601, phone (502) 564-7910, fax (502) 696-3806, email Christopher.harlow@ky.gov.

REGULATORY IMPACT ANALYSIS AND TIERING STATEMENT

Contact Person:Christopher Harlow

(1) Provide a brief summary of:

(a) What this administrative regulation does:
This administrative regulation establishes the requirements for Manufacturers and virtual manufacturers.

(b) The necessity of this administrative regulation:
KRS 315.191(1)(a) authorizes the Board of Pharmacy to promulgate administrative regulations with minimum requirements for the permitting of those entities manufacture prescription drugs.

(c) How this administrative regulation conforms to the content of the authorizing statutes:
This administrative regulation establishes the requirements for Manufacturers and virtual manufacturers.

(d) How this administrative regulation currently assists or will assist in the effective administration of the statutes:
This regulation ensures compliance with federal regulations.

(2) If this is an amendment to an existing administrative regulation, provide a brief summary of:

(a) How the amendment will change this existing administrative regulation:
This amendment only amends the forms for manufacturers including the permit application and renewal application.

(b) The necessity of the amendment to this administrative regulation:
The fee has been proposed to be amended in 201 KAR 2:050. This amendment is necessary to amend the form with the new fee amount.

(c) How the amendment conforms to the content of the authorizing statutes:
KRS 315.191(1)(a) authorizes the board to promulgate administrative regulations pertaining to pharmacists and pharmacies.

(d) How the amendment will assist in the effective administration of the statutes:
The amendment will further promote, preserve, and protect public health through effective regulation of pharmacists and pharmacies.

(3) List the type and number of individuals, businesses, organizations, or state and local governments affected by this administrative regulation:
The board anticipates pharmacies and pharmacists will be affected minimally by this regulation amendment.

(4) Provide an analysis of how the entities identified in question (3) will be impacted by either the implementation of this administrative regulation, if new, or by the change, if it is an amendment, including:

(a) List the actions that each of the regulated entities identified in question (3) will have to take to comply with this administrative regulation or amendment:
Only in-state drug manufacturers and virtual manufacturers will be impacted by this regulation.

(b) In complying with this administrative regulation or amendment, how much will it cost each of the entities identified in question (3):

There are no expected costs for the entities that are permitted except for the permit and renewal fees.

(c) As a result of compliance, what benefits will accrue to the entities identified in question (3):

Processing of applications in a timely manner. (5) Provide an estimate of how much it will cost to implement this administrative regulation:

(5) Provide an estimate of how much it will cost the administrative body to implement this administrative regulation:

(a) Initially:

No costs will be incurred.

(b) On a continuing basis:

No costs will be incurred.

(6) What is the source of the funding to be used for the implementation and enforcement of this administrative regulation:

Board revenues from pre-existing fees provide the funding to enforce the regulation.

(7) Provide an assessment of whether an increase in fees or funding will be necessary to implement this administrative regulation, if new, or by the change if it is an amendment:

This amendment is only a proposed to forms. 201 KAR 2:050 does contain a proposed change to fees for applications and renewals by an increase of twenty-five ($25) dollars.

(8) State whether or not this administrative regulation establishes any fees or directly or indirectly increases any fees:

The administrative regulation does not directly establish fees; however 201 KAR 2:050 is being amended with a proposed twenty-five (25) dollar fee increase for applications and renewal applications.

(9) TIERING: Is tiering applied?

Tiering is not applied because the regulation is applicable to all entities wishing to manufacture drugs in Kentucky.

FISCAL NOTE

(1) What units, parts, or divisions of state or local government (including cities, counties, fire departments, or school districts) will be impacted by this administrative regulation?

The Kentucky Board of Pharmacy will be the only entity impacted by this administrative regulation.

(2) Identify each state or federal statute or federal regulation that requires or authorizes the action taken by the administrative regulation.

KRS 315.191(1)(a).

(3) Estimate the effect of this administrative regulation on the expenditures and revenues of a state or local government agency (including cities, counties, fire departments, or school districts) for the first full year the administrative regulation is to be in effect.

None.

(a) How much revenue will this administrative regulation generate for the state or local government (including cities, counties, fire departments, or school districts) for the first year?

This administrative regulation will not generate anything on its own. It does not contain a fee.

(b) How much revenue will this administrative regulation generate for the state or local government (including cities, counties, fire departments, or school districts) for subsequent years?

This administrative regulation does not contain a fee.

(c) How much will it cost to administer this program for the first year?

No costs are required to administer this program for the first year.

(d) How much will it cost to administer this program for subsequent years?

No costs are required to administer this program for subsequent years.

Note: If specific dollar estimates cannot be determined, provide a brief narrative to explain the fiscal impact of the administrative regulation.

Revenues (+/-):0

Expenditures (+/-):0

Other Explanation:

201 KAR 2:050 does increase fees by $25 for a manufacturing permit.

(4) Estimate the effect of this administrative regulation on the expenditures and cost savings of regulated entities for the first full year the administrative regulation is to be in effect.

(a) How much cost savings will this administrative regulation generate for the regulated entities for the first year?

None

(b) How much cost savings will this administrative regulation generate for the regulated entities for subsequent years?

None.

(c) How much will it cost the regulated entities for the first year?

$150 annually.

(d) How much will it cost the regulated entities for subsequent years?
$150 annually.

Note: If specific dollar estimates cannot be determined, provide a brief narrative to explain the fiscal impact of the administrative regulation.

Cost Savings (+/-):0

Expenditures (+/-):$150

Other Explanation:
This is the cost of the manufacturing permit.

(5) Explain whether this administrative regulation will have a major economic impact, as defined below.
"Major economic impact" means an overall negative or adverse economic impact from an administrative regulation of five hundred thousand dollars ($500,000) or more on state or local government or regulated entities, in aggregate, as determined by the promulgating administrative bodies. [KRS 13A.010(13)] This regulation does not have major economic impact.