

**MARYLAND BOARD OF PHARMACY
REPORT TO THE GOVERNOR AND THE
GENERAL ASSEMBLY**

ON THE

**IMPLEMENTATION OF TITLE 12,
SUBTITLE 4A OF THE HEALTH
OCCUPATIONS ARTICLE**

January 1, 2014

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EXECUTIVE SUMMARY

In the summer and fall of 2012, contaminated injectable steroids produced by a Massachusetts-based compounding pharmacy caused a multistate outbreak of fungal infections, including fatal fungal meningitis infections. The contaminated steroids were shipped to seven facilities in Maryland. At least 26 people were infected by the contaminated steroids administered in Maryland; three of those people died. In response, Health Occupations Article, Title 12, Subtitle 4A, Annotated Code of Maryland, Sterile Compounding Permits (HO §12-4A), was passed in the 2013 Legislative Session as House Bill 986, Chapter 397. This new law gave the Maryland Board of Pharmacy (the “Board”) authority to oversee all sterile compounding in Maryland. This is the Board’s report, pursuant to HB 986 State Board of Pharmacy – Sterile Compounding – Permits, Section 3, Chapter 397, 2013, on the implementation of Title 12, Subtitle 4A of the Health Occupations Article.

HO §12-4A requires a sterile compounding permit from the Board for any sterile compounding facility that is compounding pursuant to a patient specific prescription. A sterile compounding facility is defined as a pharmacy, a health care practitioner’s office, or any other setting in which sterile compounding is performed. Additionally, it requires any entity that plans to prepare sterile drug products without a patient prescription, and distribute those products into Maryland, to possess a wholesale distributor’s permit and a manufacturer’s permit or other permit designated by the U.S. Food and Drug Administration (FDA), to ensure the safety of the sterile drug products. Those entities that plan to prepare sterile drug products without a patient specific prescription, and do not qualify for an FDA permit, may apply for a waiver from the Board under strict circumstances.

The Board created a Sterile Compounding Subcommittee (the “Subcommittee”) to draft regulations and spearhead the implementation process. This committee has worked diligently to draft regulations, solicit public comment, create new applications and assist Board staff in preparing for this new complex licensure category. The Subcommittee drafted the regulations in two phases. The first phase entailed developing regulations for entities that manufacture sterile drug products and conditions for qualifying and operating under the sterile drug product waiver. Sterile drug products are drug products that must be prepared using aseptic techniques and are not required to be prepared in response to a patient specific prescription. An entity would have to obtain an appropriate FDA manufacturer permit and also acquire a wholesale distributor permit from the Board. For those entities that wish to manufacture sterile drug products and distribute them into Maryland, and do not have an FDA permit, they may apply to the Board for a waiver. The regulations set forth the stringent requirements to obtain such a waiver.

The second phase involved drafting requirements to obtain a sterile compounding permit. The Subcommittee revised the existing COMAR 10.34.19 Sterile Pharmaceutical Compounding, to include all sterile compounding facilities, which under HO §12-4A, are defined as pharmacies, health care practitioner’s offices, or any other setting in which sterile compounding is performed. Prior to HB 986, COMAR 10.34.19 pertained only to sterile compounding pharmacies. The revisions also include a minor change to Regulation .06 Special Handling, Packaging, Labeling, and Beyond Use Dating, to allow only a pharmacy to deliver sterile compounded prescriptions to a patient. Other revisions were made to Regulation .07 Record-Keeping Requirements, to ensure

that a sterile compounding facility would retain completed patient prescription records for at least 5 years, either at the inspection site or retrievable by computer or other electronic means.

Upon receiving informal comments from a variety of stakeholders, the Subcommittee met and revised the proposed regulations to reflect recommendations and suggestions received. The Board prepared one detailed response discussing all the concerns and explaining why revisions were, or were not, made. The major revisions include:

- Deleting unnecessary definitions and revising definitions for clarification purposes;
- Clarification that a sterile compounding facility would be required to have a controlled environment that meets USP 797 Standards;
- Clarification that during an inspection, a sterile compounding facility would provide microbial testing of a sampling of the sterile compounded preparations of the sterile compounding facility, if applicable according to USP 797 Standards. The Board recognizes that some testing would not be immediately available;
- Under the sterile drug product regulation, the Board added “if applicable” after the requirement of a wholesale distributor permit as in some instances the wholesale distributor permit would not be required;
- Expansion of the source of a current drug shortage index beyond the FDA to include “or other nationally recognized index;” and
- Revising the list of health care providers who will assist the Board in determining clinical need for a waiver to simply those relevant professional as determined by the Board.

This report discusses the Board’s strategy to have appropriate staff in place to implement all facets of HB 986. The Board would like to recruit new staff early in 2014 so that training may be completed and staff will be ready for implementation by April 1, 2014. The report sets forth a timeline for promulgation of regulations and the hiring and training of staff.

Finally, the federal Drug Quality and Security Act passed and was signed by President Obama the end of November 2013. This legislation addresses compounding nationally and establishes a U.S. Food and Drug Administration (FDA) permit for “outsourcing facilities” that perform sterile compounding without a patient specific prescription. The Board’s Sterile Compounding Subcommittee will meet in early January 2014, to consider if amendments would be necessary to Maryland’s Health Occupations Article, Title 12, Subtitle 4A Sterile Compounding Permits, so that it does not conflict with the new federal law.

IMPLEMENTATION OF HEALTH OCCUPATIONS ARTICLE, TITLE 12, SUBTITLE 4A – STERILE COMPOUNDING – PERMITS

The Board formed a Sterile Compounding Subcommittee consisting of Board members, Board staff, Board Counsel and a representative from the Department of Health and Mental Hygiene (DHMH), to draft regulations and to create a timeline for implementation. The Board staff, made up of 5 units, has also been involved in many capacities in promulgating regulations; drafting applications for the sterile compounding permit and the sterile drug product waiver; assisting in the hiring process for new staff to evaluate applications and inspect pharmacies and sterile drug product manufacturers; drafting inspection forms for sterile drug product manufacturers and training inspectors; and working with the database contractor to create an online database to track sterile compounders and manufacturers of sterile drug products. All proposed language, policies and substantive decisions are presented to the full Board for approval before release for public comment and final promulgation. The Board anticipates the implementation of Health Occupations Article, Title 12, Subtitle 4A, will be complex, therefore requiring the entire phase-in period, through April 1, 2014 to implement.

Process for Developing Regulations

The Subcommittee began meeting to draft regulations in June 2013. At the request of DHMH, a solicitation for comment regarding the upcoming proposed regulations was posted on the DHMH website. (See Appendix I.) Comments were received from a pharmacy association, health maintenance organization, surgical society, hospital pharmacy, several veterinarians, and over 70 pet owners and included detailed questions and suggested specific content for the regulations to be drafted. Since many of the comments were duplicative, the Board prepared five sets of responses that were used to respond to all of the stakeholder comments. (See Appendix II.) The Subcommittee drafted the regulations based on statutory requirements and incorporating appropriate suggestions received from the stakeholders.

Since USP 797 is the national and international standard adopted for sterile compounding and already incorporated into the existing COMAR 10.34.19 Sterile Pharmaceutical Compounding, the Board chose COMAR 10.34.19 to revise in accordance with HO §12-4A. The Subcommittee used a two-phased approach to address the new statutory requirements. The first phase addressed the “sterile drug products” requirements and the criteria for receiving a Board waiver of provisions in the new law as allowed by statute. The second phase entailed amending COMAR 10.34.19, which is only currently applicable only to pharmacies, to require any entity that performs sterile pharmaceutical compounding to acquire a Maryland “sterile compounding permit” and expands existing regulatory requirements in addition to other required licenses and permits (e.g., pharmacy permit, physician license, etc.).

For the purposes of this report the proposed requirements for acquiring a “sterile compounding permit” will be described first since it will be the primary venue used in Maryland to perform sterile compounding.

Sterile Compounding Permit

The sterile compounding permit will be issued to pharmacies and other sterile compounding facilities in which sterile compounding is performed pursuant to a patient specific prescription. Sterile compounding means compounding of biologics, diagnostics, drugs, nutrients, and radiopharmaceuticals that, under UPS 797, are prepared using aseptic techniques. The draft regulations for the sterile compounding permit were amended to reflect the definitions in HB 986 for adverse events, compounding, designee, health care practitioner, sterile compounding, sterile compounding facility, and sterile drug product. The definitions were added to clarify terms to assure a common perspective when the terms are used.

A large portion of the draft proposed regulations for the sterile compounding permit revised the existing COMAR 10.34.19 to accommodate the new law which requires that any pharmacy, health care practitioner's office, or any other setting in which sterile compounding is performed is required to obtain a sterile compounding permit. Most revisions were minor and included striking the word "pharmacist" and replacing it with "health care practitioner" and striking the word "pharmacy" and replacing it with "sterile compounding facility." Revisions also included a minor change to Regulation .06 Special Handling, Packaging, Labeling, and Beyond Use Dating, to ensure that only a pharmacy would be the entity that is allowed to deliver sterile compounded prescriptions to a patient. An additional revision was made to Regulation .07 Record-Keeping Requirements, to ensure that a sterile compounding facility would keep completed patient prescription records in a retrievable manner for at least 5 years, either at the inspection site or retrievable by computer or other electronic means.

Some of the amendments addressed new sterile compounding permit application requirements. They include: minimum application requirements; notification to the Board of any changes to information provided on the initial or renewal applications; a requirement that each site is required to obtain a separate permit and is not transferable; and renewal requirements. Two new requirements were created to address minimum requirements for inspections of sterile compounding permit holders and reporting requirements. Inspections may be performed by a designee of the Board, the FDA, or other appropriate state entity which indicates compliance with USP 797 Standards. Reporting requirements of sterile compounding permit holders were also added. A sterile compounding permit holder will be required to document and perform routine testing as required by USP 797 Standards for the appropriate risk levels of sterile compounded preparations. To ensure protection of the public, a sterile compounding permit holder will be required to report to the Board within 5 calendar days:

- (1) Adverse events including corrective actions taken or proposed;
- (2) Deficiencies related to the sterile compounding process;
- (3) Disciplinary action in other states or by other state agencies;
- (4) Changes in accreditation status;
- (5) Disciplinary actions taken against a health care practitioner who is an owner operator or employee of the sterile compounding permit holder; and
- (6) Disciplinary action taken against any other known permit, or any other authorization, held by the sterile compounding permit holder.

The proposed regulations for the sterile compounding permit requirements were drafted by the Subcommittee and approved by the full Board at the October 16, 2013 Public Board Meeting. The proposed regulations were released for “informal comment” to an extensive list of stakeholders on October 25, 2013 for a two week comment period. The draft released is attached as Appendix III.

Sterile Drug Products and Waiver Criteria

“Sterile drug products” was newly defined in Maryland statute to mean *a drug product that must be prepared using aseptic techniques and is not required to be prepared in response to a patient specific prescription*. In essence, preparation of sterile drug products is manufacturing, which provides the rationale for determining that an entity that prepares and distributes sterile drug products in Maryland would be required to obtain an appropriate FDA manufacturer permit. The revisions in the chapter that describe what is required to manufacture sterile drug products is straight forward; based on existing requirements. An entity would have to obtain the appropriate FDA manufacturer permit and also have a wholesale distributor permit from the Board. Since all manufacturers who distribute in Maryland are considered distributors, they would also be required to acquire a Board-issued wholesale distributor permit.

The draft regulations for the sterile drug products and waiver criteria were drafted to reflect the definitions in HB 986 for adverse events, compounding, designee, health care practitioner, sterile compounding, sterile compounding facility, and sterile drug product. The definitions, again, were added to clarify terms to assure a common perspective when the terms are used. The draft regulations also included requirements for the waiver application, inspections, adverse event reporting, record keeping, documentation of administration of sterile drug products, renewal procedures, and procedures for amendments to the waiver.

The statute, and proposed corresponding regulations, allow for a waiver for entities that do not have an FDA permit, but wish to manufacture sterile drug products and distribute them into Maryland under very strict criteria. The waiver is time-limited and can only be approved for a specific sterile drug product where exigent circumstances exist under the following criteria:

- (a) The specified sterile drug product in the size and strength needed is:
 - (i) Listed on the current drug shortages index by the U.S. Food and Drug Administration or other nationally recognized index; or
 - (ii) Only prepared and distributed by the person applying for the waiver; and
 - (b) The absence of the specified sterile drug product would result in a patient care or a patient safety risk; and
- (2) There is a clinical need.

The Board will determine when there is a “clinical need” with input from relevant professionals as determined by the Board. Criteria for determining whether a waiver is approved may not be based on financial or business concerns.

The proposed regulations for sterile drug products and the waiver requirements were approved by the Board at the September 20, 2013 Public Board meeting and were released for “informal

comment” to an extensive list of stakeholders on October 11, 2013 for a two week comment period. The released draft is attached as Appendix IV.

Informal Comments and Board Response

The Board received eleven comments as a result of the informal release of the proposed Sterile Compounding Permit regulations and the proposed Sterile Drug Product and Waiver regulations. Comments were received from the Maryland Society of Health System Pharmacists, St. Agnes Hospital, Maryland Hospital Association, Donald Taylor, Mel Rubin, Dan Doherty, Professional Arts Pharmacy, JCB Laboratories, Omnicare, Inc., Pharmacy Compounding Accreditation Board, and DHMH. The Subcommittee reviewed the comments and responded with one letter addressing all the concerns. That response was approved by the Board at the November 20, 2013 Public Board Meeting and emailed to stakeholders on December 4, 2013. Below are the revisions and suggestions from the informal comments and the Board’s response:

The draft proposed regulations released for informal comment (See Appendices III and IV) were incorporated into one proposal with the following renumbering of the regulations:

- .17 Sterile Compounding Permit Application Requirements.
- .18 Minimum Requirements for Inspections of Sterile Compounding Permit Holders.
- .19 Reporting Requirements for Sterile Compounding Permit Holders.
- .20 Sterile Drug Products.
- .21 Sterile Drug Product Waiver.

.03 Definitions.

“Adverse Event”

It was suggested that this definition be revised to read “Adverse events” means: (a) Any adverse patient outcome related to the *sterility of the sterile* compounding process. The Board considered this wording, but determined that only adding the word “*sterile*” would be sufficient so as not to place limits on what would be considered an adverse event.

It was noted in “(b) Evidence of environmental contamination, including microbial contamination above the threshold as set forth in USP 797 Standards.” that USP 797 would consider a facility contaminated even below the threshold if the bacteria are pathogenic. The Board responds that there is currently a threshold in USP 797 Standards for pathogenic bacteria and no revisions will be made.

“Biological safety cabinet”

It was suggested that the Board include two types of biological safety cabinets in the definition. The Board, to be consistent with USP 797 Standards, will be making no revisions to this definition.

“Clean room”

It was noted that this definition did not take into consideration that some “open architecture” clean rooms consist of only an ISO-5 environment, therefore; the Board added “*a room with an ISO-5 environment or*” to the beginning of the definition.

“Compounding”

It was suggested to remove the word “assembling” from the definition of “compounding.” The Board determined that the word “assembling” is necessary in the definition since “assembling” does occur in some locations and it is also included in the definition set forth in the law. See Health Occupations Article, 12-101, Annotated Code of Maryland.

“Designee”

It was suggested that the Board consider adding standards for the Board’s approval of a “designee.” The Board decided to add a phrase “*trained in USP 797 Standards and/or FDA good manufacturing practices*” after “public agency or private entity” so that it would be clear that any designee would be properly trained to inspect sterile compounding facilities.

“Health Care Practitioner”

It was asked if dentists, podiatrists, and veterinarians are currently allowed to compound drugs. The Board defers to the licensing boards of these health professions, but the Board’s understanding is that it is within these professions’ scope of practice. See Health Occupations Article, 12-102, Annotated Code of Maryland, that allows these individuals to personally prepare prescriptions.

“Low risk,” “Medium risk,” and “High risk” were removed from the proposal since those terms are duplicative of the definition of risk level which references USP 797 Standards.

“Sterile compounding facility”

The definition of “sterile compounding facility” was revised to clarify the environment where sterile compounding would be performed and where sterile compounding permits are required.

(16-2) “Sterile compounding facility” means a pharmacy, a health care practitioner’s office, or any other setting in which sterile compounding is performed in a controlled environment as required by USP 797 Standards.

“Sterile drug product”

It was noted that generally the word “product” refers to a manufactured drug. In the HB986, however; it is included in the definition of “sterile drug product” and the Board is bound by the definition in the statute.

Please note that the definitions have been renumbered for clarity.

.09 Minimum Facility Requirements.

At the beginning of Regulation .09, under A. Controlled Environment, the regulations require that a sterile compounding facility have a controlled environment. Concern was expressed that this would require the same facility and supply requirements for a pharmacy as “immediate use” compounding on a nursing unit or operating room in a hospital. It was suggested that there be an exemption in these regulations for “immediate use.” The Board will not be adding an exemption because USP 797 Standards already include an exemption for “immediate use.” The Board will, however; add to the end of the first subsection the following for clarification purposes:

(1) The [pharmacy] sterile compounding facility shall have a controlled environment that meets USP 797 Standards.

B. and C. Controlled Environment – Clean Room and Anteroom

It was suggested to clarify regarding the barrier isolator exemption. The Board will not be adding clarification here as it is addressed in USP 797 Standards.

.17 Sterile Compounding Permit Application Requirements. (.19 in the released draft)

In Section D(7) the applicant is required to “submit reports and corrective actions taken or proposed in response to adverse events indentified 12 months before submission of the application;” A comment was received that asked whether this would be required for renewal since it would be duplicative. The Board will not be asking for these reports upon renewal. See Section H for the renewal requirements.

Section F states: “A separate sterile compounding permit is required for each site at which sterile compounding is performed.”

Clarification has been requested regarding the scope of practitioners and physical plant covered under a single permit. There was concern that nursing units, hospital clinics, physician’s offices and pharmacies would be required to obtain this permit if sterile compounding. It is the Board’s understanding that nursing units do not perform sterile compounding, except perhaps for immediate use. Immediate use is an USP 797 Standards exemption. If a person is compounding in a controlled environment, then a sterile compounding permit would be required.

.18 Minimum Requirements for Inspections of Sterile Compounding Permit Holders. (.20 in the released draft)

It was recommended to revise subsection B(3) to be consistent with USP 797 Standards so that it would read: “The sterile compounding permit holder shall provide as a part of the inspection process: (3) Microbial testing of a sampling of the sterile compounded preparations of the sterile compounding facility *if applicable according to USP 797 Standards.*”

The Board agrees with this revision since there may be circumstances when sampling tests would not be available for inspection. This would occur because testing the preparation might compromise the preparation’s integrity for a specified patient.

.19 Reporting Requirements for Sterile Compounding Permit Holders. (.21 in the released draft)

It was suggested that reporting adverse events including corrective actions taken or proposed should be reported within 15 business days after sampling results are conclusive, instead of 5 days as required by the proposed regulations. Even though some sampling results may take longer than 5 days, the Board would like whatever information a permit holder has as soon as possible within the 5 day timeframe. The permit holder can send further results as they become available, but the Board wants to know if there is a problem as soon as the permit holder knows.

Additionally, it was suggested that reporting of deficiencies also be extended to 15 business days. The Board does not agree, and again, wants to know of deficiencies as soon as possible within the 5 day timeframe.

The Board made a revision for clarification to Section B(2) to clarify that deficiencies would be related to the sterile compounding process: “B. Report to the Board within 5 calendar days: (2) Deficiencies *related to the sterile compounding process.*”

.20 Sterile Drug Products. (.17 in the released draft)

This section, taken directly from HB986, sets forth the requirements for persons that are preparing and distributing sterile drug products. Those persons require an U.S. Food and Drug Administration (FDA) manufacturer’s permit and a Wholesale Distributor Permit from the Board. Those persons who prepare sterile drug products would not be required to have a sterile compounding permit. The only revision that the Board will make to this section concerns the requirement that a person that prepares and distributes sterile drug products shall hold a wholesale distributor’s permit, *if applicable*. This was added to accommodate the practice of intracompany transfers of sterile drug products, which would not require a wholesale distributor permit. This often occurs within health systems.

Keep in mind that a hospital that prepares patient specific sterile compounded medications would require a Sterile Compounding Permit and would not fall under this section.

.21 Sterile Drug Product Waiver. (.18 in the released draft)

In the proposed Section A(1) it specifies that the Board may issue a waiver to a person that prepares and distributes sterile drug products only for a specified sterile drug product. A comment was received that asked the Board to consider granting a waiver for compounding pharmacies that covered all the medications compounded within that pharmacy if the pharmacy were able to meet all of the requirements of the Board, including the new Sterile Compounding Permit requirements. The Board is not able to make this change since the law specifies that waivers may be granted only for a specified drug product.

In the proposed Section A(1)(a)(i) it lists criteria for exigent circumstances. One of those criteria is that the sterile drug product is listed on the current drug shortages index by the FDA. It was suggested that there might be timelier or more accurate sources for drug shortage information. To allow for other sources the Board revised this section by adding: “*or other nationally recognized index;*”

In the proposed Section A(1)(a)(ii) one of the criteria for exigent circumstances is that the specified drug product must only be prepared and distributed by the applicant or the person applying for the waiver. It was questioned in one of the comments whether this may restrict who may apply to compound a specific medication on the drug shortage list. The language in this section does not restrict who may apply. It only requires that whoever is applying must do the actual preparation and distribution.

Additionally, a comment was received that questioned who was meant by “person applying for the waiver.” Person in this context would be the facility applying to perform the compounding of a sterile drug product, not the individual completing the application.

In the proposed Section A(2)(a) it lists the health care providers in the State who will assist the Board in determining clinical need for a waiver. A comment was received that questioned why the Board has limited the stakeholder feedback to licensed health care providers from specified trade associations. Upon consideration, the Board agrees and revised this section to read:

“For which there is a clinical need as determined by the Board with input from relevant professionals as determined by the Board;”

In the proposed Section A(2)(b) “clinical need” may not be based on financial or business concerns. A comment was received requesting that clinical need may not *primarily* be based on financial or business concerns since there may be situations where a financial concern may be one component of a need. The Board will not be adding a financial component to criteria for clinical need as these concerns do not fit within a patient’s exigent circumstances or a patient’s clinical need for a medication.

In the proposed Section A(3)(b) the applicant is required to meet requirements such as identifying “in the application the highest USP 797 risk levels of compounding engaged in by the applicant.” A comment was received that suggested that if the facility is FDA registered, the FDA may require good manufacturing practice compliance rather than USP compliance. The Board notes that an applicant applying for a waiver would apply because that applicant does not have an FDA permit.

Additionally, another comment was received about this section with concerns that only one level of risk would be reported. The Board notes that it would only need to know the highest risk level of preparation. If an applicant meets the standards for a high risk level than the applicant would also meet lower risk levels as well.

In the proposed Section A(3)(g), it was noted by more than one individual, that the word “If” was missing from the beginning of this sentence. The Board has added it in.

In the proposed Section A(3)(h), the applicant is required to submit evidence of good standing with any other Maryland licensing entity or the licensing entity in the state in which the applicant is located. It was asked if the Board should also require evidence of good standing from the FDA. Again, if the applicant is applying for a sterile drug product waiver, it would not have an FDA permit.

In the proposed Section H, the holder of a sterile drug product waiver shall submit amendments to the waiver in advance to the Board for approval, including the addition of a specified sterile drug product. Concern was expressed that in cases when a patient’s need is urgent, an exception to this requirement may be warranted. The Board assures the public that it will give urgent patient needs priority when approving sterile drug product waivers or amendments to sterile drug product waivers.

Please note that renumbering has occurred in the final proposal.

General Comments

Please be advised that the law in Maryland is clear. Health Occupations Article, 12-101, Annotated Code of Maryland.

“Compounding” means the preparation, mixing, assembling, packaging, or labeling of a drug or device:

(i) As the result of a practitioner’s prescription drug order or initiative based on the practitioner/patient/pharmacist relationship in the course of professional practice; or

(ii) For the purpose of, or incident to, research, teaching, or chemical analysis and not for the sale or dispensing of the drug or device.

(2) “Compounding” includes the preparation of drugs or devices in anticipation of a prescription drug order based on routine, regularly observed prescribing patterns.

This does not allow a practitioner to write drug orders for office use or allow a pharmacy to compound a sterile product for use in an office.

There was some confusion expressed in one comment about what is meant by “distribute,” “distribution,” and “dispense” within HB986. HB986 requires a practice to acquire a Sterile Compounding Permit regardless of whether the medication is “administered,” “dispensed,” or “distributed.” The legislation is about sterile compounding of a product. Non-sterile compounding, such as amalgam filling in the restoration of a tooth, is not regulated by this legislation.

A few of the informal comments pointed out formatting and grammatical errors in the proposed regulations. The Board made corrections and revisions where necessary. The final version of the proposed regulations, incorporating the changes above, was also approved by the Board on November 20, 2013. (See Appendix V) The Board submitted the proposed regulations to DHMH for sign-off and submission to the Maryland Register for publication on November 21, 2013.

Federal Legislation

The federal Drug Quality and Security Act passed and was signed by President Obama the end of November 2013. This legislation addresses compounding nationally and establishes a U.S. Food and Drug Administration (FDA) permit for “outsourcing facilities” that perform sterile compounding without a patient specific prescription. The Board’s Sterile Compounding Subcommittee will meet in early January 2014, to consider if amendments would be necessary to Maryland’s Health Occupations Article, Title 12, Subtitle 4A Sterile Compounding Permits, so that it does not conflict with the new federal law.

Hiring and training of staff

In the fiscal note for HB 986, the Board indicated that the program would increase operations at the Board. In addition to its existing regulatory authority over sterile compounding pharmacies in Maryland, the Board would assume additional regulatory responsibilities to ensure the safety of non-resident sterile compounding pharmacies and sterile compounding facilities that perform sterile pharmaceutical compounding for Maryland patients. The Board projected that at least four additional staff will need to be recruited to meet its new responsibilities. The additional personnel minimally needed are:

- Two Pharmacists III, Grade 18, Step 8, to assist existing inspection personnel in performing field inspections of compounding pharmacies and other establishments located in Maryland (e.g., hospital, long term care and home infusion pharmacies, and wholesale distributors, sterile compounded products distributors, etc), and review sterile compounding reports provided from non-resident entities;
- A Laboratory Scientist Surveyor I, Grade 16, Step 8, to work in-house to review compounding pharmacy applications and to review and interpret scientific reports provided by compounding pharmacies to insure compliance; and
- An Office Services Clerk, Grade 8, Step 3, to perform licensing tasks related to the projected increase in applications submitted to the Board and issue compounding pharmacy permits.

In addition the Board will need to acquire two new vehicles to conduct the inspections required by HB 986.

During the first year of operations, the Board projects that it will be able to absorb start-up costs (\$77,785) using funds available in its projected surplus. Cost for implementing the new regulations are guesstimates only. The Board does not know how many types of sterile compounders are operating in Maryland in addition to the approximately 110 sterile compounding pharmacies. The Board's projections are based on its projection of an approximate total of 300 entities that would require a sterile compounding permit to operate in Maryland.

The Board has requested DHMH to take steps that will allow recruitment of staff in the positions to be recruited and begin training no later than January 2014.

Summary of Implementation Timeline

The Sterile Compounding Permit and Sterile Drug Products regulation revisions were drafted separately and released for comment separately. Both parts will be combined in the final proposal that is submitted for promulgation. Below is a timeline for implementation of HB 986 and promulgating regulations:

- 10/11 - 10/25 - Board released Sterile Drug Product regulations .01, .17 and .08 for informal comment (sterile drug products and waiver).
- 10/25 - 11/8 - Board released Sterile Compounding Permit regulations for informal comment.

- 10/25 - 11/13 - Subcommittee reviews all comments received, drafts responses to comments, makes revisions, as necessary, to both the Sterile Drug Product and Sterile Compounding Permit draft regulations.
- 11/20 – Board approves the entire chapter of revisions that will include new fees for the Sterile Compounding Permit and the Sterile Drug Product Waiver.
- 11/21 – Board submission of a revised 10.34.19 Sterile Compounding Preparations and Sterile Drug Products, with all revisions as an Emergency Proposal with an identical regular proposal.

Operational Implementation:

- 10/15/2014 – 2/15/2014 – Preparation of applications, inspection forms and internal procedures.
- 12/10/13 – 1/10/2014 - New staff recruitment.
- 1/10/2014 - 4/1/14 - Train new and existing staff on regulatory requirements and operation procedures.

Fees:

The Board also determined the economic impact of this program on the Board’s current resources and staffing needs to determine what fees to impose for the new licensing category. The new fees were added to COMAR 10.34.09 Fees, and are included in the regulatory proposal submitted to DHMH. An economic impact statement is included in Appendix V.

CONCLUSION

The Board has worked diligently to implement HB 986 State Board of Pharmacy – Sterile Compounding – Permits, Chapter 397, 2013, so that the risk of contaminated injectables being dispensed to Maryland patients are significantly reduced. The Board immediately appointed a Subcommittee to draft regulations and spearhead the implementation process. The Subcommittee began work in June, preceding the effective date of the new law, to draft regulations, solicit public comment, create new applications, and assist Board staff in preparing for the new complex licensure category.

Since the effective date of the HB 986, the Subcommittee has drafted revisions to COMAR 10.34.19 Sterile Pharmaceutical Compounding, which address the new sterile compounding permit and the regulation of the manufacture of sterile drug products. The Board has received some initial comments from a solicitation for comment that was placed in the DHMH website. After drafting revisions to COMAR 10.34.19 and adding in new regulations to address HB 986, the Board has released drafts to the public for informal comment in two phases.

The first informal release addressed sterile drug products and the sterile drug product waivers. Within this release were revisions to the scope of the chapter and also definitions consistent with the new law. Also in this release were new regulations to address what is required if an entity chooses to manufacture sterile drug products in Maryland. Finally, this release contains a new regulation how an entity may apply for a waiver from requirements to produce sterile drug products without an FDA permit.

The second informal release addressed the sterile compounding permit. Within this release were the same revisions to the definitions section as in the sterile drug product release. This version also contained revisions to 9 other regulations which consisted of striking the word “pharmacist” and replacing it with “health care practitioner” and striking the word “pharmacy” and replacing it with “sterile compounding facility.” Revisions also included a minor change to Regulation .06 Special Handling, Packaging, Labeling, and Beyond Use Dating, to ensure that only a pharmacy would be the entity that is allowed to deliver sterile compounded prescriptions to a patient. An additional revision was made to Regulation .07 Record-Keeping Requirements, to ensure that a sterile compounding facility would keep completed patient prescription records in a retrievable manner for at least 5 years, either at the inspection site or retrievable by computer or other electronic means. There were 3 new regulations included in this release addressing Sterile Compounding Permit Application Requirements; Minimum Requirements for Inspections of Sterile Compounding Permit Holders; and Reporting Requirements for Sterile Compounding Permit Holders.

Upon receiving informal comments from a variety of stakeholders, the Subcommittee met and revised the proposed regulations to reflect recommendations and suggestions received. The draft proposed regulations released for informal comment were incorporated into one proposal and submitted to DHMH for sign-off and the promulgation process. The Board prepared one detailed response discussing all the concerns and explaining why revisions were, or were not, made. The major revisions include:

- Deleting unnecessary definitions and revising definitions for clarification purposes;
- Clarification that a sterile compounding facility would be required to have a controlled environment that meets USP 797 Standards;
- Clarification that during an inspection, a sterile compounding facility would provide microbial testing of a sampling of the sterile compounded preparations of the sterile compounding facility, if applicable according to USP 797 Standards. The Board recognizes that some testing would not be immediately available;
- Under the sterile drug product regulation, the Board added “if applicable” after the requirement of a wholesale distributor permit as in some instances the wholesale distributor permit would not be required;
- Expansion of the source of a current drug shortage index beyond the FDA to include “or other nationally recognized index;” and

- Revising the list of health care providers who will assist the Board in determining clinical need for a waiver to those relevant professionals as determined by the Board.

Along with amending regulations and drafting new regulations, the Subcommittee and Board staff has worked to timely implement all phases of this new level of licensure and waiver. New applications for sterile compounding permits and sterile drug product waivers have been created and are in the Board approval process. Board is pursuing approval to recruit permanent staff to evaluate applications and inspect pharmacies and sterile drug product manufacturers. A plan has been created to draft inspection forms for sterile drug product manufacturers and training inspectors. The Board's database will also need revisions and additions to allow for a new licensure category and to store records and activities of sterile compounders and manufacturers of sterile drug products.

HO §12-4A affects every unit of the Board and each unit has been working toward the implementation deadline of April 1, 2014. The report includes a timeline that the Board has adhered to so that revisions to regulations, new applications, new inspection forms, new staff and staff training will be completed for full implementation on April 1, 2014. With the passage of the federal Drug Quality and Security Act it remains to be seen whether or not additional statutory revisions will be necessary to avoid conflict with the federal law and continue to protect the public.

APPENDIX I

BOP public comment compounding

Maryland Board of Pharmacy Request for Public Comment: Compounding Statute-Related Questions

In the summer and fall of 2012, contaminated injectable steroids produced by the Massachusetts-based New England Compounding Center caused a multistate outbreak of fungal infections, including fatal fungal meningitis infections. The contaminated injectable steroids were shipped to seven facilities in Maryland. At least 26 people were infected by the contaminated steroids administered in Maryland; three of those people have died. In response to this situation, a new statute was enacted which provides the Maryland Board of Pharmacy more authority to oversee sterile compounding. The Board is soliciting public input on several related questions. First, the statute allows the board to set additional requirements for a separate license for sterile compounding.

- ***What special requirements for sterile compounding should the Board consider?***

Second, the new statute prohibits the sale of sterile medications not produced by FDA licensed manufacturers or made pursuant to a sterile compounding license; however, the law permits the Board of Pharmacy to waive - in special, specified situations - these requirements and allow products manufactured in bulk in a facility that is not FDA licensed and where products are not traditionally compounded. Such a waiver may be issued only in exigent circumstances for drugs for which there is a clinical need.

- ***What are such exigent circumstances that might necessitate a waiver?***
- ***What are examples of specific sterile products and clinical situations that might meet criteria for such a waiver?***
- ***What process can the Board use to keep a current list of products for which there is a need for a waiver?***
- ***In addition to provision of reports of inspections, a statement of compliance with USP 797, and review and report of any adverse regulatory action, what else should be required of people or facilities producing and distributing "waived" sterile products?***
 - ***How can the Board know when the need for a "waived" sterile product no longer exists?***
- ***Should there be an emergency waiver process, and if so, when would that be needed and how might that work?***

Please submit all responses to the Maryland Board of Pharmacy no later than July 25, 2013.

E-Mail: DHMH.MDBOP@Maryland.gov

(please put "Sterile Compounding Comments Attn: Anna Jeffers" in subject line)

Mail: Maryland Board of Pharmacy

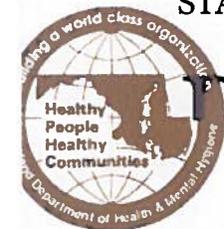
4201 Patterson Avenue

Baltimore, MD 21201

Attn: Anna Jeffers

APPENDIX II

STATE OF MARYLAND



DHMH

Department of Health and Mental Hygiene

*Martin O'Malley, Governor – Anthony G. Brown, Lt. Governor –
Joshua M. Sharfstein, MD, Secretary*

MARYLAND BOARD OF PHARMACY

4201 Patterson Avenue • Baltimore, Maryland 21215-2299

Lenna Israbian-Jamgochian, Board President - LaVerne G. Naesea, Executive Director

September 20, 2013

Soumi Saha, PharmD, JD
Government Relations and Regulatory Affairs Coordinator
Kaiser Permanente
2010 East Jefferson Street
Department of Pharmacy Services, 3-West
Rockville, MD 20852

Meghan Davlin Swarthout, PharmD, MBA, BCPS
Heather Hurley, PharmD, BCPS
Co-Chairs, Legislative Committee
Maryland Society of Health System Pharmacists
800 SW Jackson Street, Suite 1500
Topeka, KS 66615
mdavlin1@jhmi.edu

Dear Dr. Hurley, Dr. Swarthout, and Dr. Saha:

Thank you for providing comments in reference to the HB 986 State Board of Pharmacy – Sterile Compounding – Permits, Chapter 397, 2013, (HB986), prior to the promulgation of the regulations. The Board's solicitation for comment included a series of questions for stakeholders to consider. Those questions are set forth below with a summary of comments received from both Kaiser Permanente and the Maryland Society of Health System Pharmacists followed by the Board's response.

1. What special requirements for sterile compounding should the Board consider?

It was suggested that the Board consider the following special requirements for sterile compounding:

a. Federal legislative impact.

It was noted that there are inconsistencies between the proposed federal legislation and HB 986.

The proposed federal legislation does not allow a compounding manufacturer to register as a pharmacy in any state so that there is a clear distinction between federal and state oversight. This is problematic for those entities that perform sterile compounding and also manufacture sterile drug products. The Board is following the federal legislation and understands that revisions may need to be made to the new Subtitle 4A, Sterile Compounding Permits, in the future.

b. Transfer of products within health systems.

It was suggested that the Board consider in the proposed regulations the transfer of patient specific compounded medications within a hospital's pharmacies or a health system's pharmacies. Please be advised that these types of transfers may be considered "intracompany" and would not be subject to HB 986.

c. Transfer between health systems.

It was also suggested that the Board consider allowing the transfer of sterile compounds between hospitals or health systems to occur when needed urgently for patient care. The Board is taking into consideration, and HB 986 accommodates, drug shortages. Transfers between health systems are not "intracompany" and would be subject to HB 986.

2. What are such exigent circumstances that might necessitate a waiver?

It was suggested that the Board consider the following categories of exigent circumstances that may necessitate a waiver:

a. Drug Shortages.

HB 986 was crafted to address drug shortages and a mechanism for the provision of compounded medications and sterile drug products to Maryland citizens when there is a true drug shortage.

b. Emergent In-Office Use.

It was pointed out that the ability to obtain non-patient specific sterile compounds for emergent in-office use is critical for the immediate treatment of urgent conditions that require timely administration of medications to prevent negative health care outcomes. It was recommended that the definition of "emergent" include any diagnosis where treatment with a sterile compounded medication within 72 business hours is clinically necessary to prevent adverse health outcomes.

The Board notes that within a 72 hour window a patient specific prescription could be made available to obtain the medications needed and would not be an emergent reason for a waiver. In addition, compounding under urgent conditions becomes a patient safety risk.

Additionally, the Board will place in the proposed regulations a provision that does not allow a waiver based on criteria based on financial or business concerns. The Board believes this supports the intent of the legislation that allows a waiver for which there is a clinical need and there are emergent circumstances that, as determined by the Board, otherwise prevent health care providers from obtaining, in the size and strength needed, the specified sterile compounded preparations or sterile drug products for which there is a clinical need.

c. Non-Compounding Manufacturers

It was suggested that entities that could not obtain an FDA permit be automatically waived from the requirements of a wholesale distributor permit.

Additionally, it was noted that federal legislation is pending that precludes an entity that is licensed as a pharmacy from receiving a compounding manufacturer permit from the FDA in order to differentiate between federal and state oversight. Those entities that have dual business purposes, patient specific and sterile drug products would not be able to register with the FDA and would not be eligible to ship non-patient specific sterile drug products into MD without a waiver.

The Board notes that this is the intent of HB 986 – to provide a mechanism to provide a waiver for those entities that do not qualify for a sterile compounding permit or are not able to obtain an FDA permit and to know exactly which entities are dispensing or distributing sterile drug products to Maryland citizens.

A suggestion for dual business entities that perform patient specific compounding and compound sterile drug products would be for those entities to establish separate entities for each purpose.

d. USP 797 low risk compounding

It was suggested that hospitals and health systems that only prepare low risk compounds, as defined in USP <797>, be eligible for a sterile compounding permit waiver.

The waiver is not intended for pharmacies that are compounding as defined in USP <797>. Pharmacies performing compounding under USP <797> are required to obtain the Sterile Compounding Permit.

3. What are examples of specific sterile products and clinical situations that might meet criteria for such a waiver?

Several comments were received which listed specific sterile products and clinical situations that might meet the criteria for a waiver. HB 986 is very specific when a waiver may be issued.

HB 986 sets forth that the Board may issue a waiver of the Maryland requirements for FDA manufacturers to a person that prepares and distributes sterile drug products into, out of, or within the State only for a specified sterile drug product where exigent circumstances exist. The criteria for exigent circumstances may include that the specified sterile drug product is listed on the current drug shortages index by the U.S. Food and Drug Administration or the specified drug product is only prepared and distributed by the person applying for the waiver. Additionally, the absence of the specified sterile drug product would result in a patient care or a patient safety risk may be considered. Clinical need will be determined by the Board with input from health care providers in the State such as the Maryland Hospital Association; the Maryland Society of Health-Systems Pharmacists; the Maryland State Medical Society; and other relevant professionals as determined by the Board. The criteria may not be based on financial or business concerns;

4. What process can the Board use to keep a current list of products for which there is a need for a waiver?

It was suggested that the Board form an expert taskforce with representation from different areas of pharmacy to review, approve, and oversee the list of products for which there is a need for a waiver with final approval of the list by the Board.

The Board plans to use the FDA Drug Shortage List when considering granting a waiver.

5. In addition to provision of reports of inspections, a statement of compliance with USP 797, and review and report of any adverse regulatory action, what else should be required of people or facilities producing and distributing “waived” sterile products?

No additional requirements were suggested in the comments received.

6. How can the Board know when the need for a “waived” sterile product no longer exists?

It was suggested that the expert taskforce suggested above would be responsible for reviewing the list of “waiver” sterile products and make recommendation to the Board regarding when the need for a product waiver no longer exists.

The Board plans to use the FDA Drug Shortage List when considering the need to continue a waiver.

7. Should there be an emergency waiver process, and if so, when would that be needed and how might that work?

There was a suggestion that an emergency waiver process be available for short notice drug shortages caused by urgent recalls or other emergent situations, including natural disasters. It was also suggested that facilities be allowed to compound to meet urgent needs while their waiver application is pending.

HB 986 establishes a process to allow for waivers for exigent circumstances. For situations that require immediate action, specifically during natural disasters or federal or State emergencies, the Secretary may override HB 986 and allow for the necessary compounding to meet the health needs of Marylanders.

8. Additional comments.

It was suggested that formal training be conducted for Board of Pharmacy inspectors concerning USP <797>. Please know that the Board’s inspectors have received extensive training in USP <797> as COMAR 10.34.19 Sterile Pharmaceutical Compounding has been effective since 2009 incorporating all the revisions to USP <797>. The Board inspects all pharmacies annually and has been thoroughly inspecting compounding pharmacies for compliance with USP <797> since 2009.

It was suggested that annual inspections of pharmacies, and annual inspections of those pharmacies that hold sterile compounding permits, occur at the same time. The Board is conscious of preserving resources and will make every effort to inspect pharmacies, regardless of permit status, only once a year, unless otherwise warranted.

It was also suggested that decentralized pharmacies within a hospital system have clear direction regarding sterile compounding. All pharmacies that obtain a sterile compounding permit will be subject to the same laws and regulations.

Thank you again for your thorough consideration of the solicitation for comment posted on the Department of Health and Mental Hygiene's website. Drafts of the regulations will be released informally this fall. Please also monitor the Maryland Register for the initial publication of the proposed revisions to COMAR 10.34.19 Sterile Pharmaceutical Compounding.

<http://www.dsd.state.md.us/MDRegister/mdregister.aspx> A 30 day comment period will follow. Should you have questions or additional concerns, please feel free to contact Anna D. Jeffers, Legislation and Regulations Manager at (410) 764-4794.

Sincerely,



LaVerne G. Naesea
Executive Director

cc: Linda Bethman, Board Counsel, Board of Pharmacy
David Blythe, M.D., Deputy Secretary of Infectious Diseases, DHMH
Mitra Gavvani, Member of Subcommittee on Revisions to Sterile Compounding Regulations
Lenna Israbian-Jamgochian, President, Maryland Board of Pharmacy
Anna D. Jeffers, Legislation and Regulations Manager, Board of Pharmacy

STATE OF MARYLAND



Department of Health and Mental Hygiene

Martin O'Malley, Governor – Anthony G. Brown, Lt. Governor –
Joshua M. Sharfstein, MD, Secretary

MARYLAND BOARD OF PHARMACY
4201 Patterson Avenue • Baltimore, Maryland 21215-2299
Lenna Israbian-Jamgochian, Board President - LaVerne G. Naesea, Executive Director

September 20, 2013

Gregory P. Smith, RPh, MBA
Director of Pharmacy
Saint Agnes Hospital
900 S. Caton Avenue
Baltimore, MD 21229
Gsmith1@stagnes.org

Dear Mr. Smith:

Thank you for providing comments in reference to the HB 986 State Board of Pharmacy – Sterile Compounding – Permits, Chapter 397, 2013, (HB986), prior to the promulgation of the regulations. Below are responses to your questions:

Does this pertain to compounding for own use?

HB 986 pertains to compounding pursuant to a patient specific prescription and also to the preparation of sterile drug products which are prepared using aseptic techniques and are not required to be prepared in response to a patient specific prescription.

Do hospitals need to get the additional permit?

All pharmacies licensed in Maryland will be required to obtain a sterile compounding permit if they are performing sterile compounding.

Is there a difference between anticipatory compounding and patient specific?

Yes. Please see COMAR 10.34.19.08 which pertains to “batch preparation” or anticipatory compounding. Patient specific prescriptions are the basis for “batch preparations.”

.08 Batch Preparation.

A. A pharmacist may prepare batched sterile preparations for future use in limited quantities supported by prior valid prescriptions or physician orders before receiving a valid written prescription or medication order.

B. Batch preparation of specific compounded sterile preparations is acceptable if the:

- (1) Pharmacist can document a history of valid prescriptions or physician orders that have been generated solely within an established professional prescriber-patient-pharmacist relationship; and
- (2) Pharmacy maintains the prescription on file for such preparations dispensed.

Will there be different standards based on whether the compound is low risk, medium risk, or high risk?

No.

Shipping concerns due to environment (temperature) and security.

Please see COMAR 10.34.25 Delivery of Prescriptions, which applies to shipping of all prescription medications by a Maryland pharmacy.

Thank you again for your thorough consideration of the solicitation for comment posted on the Department of Health and Mental Hygiene's website. Drafts of the proposed regulations will be released informally. Please monitor the Maryland Register for the initial publication of the proposed revisions to COMAR 10.34.19 Sterile Pharmaceutical Compounding. <http://www.dsd.state.md.us/MDRegister/mdregister.aspx> A 30 day comment period will follow. Should you have questions or additional concerns, please feel free to contact Anna D. Jeffers, Legislation and Regulations Manager at (410) 764-4794.

Sincerely,



LaVerne G. Naesea
Executive Director

cc: Linda Bethman, Board Counsel, Board of Pharmacy
David Blythe, M.D., Deputy Secretary of Infectious Diseases, DHMH
Mitra Gavvani, Member of Subcommittee on Revisions to Sterile Compounding Regulations
Lenna Israbian-Jamgochian, President, Maryland Board of Pharmacy
Anna D. Jeffers, Legislation and Regulations Manager, Board of Pharmacy

STATE OF MARYLAND



Department of Health and Mental Hygiene

Martin O'Malley, Governor – Anthony G. Brown, Lt. Governor –
Joshua M. Sharfstein, MD, Secretary

MARYLAND BOARD OF PHARMACY

4201 Patterson Avenue • Baltimore, Maryland 21215-2299

Lenna Israbian-Jamgochian, Board President - LaVerne G. Naesea, Executive Director

September 20, 2013

Basil Morgan, MD, President
Maryland Society of Eye Physicians and Surgeons
1211 Cathedral Street
Baltimore, MD 21201
BEV@AMG101.COM

Dear Dr. Morgan:

Thank you for providing comments in reference to the HB 986 State Board of Pharmacy – Sterile Compounding – Permits, Chapter 397, 2013, (HB986), prior to the promulgation of the regulations. The Maryland Society of Eye Physicians and Surgeons urged the Board to include office use exemptions for compounded biologics and other FDA marketed drugs to ensure that ophthalmologists have access to them for their patients to receive critical, sight-saving treatment.

Please be advised that the law in Maryland is clear. Health Occupations Article, 12-101, Annotated Code of Maryland. HB 986 has not changed this definition.

“Compounding” means the preparation, mixing, assembling, packaging, or labeling of a drug or device:

(i) As the result of a practitioner’s prescription drug order or initiative based on the practitioner/patient/pharmacist relationship in the course of professional practice; or

(ii) For the purpose of, or incident to, research, teaching, or chemical analysis and not for the sale or dispensing of the drug or device.

“Compounding” includes the preparation of drugs or devices in anticipation of a prescription drug order based on routine, regularly observed prescribing patterns.

Compounded medications obtained for office use that are commercially available may be purchased from an FDA manufacturer. For those compounded medications that are not commercially available, and there is an emergent need as determined by the Board using the criteria in HB 986, there will be a waiver available. The waiver is intended for entities that are licensed as wholesale distributors and where there is no FDA permit available.

Thank you again for your thorough consideration of the solicitation for comment posted on the Department of Health and Mental Hygiene's website. Drafts of the proposed regulations will be released informally this fall. Please also monitor the Maryland Register for the initial publication of the proposed revisions to COMAR 10.34.19 Sterile Pharmaceutical Compounding.

<http://www.dsd.state.md.us/MDRegister/mdregister.aspx> A 30 day comment period will follow.

Should you have questions or additional concerns, please feel free to contact Anna D. Jeffers, Legislation and Regulations Manager at (410) 764-4794.

Sincerely,



LaVerne G. Naesea
Executive Director

cc: Linda Bethman, Board Counsel, Board of Pharmacy
David Blythe, M.D., Deputy Secretary of Infectious Diseases, DHMH
Mitra Gavvani, Member of Subcommittee on Revisions to Sterile Compounding Regulations
Lenna Israbian-Jamgochian, President, Maryland Board of Pharmacy
Anna D. Jeffers, Legislation and Regulations Manager, Board of Pharmacy
Beverly Lynch, Executive Director, MSEPS

STATE OF MARYLAND



Department of Health and Mental Hygiene

Martin O'Malley, Governor – Anthony G. Brown, Lt. Governor –
Joshua M. Sharfstein, MD, Secretary

MARYLAND BOARD OF PHARMACY

4201 Patterson Avenue • Baltimore, Maryland 21215-2299

Lenna Israbian-Jamgochian, Board President - LaVerne G. Naesea, Executive Director

September 20, 2013

Jean B. Townsend, VMD

jbtvet@jeanlarry.net

Dear Dr. Townsend:

Thank you for providing comments in reference to the HB 986 State Board of Pharmacy – Sterile Compounding – Permits, Chapter 397, 2013, (HB986), prior to the promulgation of the regulations.

Until the new sterile compounding laws become effective (both State and federal), veterinarians may continue to compound and dispense sterile products in accordance with applicable standards of practice to their patients only. Keep in mind that HB 986 applies to sterile compounding only. Veterinarians may compound a limited quantity of a particular medication in anticipation of immediate future need as based on previously documented prescriptions filled for that medication. Veterinarians who wish to engage in sterile compounding after the implementation of the new Maryland law must obtain an additional permit from the Board of Pharmacy and comply with certain minimum standards. Veterinarians who compound non-sterile products do not require an additional permit from the Board.

If using a pharmacy, a pharmacy would have the ability to compound in anticipation of receipt of a patient specific prescription. Any compounded prescription that is dispensed must be pursuant to a patient specific prescription. See COMAR 10.34.19.08. This regulation may provide a solution to some veterinarian concerns. The veterinarian should work with the pharmacy to arrange availability in emergency situations.

Thank you again for your thorough consideration of the solicitation for comment posted on the Department of Health and Mental Hygiene's website. Drafts of the proposed regulations will be released informally. Please monitor the Maryland Register for the initial publication of the proposed revisions to COMAR 10.34.19 Sterile Pharmaceutical Compounding.

<http://www.dsd.state.md.us/MDRegister/mdregister.aspx> A 30 day comment period will follow.

Should you have questions or additional concerns, please feel free to contact Anna D. Jeffers, Legislation and Regulations Manager at (410) 764-4794.

Sincerely,

A handwritten signature in blue ink, appearing to read "LaVerne G. Naesea".

LaVerne G. Naesea
Executive Director

cc: Linda Bethman, Board Counsel, Board of Pharmacy
David Blythe, M.D., Deputy Secretary of Infectious Diseases, DHMH
Laura Downes, Executive Director, Board of Veterinary Medical Examiners
Mitra Gavvani, Member of Subcommittee on Revisions to Sterile Compounding Regulations
Lenna Israbian-Jamgochian, President, Maryland Board of Pharmacy
Anna D. Jeffers, Legislation and Regulations Manager, Board of Pharmacy

STATE OF MARYLAND



Department of Health and Mental Hygiene

Martin O'Malley, Governor – Anthony G. Brown, Lt. Governor –
Joshua M. Sharfstein, MD, Secretary

MARYLAND BOARD OF PHARMACY

4201 Patterson Avenue • Baltimore, Maryland 21215-2299

Lenna Israbian-Jamgochian, Board President - LaVerne G. Naesea, Executive Director

September 20, 2013

Dear Pet Owner:

Thank you for providing comments in reference to the HB 986 State Board of Pharmacy – Sterile Compounding – Permits, Chapter 397, 2013, (HB986), prior to the promulgation of the regulations.

HB 986 applies to sterile compounding only. Many compounded pet medications are not sterile under USP <797> and HB 986 does not apply to those compounds.

The purpose of HB 986 and the pending regulations is to ensure the quality and safety of the drugs that pets receive.

Until the new sterile compounding laws become effective (both State and federal), veterinarians may continue to compound and dispense sterile products in accordance with applicable standards of practice. Veterinarians may compound a limited quantity of a particular medication in anticipation of immediate future need as based on previously documented prescriptions filled for that medication. Veterinarians who wish to engage in sterile compounding after the implementation of the new Maryland law must obtain an additional permit from the Board of Pharmacy and comply with certain minimum standards. Veterinarians who compound non-sterile products do not require an additional permit from the Board.

If using a pharmacy, a pharmacy would have the ability to compound in anticipation of receipt of a patient specific prescription. Any compounded prescription that is dispensed must be pursuant to a patient specific prescription. See COMAR 10.34.19.08. This regulation may provide a solution to some veterinarian concerns. The veterinarian should work with the pharmacy to arrange availability in emergency situations.

Thank you again for your thorough consideration of the solicitation for comment posted on the Department of Health and Mental Hygiene's website. Drafts of the proposed regulations will be released informally. Please monitor the Maryland Register for the initial publication of the proposed revisions to COMAR 10.34.19 Sterile Pharmaceutical Compounding.

<http://www.dsd.state.md.us/MDRegister/mdregister.aspx> A 30 day comment period will follow.

Should you have questions or additional concerns, please feel free to contact Anna D. Jeffers, Legislation and Regulations Manager at (410) 764-4794.

Sincerely,



LaVerne G. Naesea
Executive Director

cc: Linda Bethman, Board Counsel, Board of Pharmacy
David Blythe, M.D., Deputy Secretary of Infectious Diseases, DHMH
Laura Downes, Executive Director, Board of Veterinary Medical Examiners
Mitra Gavvani, Member of Subcommittee on Revisions to Sterile Compounding Regulations
Lenna Israbian-Jamgochian, President, Maryland Board of Pharmacy
Anna D. Jeffers, Legislation and Regulations Manager, Board of Pharmacy

APPENDIX III

Chapter 19 Sterile [Pharmaceutical] Compounding Preparations and Sterile Drug Products

Authority: Health Occupations Article, §§12-205, 12-503, [and] 12-505, and 12-4A -01 – 12-4A-11, Annotated Code of Maryland

.03 Definitions.

A. In this chapter, the following terms have the meanings indicated.

B. Terms Defined.

(1) "Adverse events" means:

(a) Any adverse patient outcome related to the compounding process; or

(b) Evidence of environmental contamination, including microbial contamination above the threshold set forth in USP 797 Standards.

[(1)] (1-1) "Antineoplastic" means an agent that prevents the development, growth, or proliferation of malignant cells.

(2) "Anteroom" means the area, room, or rooms where personnel perform hand hygiene and garbing immediately adjacent to the designated clean room where the compounding of sterile preparations is performed.

(3) Batch.

(a) "Batch" means a preparation compounded in advance of receipt of a prescription, or a preparation compounded in a supply that will be used on more than one dispensing to a patient or patients or any preparation compounded in excess of the filling of an individual prescription.

(b) "Batch" includes a limited quantity of identical preparations compounded in a single, discrete process, by the same individuals, carried out during one limited time period.

(4) "Biological safety cabinet" means a containment unit:

(a) Suitable for work involving agents that pose higher risk of exposure to operators during compounding; and

(b) Used when there is a need for protection of the preparation, personnel, and environment.

(5) "Clean room" means an International Standards Organization (ISO) Class 7 environment that meets USP 797 Standards, inside which compounding occurs within an ISO Class 5 engineering control device such as a laminar airflow workstation or a biological safety cabinet.

(5-1) "Closed system vial transfer device (CSTD)" means a closed system drug transfer device that mechanically, not by means of vents or filters, prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug aerosols or vapors into the environment.

(5-2) "Compounding" means the preparation, mixing, assembling, packaging, or labeling of a drug only:

(a) As the result of a practitioner's prescription drug order or initiative based on the practitioner/patient relationship in the course of professional practice; or

(b) For the purpose of, or incidental to, research, teaching, or chemical analysis and not for the sale or dispensing of the drug or device; or

(c) In anticipation of a prescription drug order based on routine, regularly observed prescribing patterns.

(6) "Compounded sterile preparation" means sterile medication preparations, such as intravenous, epidural, and intraocular medications, compounded in the [pharmacy] ***sterile compounding facility*** using currently accepted aseptic compounding techniques under acceptable compounding conditions.

(7) "Compounding aseptic isolator" means an enclosed positive or negative pressure environment especially designed for sterile preparation compounding that maintains a physical barrier between the workspace and the operator.

(8) "Controlled environment" means a designated area for compounding sterile preparations that consists of a clean room and an anteroom.

(9) "Cytotoxic" means drug entities that are damaging or debilitating to cells, tissues, or organs.

(9-1) "Designee" means a public agency or private entity approved by the Board to conduct inspections of sterile compounding facilities or entities that prepare sterile drug products.

(9-2) "Health Care Practitioner" means a licensed dentist, pharmacist, physician, podiatrist, or veterinarian who is authorized to perform sterile compounding for dispensing or administering directly to their patients.

(9-3) "High risk" means a compounding process as defined in U.S. Pharmacopeia (USP)

General Chapter 797 Pharmaceutical Compounding – Sterile Preparations (USP 797 Standards).

(10) "Laminar air flow workstation" means an ISO Class 5 ("Class 100") laminar airflow hood inside which sterile compounding occurs.

(10-1) "Low risk" means a compounding process as defined in U.S. Pharmacopeia (USP)

General Chapter 797 Pharmaceutical Compounding – Sterile Preparations (USP 797 Standards).

(11) "Media fill verification" means a process of practical examination to verify the aseptic technique of personnel or an aseptic process by manual manipulation of microbiological growth media which simulates compounding processes and techniques used in actual compounding procedures.

(11-1) "Medium risk" means a compounding process as defined in U.S. Pharmacopeia

(USP) General Chapter 797 Pharmaceutical Compounding – Sterile Preparations

(USP 797 Standards).

(12) "Parenteral" means routes of drug administration or fluid administration other than via the gastrointestinal tract.

(13) "Pharmacist" means an individual who is licensed to practice pharmacy regardless of the location where the activities of practice are performed.

(14) "Pharmacy" means an establishment in which prescription or nonprescription drugs or devices are compounded, dispensed, or distributed.

(15) "Pyrogen testing" means an analysis of sterile preparations for the presence of cell material from microbiological organisms in sufficient quantity to elicit a febrile reaction.

(15-1) "Risk level" means a risk level of low, medium or high as defined in USP

797 Standards.

(16) "Sterile" means free from living microorganisms or any other contaminants.

(16-1) "Sterile compounding" means compounding of biologics, diagnostics, drugs, nutrients, and radiopharmaceuticals that, under USP 797 Standards, are prepared using aseptic techniques.

(16-2) "Sterile compounding facility" means a pharmacy, a health care practitioner's office, or any other setting in which sterile compounded compounding is performed.

(16-3) "Sterile drug product" means a drug product that:

(a) Is prepared using aseptic techniques; and

(b) Is not required to be prepared in response to a patient specific prescription.

(17) "Total parenteral nutrition" means providing caloric needs by the parenteral route for a patient who is unable to ingest sufficient calories.

(18) "USP 795 Standards" means standards set forth in the US Pharmacopeia (USP) General Chapter 795 Pharmaceutical Compounding—Non-Sterile Preparations.

(19) "USP 797 Standards" means standards set forth in the U.S. Pharmacopeia (USP) General Chapter 797 Pharmaceutical Compounding—Sterile Preparations.

.04 [Pharmacy] Sterile Compounding Facility Environment.

The compounding, preparation, and dispensing of compounded sterile preparations shall be accomplished in a [pharmacy] **sterile compounding facility** environment subject to State and federal laws, regulations, and standards.

.05 General Requirements.

A licensed [pharmacist] **health care practitioner** who has [appropriate practical and didactic] training in compounding sterile preparations, clean room technology, laminar flow technology, quality assurance techniques, and clinical application of intravenous drug therapy shall control and supervise the section of the [pharmacy] **sterile compounding facility** that prepares compounded sterile preparations and is responsible for, at a minimum, the following:

A. Preparation of compounded sterile preparations within the [pharmacy or pharmacy satellite] **sterile compounding facility**;

B. Storage of materials pertinent to the preparation of compounded sterile preparations, including drugs, chemicals, and biologicals, and the establishment of specifications for procurement of the materials;

C. Labeling of containers of compounded sterile preparations compounded within the [pharmacy] ***sterile compounding facility***;

D. Recording of transactions of the [pharmacy] ***sterile compounding facility*** as may be applicable to State and federal laws and regulations, as may be necessary to maintain accurate control over, and accountability for, pharmaceutical materials; and

E. Ensuring that licensed [pharmacists] ***health care practitioners*** meeting the requirements of §A of this regulation, or registered pharmacy technicians under direct supervision of a licensed pharmacist meeting the requirements of §A of this regulation, prepare, compound, and dispense compounded sterile preparations.

.06 Special Handling, Packaging, Labeling, and Beyond Use Dating.

A. The [pharmacy] ***sterile compounding facility*** shall make available special handling and packaging materials to maintain container integrity and drug stability of the prepared prescription orders, including antineoplastic or other hazardous sterile preparations, during [delivery] ***handling, and before administration***, to the patient including:

(1) A reasonable effort to provide tamper-evident packaging if appropriate to setting;

(2) [Delivery from the pharmacy to the patient within a reasonable time; and

(3)] Proper in-transit storage consistent with preparation labeling[.] ; ***and***

(3) For a sterile compounding facility that is a pharmacy, delivery to the patient within a reasonable time.

B. The dispensed container for any compounded sterile preparation shall include labeling according to Maryland law and regulations, in addition to the following information that is required by federal law:

(1) The date of preparation unless otherwise readily retrievable from prescription records;

(2) Time prepared, if applicable;

(3) The pertinent requirements for proper storage;

(4) The name of the prescriber, unless in an inpatient hospital setting;

(5) The name of the patient;

- (6) Directions for use;
- (7) The name of the base solution for infusion preparations;
- (8) The name and concentration or amount of active drugs contained in the final sterile preparation;
- (9) The name or identifying initials of the [pharmacist] *health care practitioner* who checked or prepared the compounded sterile preparation unless otherwise readily retrievable from prescription records;
- (10) The name, address, and telephone number of the [pharmacy] *sterile compounding facility* unless in an inpatient hospital facility;
- (11) The beyond-use/expiration dating and time of the compounded sterile preparation, and if no time is stated, the time is presumed to be at 11:59 p.m. of the stated beyond use date;
- (12) Any ancillary and cautionary instructions as needed; and
- (13) A pertinent warning consistent with applicable federal and State law that cytotoxic preparations are biohazardous, when applicable.

C. A [pharmacy] *sterile compounding facility* compounding sterile infusion preparations shall provide a 24-hour telephone number to allow its patients or other health care providers who may be administering its prescriptions to contact its [pharmacists] *health care practitioners*.

D. Expiration or Beyond-Use Dating. In the absence of direct testing evidence, as detailed in the Stability Criteria and Beyond Use Dating section of USP 795 Standards, the [pharmacist] *health care practitioner* shall use "beyond-use dating" as determined by USP 797 Standards and reference materials as cited in Regulation .16 of this chapter.

.07 Record-Keeping Requirements.

A. Patient Prescription Records.

- (1) The [pharmacy] *sterile compounding facility* shall maintain records of patient prescriptions.
- (2) Patient prescription records shall contain:
 - (a) Available medical information consistent with prevailing [pharmacy] *sterile compounding* standards; and
 - (b) The complete record of the formulations of the solutions that were compounded.
- (3) The [pharmacy] *sterile compounding facility* shall keep completed patient prescription records in a retrievable manner for at least 5 years[.], *either*:

(a) At the inspection site; or

(b) So as to be immediately retrievable by computer or other electronic means.

B. Compounded Sterile Preparations Records.

(1) For a [pharmacy] ***sterile compounding facility*** preparing compounded sterile preparations, the following records shall be maintained for at least 5 years:

(a) The training and competency evaluation of employees in sterile preparation procedures;

(b) Refrigerator and freezer temperatures;

(c) Certification of the sterile compounding environment, including ISO 5 workstations and the clean and anterooms;

(d) Other facility quality control logs specific to the [pharmacy's] ***sterile compounding facility's*** policies and procedures, for example, cleaning logs for facilities and equipment;

(e) Records documenting inspection for expired or recalled pharmaceutical preparations or raw ingredients;

(f) Preparation records including compounding work sheets, and records of the registered pharmacy technicians' checking/sign-off process; and

(g) Preparation records including compounding work sheets and records of the [pharmacists'] ***health care practitioners'*** checking/sign-off process.

(2) In addition to the records requirement in §B(1) of this regulation, for batch compounded sterile preparations, a [pharmacy] ***sterile compounding facility*** compounding sterile batch preparations for future use shall have records indicating the:

(a) Drug and ingredient names;

(b) Lot numbers;

(c) Expiration dates;

(d) Drug/diluent amounts; and

(e) Date on which the compounded sterile batch preparations were prepared.

(3) A [pharmacy] ***sterile compounding facility*** shall maintain records of media fill verification results for 5 years.

.08 Batch Preparation.

A. A [pharmacist] **health care practitioner** may prepare batched sterile preparations for future use in limited quantities supported by prior valid prescriptions or physician orders before receiving a valid written prescription or medication order.

B. Batch preparation of specific compounded sterile preparations is acceptable if the:

(1) [Pharmacist] **Health care practitioner** can document a history of valid prescriptions or physician orders that have been generated solely within an established professional [prescriber-patient-pharmacist] **prescriber-patient-health care practitioner** relationship; and

(2) [Pharmacy] **Sterile compounding facility** maintains the prescription on file for such preparations dispensed.

.09 Minimum Facility Requirements.

A. Controlled Environment.

(1) The [pharmacy] **sterile compounding facility** shall have a controlled environment.

(2) A [pharmacist] **health care practitioner** shall ensure that the controlled environment is:

(a) Accessible only to designated personnel; and

(b) Used only for the preparation of compounded sterile preparations, or such other tasks that require a controlled environment.

(3) The permit holder shall ensure that the controlled environment is:

(a) Structurally isolated from other areas within the [pharmacy] **sterile compounding facility** by means of restricted entry or access; and

(b) Air conditioned to maintain a temperature of the controlled environment according to USP 797 standards.

B. Controlled Environment—Clean Room. The permit holder shall ensure that the clean room in the controlled environment:

(1) Meets USP 797 Standards for design and USP 797 performance criteria quality standards for clean rooms;

(2) Contains no sinks or floor drains;

(3) Contains work surfaces constructed of smooth, impervious materials, such as stainless steel or molded plastic, so that the work surfaces may be readily cleaned and sanitized;

(4) If cytotoxic agents are routinely used in compounding preparations, contains room or rooms equipped with special pressurization requirements consistent with USP 797 Standards and the National Institute for Occupational Safety and Health (NIOSH) standards;

(5) Has in place appropriate environmental engineering control devices capable of maintaining USP 797 air-quality standards during normal compounding activity; and

(6) Contains the following equipment:

(a) A laminar airflow workstation or other suitable International Standards Organization (ISO) Class 5 compounding environment;

(b) Waste containers that are approved by Occupational Safety and Health Administration (OSHA) for used needles and syringes, and for chemotherapy waste; and

(c) Ancillary supplies required for proper compounding.

C. Controlled Environment—Anteroom. The permit holder shall ensure that the anteroom in the controlled environment:

(1) Meets USP 797 Standards for design and USP 797 performance criteria quality standards for anterooms; and

(2) Contains the following equipment:

(a) A sink with hot and cold running water;

(b) Waste containers for personal protective equipment;

(c) An eyewash station or sink design suitable for flushing an eye injury; and

(d) A hazardous waste spill kit, if applicable.

D. The requirements specified in §§B(1) and C(1) of this regulation are not applicable if a compounding aseptic isolator is used to compound sterile preparations in accordance with the:

(1) Compounding aseptic isolator conditions set forth in USP 797 Standards; and

(2) Isolator vendor or manufacturer specifications.

.10 Minimum Requirements for Equipment. (text unchanged)

.11 Minimum Requirements for Supplies.

A [pharmacy] ***sterile compounding facility*** engaging in compounding sterile preparations shall maintain adequate stock levels of the following supplies according to USP 797 Standards, including but not limited to:

A. Personal protective equipment:

- (1) Sterile gloves;
- (2) Masks;
- (3) Non-shedding gowns;
- (4) Shoe covers;
- (5) Hair covers;
- (6) Beard covers; and
- (7) Other personal protective equipment;

B. Disposable syringes and needles in necessary sizes;

C. Disinfectant cleaning agents as specified in USP 797 Standards, including 70 percent sterile isopropyl alcohol;

D. Disposable lint free towels;

E. Hand washing materials, including antimicrobial skin cleanser;

F. Adequate equipment and materials for antineoplastic or cytotoxic agent spills;

G. Supplies necessary for the aseptic preparation of compounded sterile preparations; and

H. Closed system vial transfer devices (CSTD), as required for cytotoxic compounding, if applicable.

.12 Minimum Requirements for Policies and Procedures. (text unchanged)

.13 Attire. (text unchanged)

.14 Training of Staff, Patient, and Caregiver.

A. The [pharmacist] **health care practitioner** shall make counseling available to the patient or primary caregiver, or both, concerning proper use of compounded sterile preparations and related supplies furnished by the [pharmacy] **sterile compounding facility**.

B. The permit holder shall ensure that [pharmacy] **sterile compounding facility** personnel engaging in compounding sterile preparations are trained and demonstrate competence in the safe handling and compounding of compounded sterile preparations and parenteral solutions, including cytotoxic agents if applicable.

C. The permit holder shall maintain records of training and demonstrated competence for individual employees for 5 years.

D. The permit holder shall ensure the continuing competence of [pharmacy] **sterile compounding facility** personnel engaged in compounding sterile preparations.

E. A [pharmacy] **sterile compounding facility** that compounds sterile preparations shall comply with the following training requirements:

(1) The [pharmacy] **sterile compounding facility** shall establish and follow a written program of training and performance evaluation designed to ensure that individuals working in the designated area have the knowledge and skills necessary to perform the assigned tasks properly and include at least the following:

(a) Aseptic technique with media fill verification at a frequency defined by risk level as described in USP 797 Standards:

(i) 12 months for low and medium risk; and

(ii) 6 months for high risk;

(b) Pharmaceutical calculations and terminology;

(c) Compounding sterile preparation documentation process;

(d) Quality assurance procedures;

(e) Aseptic preparation procedures;

(f) Proper cleansing, gowning, and gloving techniques;

(g) General conduct in the controlled area;

(h) Cleaning, sanitizing, and maintaining equipment used in the controlled area;

(i) Sterilization techniques for high risk preparations; and

(j) Container, equipment, and closure system selection.

(2) Individuals assigned to the controlled area shall successfully complete practical skills training in aseptic technique and aseptic area practices.

(3) Evaluations shall include:

(a) Written testing;

(b) Observation for adherence to aseptic technique and aseptic area policies and procedures; and

(c) Media fill verification as set forth in §E(1)(a) of this regulation.

.15 Quality Assurance. (text unchanged)

.16 Reference Library.

Minimum reference materials in a [pharmacy] *sterile compounding facility* shall include:

A. U.S. Pharmaceutical, General Chapter 797, Pharmaceutical Compounding—Sterile Preparations and other applicable reference materials in order to perform sterile compounding;

B. Reference materials containing drug stability and compatibility data; and

C. Reference materials concerning drug interactions and incompatibility.

ALL NEW (actual numbering of the regulations TBD)

.19 Sterile Compounding Permit Application Requirements.

A. A sterile compounding facility shall hold a sterile compounding permit issued by the Board before the sterile compounding facility may perform sterile compounding in the State.

B. A sterile compounding permit is required in addition to and does not replace any other permit or license a sterile compounding facility holds.

C. A sterile compounding facility that performs sterile compounding outside the state shall hold a sterile compounding permit issued by the Board before the sterile compounded preparations of the sterile compounding facility are dispensed in the State.

D. Minimum Application Requirements.

(1) To obtain a sterile compounding permit or renewal of a sterile compounding permit an applicant shall:

(a) Submit an application form approved by the Board that includes:

(i) Name;

(ii) Address and contact information; and

(iii) Health care practitioner license number;

(2) The highest USP 797 risk level of compounding engaged in by the applicant;

(3) Pay a fee as set forth in COMAR 10.34.09;

(4) Submit to an inspection which indicates compliance with USP 797 Standards, and conducted by:

(a) The Board;

(b) A designee of the Board; or

(c) The U.S. Food and Drug Administration;

(5) An applicant outside the State is responsible for obtaining an inspection from a designee of the Board to demonstrate compliance with USP 797 Standards;

(6) Submit a statement of current compliance with USP 797 Standards;

(7) Submit reports and corrective actions taken or proposed in response to adverse events identified 12 months before submission of the application;

(8) Submit evidence that the sterile compounding facility employs at least one licensed health care practitioner who has training in compounding sterile preparations, clean room technology,

laminar flow technology, quality assurance techniques, and clinical application of intravenous drug therapy;

(9) Submit evidence of good standing with:

(a) Other State licensing entity; or

(b) The licensing entity in the state in which the applicant is located; and

(10) Submit any other documentation as required by the Board.

E. The applicant shall notify the Board in writing within 30 days of any change in the information given on the initial or renewal application.

F. A separate sterile compounding permit is required for each site at which sterile compounding is performed.

G. A sterile compounding permit is not transferable.

H. Renewal.

(1) A sterile compounding permit expires on May 31 of the next even-numbered year after its effective date, unless the sterile compounding permit is renewed for a 2-year term as provided in this regulation.

(2) Before a sterile compounding permit expires, the sterile compounding permit may be renewed for an additional 2-year term if the applicant:

(i) Otherwise is entitled to the permit;

(ii) Pays a renewal fee as set forth in COMAR 10.34.09; and

(iii) Submits to the Board a renewal application on the form the Board requires.

.20 Minimum Requirements for Inspections of Sterile Compounding Permit Holders.

- A. The Board shall inspect a sterile compounding permit holder at least annually.
- B. The sterile compounding permit holder shall provide as part of the inspection process:
 - (1) Quality assurance testing reports;
 - (2) Documentation of reporting adverse events as required in this chapter;
 - (3) Microbial testing of a sampling of the sterile compounded preparations of the sterile compounding facility; and
 - (4) Any other information requested to ensure compliance with USP 797 Standards.
- C. Inspections may be conducted by:
 - (a) A designee of the Board;
 - (b) The U.S. Food and Drug Administration; or
 - (c) Other appropriate state entity which indicates compliance with USP 797 Standards.
- D. The Board may inspect a sterile compounding permit holder at any time to:
 - (1) Verify compliance with permit requirements; or
 - (2) Investigate a complaint.

.21 Reporting Requirements for Sterile Compounding Permit Holders.

A sterile compounding permit holder shall:

- A. Document and perform routine testing as required by USP 797 Standards for the appropriate risk levels of sterile compounded preparations;

B. Report to the Board within 5 calendar days:

- (1) Adverse events including corrective actions taken or proposed;
- (2) Deficiencies;
- (3) Disciplinary action in other states or by other state agencies;
- (4) Changes in accreditation status;
- (5) Disciplinary actions taken against a health care practitioner who is an owner operator or employee of the sterile compounding permit holder; and
- (6) Disciplinary action taken against any other known permit, or any other authorization, held by the sterile compounding permit holder.

APPENDIX IV

Chapter 19 Sterile [Pharmaceutical] Compounding Preparations and Sterile Drug Products

Authority: Health Occupations Article, §§12-205, 12-503, [and] 12-505, and 12-4A -01 – 12-4A-11, Annotated Code of Maryland

(Please note that this draft does not include new regulations for the new Sterile Compounding Permit and other revisions to the chapter consistent with that new permit - to be released separately)

.01 Scope.

This chapter applies to a licensed pharmacy [in], ***sterile compounding facility, or other person dispensing or distributing sterile compounding preparations or sterile drug products into, out of, or within*** Maryland engaging in:

A. Compounding or mixing sterile prescription solutions or suspensions to be administered parenterally or by irrigation, inhalation, or intraocular routes; and

B. Compounding of radiopharmaceuticals, except where U.S. Pharmacopeia (USP) General Chapter 797 Pharmaceutical Compounding—Sterile Preparations addresses radiopharmaceuticals, U.S. Pharmacopeia (USP) Chapter 821 Radioactivity, and U.S. Pharmacopeia (USP) Chapter 823 Radiopharmaceuticals for Positron Emission Tomography—Compounding would apply[.]; *and*

.03 Definitions.

A. In this chapter, the following terms have the meanings indicated.

B. Terms Defined.

(1) "Adverse events" means:

(a) Any adverse patient outcome related to the compounding process; or

(b) Evidence of environmental contamination, including microbial contamination above the threshold set forth in USP 797 Standards.

[(1)] (1-1) "Antineoplastic" means an agent that prevents the development, growth, or proliferation of malignant cells.

(2) "Anteroom" means the area, room, or rooms where personnel perform hand hygiene and garbing immediately adjacent to the designated clean room where the compounding of sterile preparations is performed.

(3) Batch.

(a) "Batch" means a preparation compounded in advance of receipt of a prescription, or a preparation compounded in a supply that will be used on more than one dispensing to a patient or patients or any preparation compounded in excess of the filling of an individual prescription.

(b) "Batch" includes a limited quantity of identical preparations compounded in a single, discrete process, by the same individuals, carried out during one limited time period.

(4) "Biological safety cabinet" means a containment unit:

(a) Suitable for work involving agents that pose higher risk of exposure to operators during compounding; and

(b) Used when there is a need for protection of the preparation, personnel, and environment.

(5) "Clean room" means an International Standards Organization (ISO) Class 7 environment that meets USP 797 Standards, inside which compounding occurs within an ISO Class 5 engineering control device such as a laminar airflow workstation or a biological safety cabinet.

(5-1) "Closed system vial transfer device (CSTD)" means a closed system drug transfer device that mechanically, not by means of vents or filters, prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug aerosols or vapors into the environment.

(5-2) "Compounding" means the preparation, mixing, assembling, packaging, or labeling of a drug only:

(a) As the result of a practitioner's prescription drug order or initiative based on the practitioner/patient relationship in the course of professional practice; or

(b) For the purpose of, or incidental to, research, teaching, or chemical analysis and not for the sale or dispensing of the drug or device; or

(c) In anticipation of a prescription drug order based on routine, regularly observed prescribing patterns.

(6) "Compounded sterile preparation" means sterile medication preparations, such as intravenous, epidural, and intraocular medications, compounded in the [pharmacy] ***sterile compounding facility*** using currently accepted aseptic compounding techniques under acceptable compounding conditions.

(7) "Compounding aseptic isolator" means an enclosed positive or negative pressure environment especially designed for sterile preparation compounding that maintains a physical barrier between the workspace and the operator.

(8) "Controlled environment" means a designated area for compounding sterile preparations that consists of a clean room and an anteroom.

(9) "Cytotoxic" means drug entities that are damaging or debilitating to cells, tissues, or organs.

(9-1) "Designee" means a public agency or private entity approved by the Board to conduct inspections of sterile compounding facilities or entities that prepare sterile drug products.

(9-2) "Health Care Practitioner" means a licensed dentist, pharmacist, physician, podiatrist, or veterinarian who is authorized to perform sterile compounding for dispensing or administering directly to their patients.

(9-3) "High risk" means a compounding process as defined in U.S. Pharmacopeia (USP)

General Chapter 797 Pharmaceutical Compounding – Sterile Preparations (USP 797 Standards).

(10) "Laminar air flow workstation" means an ISO Class 5 ("Class 100") laminar airflow hood inside which sterile compounding occurs.

(10-1) "Low risk" means a compounding process as defined in U.S. Pharmacopeia (USP)

General Chapter 797 Pharmaceutical Compounding – Sterile Preparations (USP 797 Standards).

(11) "Media fill verification" means a process of practical examination to verify the aseptic technique of personnel or an aseptic process by manual manipulation of microbiological growth media which simulates compounding processes and techniques used in actual compounding procedures.

(11-1) "Medium risk" means a compounding process as defined in U.S. Pharmacopeia (USP) General Chapter 797 Pharmaceutical Compounding – Sterile Preparations

(USP 797 Standards).

(12) "Parenteral" means routes of drug administration or fluid administration other than via the gastrointestinal tract.

(13) "Pharmacist" means an individual who is licensed to practice pharmacy regardless of the location where the activities of practice are performed.

(14) "Pharmacy" means an establishment in which prescription or nonprescription drugs or devices are compounded, dispensed, or distributed.

(15) "Pyrogen testing" means an analysis of sterile preparations for the presence of cell material from microbiological organisms in sufficient quantity to elicit a febrile reaction.

(15-1) "Risk level" means a risk level of low, medium or high as defined in USP

797 Standards.

(16) "Sterile" means free from living microorganisms or any other contaminants.

(16-1) "Sterile compounding" means compounding of biologics, diagnostics, drugs, nutrients, and radiopharmaceuticals that, under USP 797 Standards, are prepared using aseptic techniques.

(16-2) "Sterile compounding facility" means a pharmacy, a health care practitioner's office, or any other setting in which sterile compounding is performed.

(16-3) "Sterile drug product" means a drug product that:

(a) Is prepared using aseptic techniques; and

(b) Is not required to be prepared in response to a patient specific prescription.

(17) "Total parenteral nutrition" means providing caloric needs by the parenteral route for a patient who is unable to ingest sufficient calories.

(18) "USP 795 Standards" means standards set forth in the US Pharmacopeia (USP) General Chapter 795 Pharmaceutical Compounding—Non-Sterile Preparations.

(19) "USP 797 Standards" means standards set forth in the U.S. Pharmacopeia (USP) General Chapter 797 Pharmaceutical Compounding—Sterile Preparations.

ALL NEW (actual numbering of the regulations TBD)

.17 Sterile Drug Products.

A. A person that prepares and distributes sterile drug products into, out of, or within the State shall:

(1) Hold a manufacturer's permit or other permit designated by the U.S. Food and Drug Administration to ensure the safety of sterile drug products; and

(2) Hold a wholesale distributor's permit issued by the Board under Health Occupations Article, Title 12, Subtitle 6C, Annotated Code of Maryland.

B. A person that prepares and distributes sterile drug products into, out of, or within the State may not be required to hold a sterile compounding permit under Health Occupations Article, 12-4A-02, Annotated Code of Maryland.

.18 Sterile Drug Product Waiver.

A. The Board may issue a waiver of the requirements in Regulation .17A(1) of this chapter to a person that prepares and distributes sterile drug products into, out of, or within the State only:

(1) For a specified sterile drug product where exigent circumstances exist under the following criteria:

(a) The specified sterile drug product in the size and strength needed is:

(i) Listed on the current drug shortages index by the U.S. Food and Drug Administration; or

(ii) Only prepared and distributed by the person applying for the waiver; and

(b) The absence of the specified sterile drug product would result in a patient care or a patient safety risk; and

(2) For which there is a clinical need as determined by the Board with input from health care providers in the State under the following criteria:

(a) The licensed health care providers may be from:

(i) The Maryland Hospital Association;

(ii) The Maryland Society of Health-Systems Pharmacists;

(iii) The Maryland State Medical Society; or

(iv) Other relevant professionals as determined by the Board; and

(b) The criteria may not be based on financial or business concerns;

(3) If the applicant meets the following requirements:

(a) Submits an application form approved by the Board;

(b) Identifies in the application the highest USP 797 risk levels of compounding engaged in by the applicant;

(c) Pays a fee as set forth in COMAR 10.34.09;

(d) Submits reports of inspections conducted within a year of the application by:

(i) The Board or its designee; or

(ii) The U.S. Food and Drug Administration;

(e) Submits a statement of compliance with USP 797 Standards;

(f) Submits reports and corrective actions taken or proposed in response to adverse events identified 12 months before submission of an application for a waiver;

(g) A pharmacy or a wholesale distributor shall employ at least one licensed pharmacist who has training in compounding sterile preparations, clean room technology, laminar flow technology, quality assurance techniques, and clinical application of intravenous drug therapy;

(h) Submits evidence of good standing with:

(1) Any other State licensing entity; or

(2) The licensing entity in the state in which the applicant is located; and

(i) Submits any other documentation as required by the Board; and

(4) The Board shall, in its discretion, determine whether to issue a waiver based upon the Board's review of the information submitted in accordance with §A(1) – (3) of this regulation.

B. A person that prepares and distributes sterile drug products into, out of, or within the State under a Board approved waiver shall submit to the Board within 5 calendar days reports of adverse events and corrective actions taken or proposed.

C. A person that prepares and distributes sterile drug products into, out of, or within the State under a Board approved waiver shall notify the Board in writing within 30 days of any change in the information given on the initial or renewal application.

D. A person that prepares and distributes sterile drug products into, out of, or within the State under a Board approved waiver shall submit reports of an inspection conducted:

(1) Within 1 year of the Board's approval of the waiver that demonstrates compliance with USP 797 Standards; and

(2) By:

(a) The Board or its designee; or

(b) The U.S. Food and Drug Administration;

E. An applicant outside the State is responsible for obtaining an inspection from a designee of the Board to demonstrate compliance with USP 797 Standards;

F. Renewal.

(1) Any waiver issued by the Board may:

(a) Not exceed a duration determined by the Board based on exigent circumstances and clinical need;

(b) Not exceed 2 years; and

(c) Be renewed if the renewal applicant submits:

(i) An application form approved by the Board;

(ii) A fee as set forth in COMAR 10.34.09; and

(iii) Meets the requirements for a waiver under §A(1) – (3) of this regulation.

G. Documentation of Administration of Sterile Drug Products.

The holder of a sterile drug product waiver shall ensure that the recipient of the sterile drug products maintain readily retrievable records of the administration and/or dispensing of the sterile drug products to patients, to include:

(1) Documentation of the lot number or other mechanism for identifying the sterile drug product for the purpose of tracing the sterile drug product back to the sterile compounding facility or other person that prepared it; or

(2) If documentation of the lot number or other identification mechanism is not feasible, documentation of the source of the sterile drug product for the purpose of tracking the sterile drug product back to the sterile compounding facility or other person that prepared it.

H. Amendments to the Waiver.

(1) The holder of a sterile drug product waiver shall submit amendments to the waiver in advance to the Board for approval, including the addition of a specified sterile drug product.

(2) The Board may approve amendments to the waiver if:

(a) The requirements of this chapter and Health Occupations Article, Title 12, Subtitle 4A, Annotated Code of Maryland are met;

(b) The applicant submits any additional information requested by the Board; and

(c) Pays to the Board an amendment fee as set forth in 10.34.09.

APPENDIX V

Title 10

DEPARTMENT OF HEALTH AND MENTAL HYGIENE

Subtitle 34 BOARD OF PHARMACY

10.34.09 Fees

Subtitle 34 BOARD OF PHARMACY

10.34.19 Sterile Compounding Preparations and Sterile Drug Product

Authority: See Attached

Notice of Proposed Action

The Secretary of Health and Mental Hygiene proposes to 1) Amend Regulation .02 under COMAR 10.34.09 Fees; and
2) Amend Regulations 01, .03.—09, .11, .14, and .16, and adopt new Regulations .17—.21 under COMAR 10.34.19 Sterile Compounding Preparations and Sterile Drug Product.

This action was considered by the Board of Pharmacy at a public meeting held November 20, 2013, notice of which was given by publication on the Board of Pharmacy web site <http://dhmh.maryland.gov/pharmacy/SitePages/Home.aspx> from October 30, 2013 – November 20, 2013, pursuant to the State Government Article, §10-506(c), Annotated Code of Maryland.

Statement of Purpose

The purpose of this action is to 1) Add new fees for sterile compounding permits and for applications for a waiver for specified drug products under COMAR 10.34.09; and
2) Revise COMAR 10.34.19 to accommodate HB 986 State Board of Pharmacy – Sterile Compounding – Permits, 2013, Chapter 397, which creates a new class of licensees. The revisions include new definitions for “adverse events,” “compounding,” “designee,” “health care practitioner,” “risk level,” “sterile compounding,” “sterile compounding facility,” and “sterile drug product.” The following existing definitions were revised to accommodate HB 986: “clean room” and “compounded sterile preparation.” Regulations 01, .03 – .09, .11, .14, and .16 were revised to accommodate HB 986 striking the word “pharmacy” and substituting “sterile compounding facility.” Additionally, the word “pharmacist” has been stricken and substituted with the word “health care practitioner.” Other minor revisions were made to these sections to bring them in line with the new sterile compounding permit requirements. The new regulations .17 - .21 provide requirements for Sterile Compounding Permit Application Requirements,

Minimum Requirements for Inspections of Sterile Compounding Permit Holders, Reporting Requirements for Sterile Compounding Permit Holders, Sterile Drug Products, and Sterile Drug Product Waivers.

Comparison to Federal Standards

There is a corresponding federal standard to this proposed action, but the proposed action is not more restrictive or stringent.

Estimate of Economic Impact

I. Summary of Economic Impact.

In the fiscal note for Senate Bill 896/House Bill 986, Chapter 397, the Board indicated that the program would increase operations at the Board. In addition to its existing regulatory authority over sterile compounding pharmacies in Maryland, the Board will assume additional regulatory responsibilities to ensure the safety of non-resident sterile compounding pharmacies and sterile compounding facilities that perform sterile pharmaceutical compounding for Maryland patients.

The Board's expenditures for FY 2014 are estimated to be \$287,785.00 as a result of HB 986 State Board of Pharmacy – Sterile Compounding – Permits, 2013, Chapter 397, and these proposed regulations. During the first year of operations, the Board projects that it will be able to absorb start-up costs (\$77,785.00) using funds available in its projected surplus and existing personnel and inspection resources. The training of existing management and inspection personnel to carry out some required functions will help absorb a portion of the costs. Also, performing dual inspections (related to the pharmacy permit and sterile compounding permit) during one annual visit to pharmacies that perform sterile compounding will defer costs related to the implementation of HB 986 State Board of Pharmacy - Sterile Compounding – Permits, Chapter 397, 2013.

The Board's revenues may increase by as much as \$210,000 in each of the next five years. HB 986 State Board of Pharmacy – Sterile Compounding – Permits, 2013, Chapter 397, will require the Board to hire two Pharmacists III, Grade 18, Step 8, to do field inspections of compounding pharmacies. The two positions will require 2 new vehicles. The Board will also need to hire a Laboratory Scientist Surveyor I, Grade 16, Step 8, to work in-house to review compounding pharmacy applications and to review and interpret scientific reports from the compounding pharmacies to insure compliance. A Grade 8, Step 3, Office Services Clerk, will be needed to process the applications and issue compounding pharmacy permits. The Board has requested DHMH and DBM to take steps support the Board's recruitment of staff in the positions to begin training no later than January 2014. Additionally, the impact on the Board's on-going operating expenses include: requiring additional staff training, additional office space and equipment to accommodate new staff, additional configuration of the Board MIS system to

allow application and tracking of permitted entities, and increases in staff and Board members' workload time (comp/per diems) related to the implementation of HB 986 State Board of Pharmacy - Sterile Compounding – Permits, Chapter 397, 2013.

Expenses and revenues for implementing the new regulations are guesstimates only. The Board does not know how many types of sterile compounders are operating in Maryland. The Board's projects 300 total entities to be regulated under this new license class based on approximately 100 pharmacies and 200 other entities (clinics, physicians, veterinarians, ophthalmologists, etc.) that may require a sterile compounding permit to operate in Maryland.

II. Types of Economic Impact.	Revenue (R+/R-)	Magnitude
	Expenditure (E+/E-)	
A. On issuing agency:		
(1) Board of Pharmacy Expenditures	(E+)	\$287,785
(2) Sterile compounding permits	(R+)	\$210,000
(3) Sterile drug product waivers	(R+)	Indeterminable
B. On other State agencies:	NONE	
C. On local governments:	NONE	
	Benefit (+) Cost (-)	Magnitude
D. On regulated industries or trade groups:		
(1) Sterile compounding facility permit	(-)	\$210,000

(2) Application fee for a waiver for specified sterile	(-)	Indeterminable
E. On other industries or trade groups:	NONE	
F. Direct and indirect effects on public:	(+)	Indeterminable

III. Assumptions. (Identified by Impact Letter and Number from Section II.)

A(1). The Board estimates that its expenditures will be \$287,785 to implement this program taking into consideration the new positions, new vehicles and new licensure program.

A(2). The Board's revenue will increase \$210,000 each year if 300 sterile compounding facilities obtain a sterile compounding permit at \$700 each. $700 \times 300 = \$210,000$

A(3). The fee for a sterile drug product waiver is \$1,750 due to the expense of reviewing the application, inspections, and consideration of criteria by the Board and other health care professionals. However, it is unknown how many entities will apply for sterile drug product waivers.

D(1). See A(2) above

D(2). See A(3) above

F. There will be a benefit to the public because sterile compounded prescriptions and sterile drug products in Maryland will be prepared under strict USP 797 standards ensuring the safety and efficacy of these prescriptions and products.

Economic Impact on Small Businesses

The proposed action has minimal or no economic impact on small businesses.

Impact on Individuals with Disabilities

The proposed action has no impact on individuals with disabilities.

Opportunity for Public Comment

Comments may be sent to Michele A. Phinney, Director, Office of Regulation and Policy Coordination, Department of Health and Mental Hygiene, 201 W. Preston Street, Room 512, Baltimore, MD 21201, or call 410-767-6499; TTY:800-735-2258, or email to dhmh.regs@maryland.gov, or fax to 410-767-6483. Comments will be accepted through . A public hearing has not been scheduled.

Economic Impact Statement Part C

A. Fiscal Year in which regulations will become effective: FY 2014

B. Does the budget for the fiscal year in which regulations become effective contain funds to implement the regulations?

C. If 'yes', state whether general, special (exact name), or federal funds will be used:

D. If 'no', identify the source(s) of funds necessary for implementation of these regulations:

E. If these regulations have no economic impact under Part A, indicate reason briefly:

F. If these regulations have minimal or no economic impact on small businesses under Part B, indicate the reason and attach small business worksheet.

The Board is not required to obtain information concerning which licensees operate small businesses, although some licensees that perform sterile pharmaceutical compounding or prepare sterile drug products may also be small businesses.

G. Small Business Worksheet:

Title 10

DEPARTMENT OF HEALTH AND MENTAL HYGIENE

Subtitle 34 BOARD OF PHARMACY

10.34.09 Fees

Authority: §§12-205, 12-206, 12-302, 12-303, 12-305, 12-308, 12-310, 12-404, 12-407, 12-601, 12-6B-02, 12-6B-03, 12-6B-04, 12-6B-07, 12-6C-03, 12-6C-04, 12-6C-05, [and] 12-6C-06, and 12-4A-02, 12-4A-04, and 12-4A-05

Annotated Code of Maryland

10.34.09.02 (November 13, 2013)

.02 Fees.

The following fees are established by the Board:

A.—D. (text unchanged)

E. Sterile Compounding Permit Fees.

(1) *Sterile compounding permit initial fee — \$700;*

(2) *Sterile compounding permit renewal fee — \$600; and*

(3) *Sterile compounding reinstatement fee. (payable if renewal fee is received after January 31) — \$600.*

F. Sterile Drug Product Waiver Fees.

(1) *Sterile drug product waiver application fee — \$1,750;*

(2) *Sterile drug product waiver application fee for an additional sterile drug product for a person with an existing sterile drug product waiver — \$700; and*

(3) *Sterile drug product waiver amendment fee — \$700.*

[E.] G. (text unchanged)

10.34.19 Sterile [Pharmaceutical] Compounding Preparations and Sterile Drug Products

Authority: Health Occupations Article, §§12-205, 12-503, [and] 12-505, and 12-4A -01 – 12-4A-11, Annotated Code of Maryland

10.34.19.01 (November 21, 2013)

.01 Scope.

This chapter applies to a licensed pharmacy [in], *sterile compounding facility, or other person dispensing or distributing sterile compounded preparations or sterile drug products into, out of, or within Maryland* engaging in:

A.—B. (text unchanged)

10.34.19.03 (November 21, 2013)

.03 Definitions.

A. (text unchanged)

B. Terms Defined.

(1) *“Adverse events” means:*

(a) *Any adverse patient outcome related to the sterile compounding process; or*

(b) *Evidence of environmental contamination, including microbial contamination above the threshold set forth in USP 797 Standards.*

[(1)] (2)—[(4)] (5) (text unchanged)

[(5)] (6) *“Clean room” means a room with an ISO-5 environment or an International Standards Organization (ISO) Class 7 environment that meets USP 797 Standards, inside which compounding occurs within an ISO Class 5 engineering control device such as a laminar airflow workstation or a biological safety cabinet.*

[(5-1)] (7) (text unchanged)

(8) *“Compounding” means the preparation, mixing, assembling, packaging, or labeling of a drug only:*

(a) *As the result of a practitioner’s prescription drug order or initiative based on the practitioner/patient relationship in the course of professional practice; or*

(b) For the purpose of, or incidental to, research, teaching, or chemical analysis and not for the sale or dispensing of the drug or device; or

(c) In anticipation of a prescription drug order based on routine, regularly observed prescribing patterns.

[(6)](9) "Compounded sterile preparation" means sterile medication preparations, such as intravenous, epidural, and intraocular medications, compounded in the [pharmacy] *sterile compounding facility* using currently accepted aseptic compounding techniques under acceptable compounding conditions.

[(7)] (10)—[(9)] (12) (text unchanged)

(13) "*Designee*" means a public agency or private entity trained in USP 797 Standards and/or FDA good manufacturing practices approved by the Board to conduct inspections of sterile compounding facilities or entities that prepare sterile drug products.

(14) "*Health Care Practitioner*" means a licensed dentist, pharmacist, physician, podiatrist, or veterinarian who is authorized to perform sterile compounding for dispensing or administering directly to their patients.

[(10)] (15)—[(15)] (20) (text unchanged)

(21) "*Risk level*" means a risk level of low, medium or high as defined in USP 797 Standards.

[(16)] (22) (text unchanged)

(23) "*Sterile compounding*" means compounding of biologics, diagnostics, drugs, nutrients, and radiopharmaceuticals that, under USP 797 Standards, are prepared using aseptic techniques.

(24) "*Sterile compounding facility*" means a pharmacy, a health care practitioner's office, or any other setting in which sterile compounding is performed in a controlled environment as required by USP 797 Standards.

(25) “*Sterile drug product*” means a drug product that:

(a) *Is prepared using aseptic techniques; and*

(b) *Is not required to be prepared in response to a patient specific prescription.*

[(17)] (26)—[(19)] (28) (text unchanged)

10.34.19.04 (November 21, 2013)

.04 [Pharmacy] *Sterile Compounding Facility Environment.*

The compounding, preparation, and dispensing of compounded sterile preparations shall be accomplished in a [pharmacy] *sterile compounding facility* environment subject to State and federal laws, regulations, and standards.

10.34.19.05 (November 21, 2013)

.05 General Requirements.

A licensed [pharmacist] *health care practitioner* who has [appropriate practical and didactic] training in compounding sterile preparations, clean room technology, laminar flow technology, quality assurance techniques, and clinical application of intravenous drug therapy shall control and supervise the section of the [pharmacy] *sterile compounding facility* that prepares compounded sterile preparations and is responsible for, at a minimum, the following:

A. Preparation of compounded sterile preparations within the [pharmacy or pharmacy satellite] *sterile compounding facility*;

B. (text unchanged)

C. Labeling of containers of compounded sterile preparations compounded within the [pharmacy] *sterile compounding facility*;

D. Recording of transactions of the [pharmacy] *sterile compounding facility* as may be applicable to State and federal laws and regulations, as may be necessary to maintain accurate control over, and accountability for, pharmaceutical materials; and

E. Ensuring that licensed [pharmacists] *health care practitioners* meeting the requirements of §A of this regulation, or registered pharmacy technicians under direct supervision of a licensed pharmacist meeting the requirements of §A of this regulation, prepare, compound, and dispense compounded sterile preparations.

10.34.19.06 (November 21, 2013)

.06 Special Handling, Packaging, Labeling, and Beyond Use Dating.

A. The [pharmacy] *sterile compounding facility* shall make available special handling and packaging materials to maintain container integrity and drug stability of the prepared prescription orders, including antineoplastic or other hazardous sterile preparations, during [delivery] *handling, and before administration*, to the patient including:

(1) (text unchanged)

(2) [Delivery from the pharmacy to the patient within a reasonable time; and

(3)] Proper in-transit storage consistent with preparation labeling[.] ; *and*

(3) *For a sterile compounding facility that is a pharmacy, delivery to the patient within a reasonable time.*

B. The dispensed container for any compounded sterile preparation shall include labeling according to Maryland law and regulations, in addition to the following information that is required by federal law:

(1)—(8) (text unchanged)

(9) The name or identifying initials of the [pharmacist] *health care practitioner* who checked or prepared the compounded sterile preparation unless otherwise readily retrievable from prescription records;

(10) The name, address, and telephone number of the [pharmacy] *sterile compounding facility* unless in an inpatient hospital facility;

(11)—(13) (text unchanged)

C. A [pharmacy] *sterile compounding facility* compounding sterile infusion preparations shall provide a 24-hour telephone number to allow its patients or other health care providers who may be administering its prescriptions to contact its [pharmacists] *health care practitioners*.

D. Expiration or Beyond-Use Dating. In the absence of direct testing evidence, as detailed in the Stability Criteria and Beyond Use Dating section of USP 795 Standards, the [pharmacist] *health care practitioner* shall use "beyond-use dating" as determined by USP 797 Standards and reference materials as cited in Regulation .16 of this chapter.

10.34.19.07 (November 21, 2013)

.07 Record-Keeping Requirements.

A. Patient Prescription Records.

(1) The [pharmacy] *sterile compounding facility* shall maintain records of patient prescriptions.

(2) Patient prescription records shall contain:

(a) Available medical information consistent with prevailing [pharmacy] *sterile compounding* standards; and

(b) (text unchanged)

(3) The [pharmacy] *sterile compounding facility* shall keep completed patient prescription records in a retrievable manner for at least 5 years[.], *either*:

(a) *At the inspection site; or*

(b) *So as to be immediately retrievable by computer or other electronic means.*

B. Compounded Sterile Preparations Records.

(1) For a [pharmacy] *sterile compounding facility* preparing compounded sterile preparations, the following records shall be maintained for at least 5 years:

(a)—(c) (text unchanged)

(d) Other facility quality control logs specific to the [pharmacy's] *sterile compounding facility's* policies and procedures, for example, cleaning logs for facilities and equipment;

(e)—(f) (text unchanged)

(g) Preparation records including compounding work sheets and records of the [pharmacists'] *health care practitioners'* checking/sign-off process.

(2) In addition to the records requirement in §B(1) of this regulation, for batch compounded sterile preparations, a [pharmacy] *sterile compounding facility* compounding sterile batch preparations for future use shall have records indicating the:

(a)—(e) (text unchanged)

(3) A [pharmacy] *sterile compounding facility* shall maintain records of media fill verification results for 5 years.

10.34.19.08 (November 21, 2013)

.08 Batch Preparation.

A. A [pharmacist] *health care practitioner* may prepare batched sterile preparations for future use in limited quantities supported by prior valid prescriptions or physician orders before receiving a valid written prescription or medication order.

B. Batch preparation of specific compounded sterile preparations is acceptable if the:

- (1) [Pharmacist] *Health care practitioner* can document a history of valid prescriptions or physician orders that have been generated solely within an established professional [prescriber-patient-pharmacist] *prescriber-patient-health care practitioner* relationship; and
- (2) [Pharmacy] *Sterile compounding facility* maintains the prescription on file for such preparations dispensed.

10.34.19.09 (November 21, 2013)

.09 Minimum Facility Requirements.

A. Controlled Environment.

- (1) The [pharmacy] *sterile compounding facility* shall have a controlled environment *that meets USP 797 Standards*.
- (2) A [pharmacist] *health care practitioner* shall ensure that the controlled environment is:
 - (a)—(b) (text unchanged)
- (3) The permit holder shall ensure that the controlled environment is:
 - (a) Structurally isolated from other areas within the [pharmacy] *sterile compounding facility* by means of restricted entry or access; and
 - (b) (text unchanged)

B.—D. (text unchanged)

10.34.19.11 (November 21, 2013)

.11 Minimum Requirements for Supplies.

A [pharmacy] *sterile compounding facility* engaging in compounding sterile preparations shall maintain adequate stock levels of the following supplies according to USP 797 Standards, including but not limited to:

A.—H. (text unchanged)

10.34.19.14 (November 21, 2013)

.14 Training of Staff, Patient, and Caregiver.

A. The [pharmacist] *health care practitioner* shall make counseling available to the patient or primary caregiver, or both, concerning proper use of compounded sterile preparations and related supplies furnished by the [pharmacy] *sterile compounding facility*.

B. The permit holder shall ensure that [pharmacy] *sterile compounding facility* personnel engaging in compounding sterile preparations are trained and demonstrate competence in the safe handling and compounding of compounded sterile preparations and parenteral solutions, including cytotoxic agents if applicable.

C. (text unchanged)

D. The permit holder shall ensure the continuing competence of [pharmacy] *sterile compounding facility* personnel engaged in compounding sterile preparations.

E. A [pharmacy] *sterile compounding facility* that compounds sterile preparations shall comply with the following training requirements:

(1) The [pharmacy] *sterile compounding facility* shall establish and follow a written program of training and performance evaluation designed to ensure that individuals working in the designated area have the knowledge and skills necessary to perform the assigned tasks properly and include at least the following:

(a)—(j) (text unchanged)

(2)—(3) (text unchanged)

10.34.19.16 (November 21, 2013)

.16 Reference Library.

Minimum reference materials in a [pharmacy] *sterile compounding facility* shall include:

A.—C. (text unchanged)

.17 Sterile Compounding Permit Application Requirements.

A. A sterile compounding facility shall hold a sterile compounding permit issued by the Board before the sterile compounding facility may perform sterile compounding in the State.

B. A sterile compounding permit is required in addition to and does not replace any other permit or license a sterile compounding facility holds.

C. A sterile compounding facility that performs sterile compounding outside the State shall hold a sterile compounding permit issued by the Board before the sterile compounded preparations of the sterile compounding facility are dispensed in the State.

D. Minimum Application Requirements.

(1) To obtain a sterile compounding permit or renewal of a sterile compounding permit an applicant shall:

(a) Submit an application form approved by the Board that includes:

(i) Name;

(ii) Address and contact information;

(iii) Health care practitioner license number; and

(iv) The highest USP 797 risk level of compounding engaged in by the applicant;

(b) Pay a fee as set forth in COMAR 10.34.09;

(c) Submit to an inspection which indicates compliance with USP 797 Standards, and conducted by:

(i) The Board;

(ii) A designee of the Board; or

(iii) The U.S. Food and Drug Administration;

- (d) If an applicant is outside the State, obtain an inspection from a designee of the Board to demonstrate compliance with USP 797 Standards;*
- (e) Submit a statement of current compliance with USP 797 Standards;*
- (f) Submit reports and corrective actions taken or proposed in response to adverse events identified 12 months before submission of the application;*
- (g) Submit evidence that the sterile compounding facility employs at least one licensed health care practitioner who has training in compounding sterile preparations, clean room technology, laminar flow technology, quality assurance techniques, and clinical application of intravenous drug therapy;*
- (h) Submit evidence of good standing with:*
 - (i) Any other State licensing entity; or*
 - (ii) The licensing entity in the state in which the applicant is located; and*
- (i) Submit any other documentation as required by the Board.*

E. The applicant shall notify the Board in writing within 30 days of any change in the information given on the initial or renewal application.

*F. A separate sterile compounding permit is required for each **sterile compounding facility** at which sterile compounding is performed.*

G. A sterile compounding permit is not transferable.

H. Renewal.

(1) A sterile compounding permit expires on May 31 of the next even-numbered year after its effective date, unless the sterile compounding permit is renewed for a 2-year term as provided in this regulation.

(2) Before a sterile compounding permit expires, the sterile compounding permit may be renewed for an additional 2-year term if the applicant:

(a) Otherwise is entitled to the permit;

(b) Pays a renewal fee as set forth in COMAR 10.34.09; and

(c) Submits to the Board a renewal application on the form the Board requires.

.18 Minimum Requirements for Inspections of Sterile Compounding Permit Holders.

A. The Board shall inspect a sterile compounding permit holder at least annually.

B. The sterile compounding permit holder shall provide as part of the inspection process:

(1) Quality assurance testing reports;

(2) Documentation of reporting adverse events as required in this chapter;

(3) Microbial testing of a sampling of the sterile compounded preparations of the sterile compounding facility if applicable according to USP 797 Standards; and

(4) Any other information requested to ensure compliance with USP 797 Standards.

C. Inspections may be conducted by:

(1) A designee of the Board;

(2) The U.S. Food and Drug Administration; or

(3) Other appropriate state entity which indicates compliance with USP 797 Standards.

D. The Board may inspect a sterile compounding permit holder at any time to:

(1) Verify compliance with permit requirements; or

(2) Investigate a complaint.

.19 Reporting Requirements for Sterile Compounding Permit Holders.

A sterile compounding permit holder shall:

A. Document and perform routine testing as required by USP 797 Standards for the appropriate risk levels of sterile compounded preparations;

B. Report to the Board within 5 calendar days:

(1) Adverse events including corrective actions taken or proposed;

(2) Deficiencies related to the sterile compounding process;

(3) Disciplinary action in other states or by other state agencies;

(4) Changes in accreditation status;

(5) Disciplinary actions taken against a health care practitioner who is an owner operator or employee of the sterile compounding permit holder; and

(6) Disciplinary action taken against any other known permit, or any other authorization, held by the sterile compounding permit holder.

.20 Sterile Drug Products.

A. A person that prepares and distributes sterile drug products into, out of, or within the State shall:

(1) Hold a manufacturer's permit or other permit designated by the U.S. Food and Drug Administration to ensure the safety of sterile drug products; and

(2) Hold a wholesale distributor's permit, if applicable, issued by the Board under Health Occupations Article, Title 12, Subtitle 6C, Annotated Code of Maryland.

B. A person that prepares and distributes sterile drug products into, out of, or within the State may not be required to hold a sterile compounding permit under Health Occupations Article, 12-4A-02, Annotated Code of Maryland.

.21 Sterile Drug Product Waiver.

A. The Board may issue a waiver of the requirements in Regulation .20A(1) of this chapter to a person that prepares and distributes sterile drug products into, out of, or within the State only:

(1) For a specified sterile drug product where exigent circumstances exist under the following criteria:

(a) The specified sterile drug product in the size and strength needed is:

(i) Listed on the current drug shortages index by the U.S. Food and Drug Administration or other nationally recognized index; or

(ii) Only prepared and distributed by the person applying for the waiver; and

(b) The absence of the specified sterile drug product would result in a patient care or a patient safety risk;

(2) For which there is a clinical need as determined by the Board with input from relevant professionals as determined by the Board;

(3) If the request for the waiver may not be based on financial or business concerns; and

(4) If the applicant meets the following requirements:

(a) Submits an application form approved by the Board;

(b) Identifies in the application the highest USP 797 risk levels of compounding engaged in by the applicant;

(c) Pays a fee as set forth in COMAR 10.34.09;

(d) Submits reports of inspections conducted within a year of the application by:

(i) The Board or its designee; or

(ii) The U.S. Food and Drug Administration;

(e) Submits a statement of compliance with USP 797 Standards;

(f) Submits reports and corrective actions taken or proposed in response to adverse events identified 12 months before submission of an application for a waiver;

(g) If a pharmacy or a wholesale distributor shall employ at least one licensed pharmacist who has training in compounding sterile preparations, clean room technology, laminar flow technology, quality assurance techniques, and clinical application of intravenous drug therapy;

(h) Submits evidence of good standing with:

(1) Any other State licensing entity; or

(2) The licensing entity in the state in which the applicant is located; and

(i) Submits any other documentation as required by the Board; and

B. The Board shall, in its discretion, determine whether to issue a waiver based on the Board's review of the information submitted in accordance with §A(1)—(4) of this regulation.

C. A person that prepares and distributes sterile drug products into, out of, or within the State under a Board approved waiver shall submit to the Board within 5 calendar days reports of adverse events and corrective actions taken or proposed.

D. A person that prepares and distributes sterile drug products into, out of, or within the State under a Board approved waiver shall notify the Board in writing within 30 days of any change in the information given on the initial or renewal application.

E. A person that prepares and distributes sterile drug products into, out of, or within the State under a Board approved waiver shall submit reports of an inspection conducted:

(1) Within 1 year of the Board's approval of the waiver that demonstrates compliance with USP 797 Standards; and

(2) By:

(a) The Board or its designee; or

(b) The U.S. Food and Drug Administration;

F. An applicant outside the State is responsible for obtaining an inspection from a designee of the Board to demonstrate compliance with USP 797 Standards;

G. Renewal.

Any waiver issued by the Board may:

(1) Not exceed a duration determined by the Board based on exigent circumstances and clinical need;

(2) Not exceed 2 years; and

(3) Be renewed if the renewal applicant submits:

(a) An application form approved by the Board;

(b) A fee as set forth in COMAR 10.34.09; and

(c) Meets the requirements for a waiver under §A(1)—(3) of this regulation.

H. Documentation of Administration of Sterile Drug Products. The holder of a sterile drug product waiver shall ensure that the recipient of the sterile drug products maintain readily retrievable records of the administration and/or dispensing of the sterile drug products to patients, to include:

(1) Documentation of the lot number or other mechanism for identifying the sterile drug product for the purpose of tracing the sterile drug product back to the sterile compounding facility or other person that prepared it; or

(2) If documentation of the lot number or other identification mechanism is not feasible, documentation of the source of the sterile drug product for the purpose of tracking the sterile drug product back to the sterile compounding facility or other person that prepared it.

I. Amendments to the Waiver.

(1) The holder of a sterile drug product waiver shall submit amendments to the waiver in advance to the Board for approval, including the addition of a specified sterile drug product.

(2) The Board may approve amendments to the waiver if:

(a) The requirements of this chapter and Health Occupations Article, Title 12, Subtitle 4A, Annotated Code of Maryland are met;

(b) The applicant submits any additional information requested by the Board; and

(c) Pays to the Board an amendment fee as set forth in 10.34.09.

JOSHUA M. SHARFSTEIN, M.D.

Secretary of Health and Mental Hygiene