FLORIDA | Board of Pharmacy

Compounding Committee

Draft Meeting Minutes

Monday, February 4, 2019
Four Points by Sheraton Tallahassee
316 W. Tennessee Street
Tallahassee, FL 32301
Contact Hotel: 850-422-0071

Mark Mikhael, PharmD
Committee Chair

Jennifer Wenhold, MSW
Acting Executive Director

Florida Board of Pharmacy Meeting Agenda
Monday, February 4, 2019
Tallahassee, FL

Participants in these public meetings should be aware that these proceedings are being recorded and that an audio file of the meetings will be posted to the board's website.

Committee Members:

Mark Mikhael, PharmD, Committee Chair (Orlando)
Richard Montgomery, BPharm, MBA (Orlando)
Blanca Rivera, BPharm, MBA (Miami)
David Wright, BPharm (Ft. Pierce)

Attorneys:

David Flynn, Senior Assistant Attorney General
Lawrence Harris, Senior Assistant Attorney General

Board Staff:

Jennifer Wenhold, MSW, Acting Executive Director
Eric Pottschmidt, MBA, Program Operations Administrator
Amber Greene, Program Operations Administrator
Jessica Hollingsworth, Government Analyst II

Monday, February 4, 2019 at 2:00 PM

Call to Order - The meeting was called to order by Committee Chair, Dr. Mikhael, at 2:00 p.m.

Roll Call - Those present during the meeting included the following:

Committee Members:

Mark Mikhael, PharmD, Committee Chair
Richard Montgomery, BPharm, MBA
Blanca Rivera, BPharm, MBA
David Wright, BPharm

I. Committee Items for Discussion

A. Rules Hearing – Rule 64B16-27.797, F.A.C.

Mr. Flynn provided a brief overview of the rules hearing from the December 2018 board meeting, where it was decided that the Compounding Committee would work with relevant stakeholders on rule language today. Dr. Mikhael reminded the committee of updating the rule to address the process of lyophilization at the October 2018 meeting, due to concern with pharmacies performing it without proper guidance. He recognized that although there has been discussion on whether lyophilization falls under manufacturing or pharmacy, the Board of Pharmacy is ok with lyophilization if it is appropriately regulated with compliance checks and directions for inspectors on what to review. He concluded that the purpose of this discussion is to create an advantageous relationship with relevant stakeholders by building the process together.

Dr. Mikhael took a brief opportunity to recognize Bob Parrado and Debra Glass, previous board members, in the audience.

Dr. Mikhael invited AnazaoHealth to address the committee, which included T.J. Morton, Attorney, Bob Mckenzie, and Dennis Davis. Mr. Montgomery expressed concern with AnazaoHealth's proposed revision not being detailed enough, particularly regarding container integrity and sterilization. Ms. Rivera added that the proposed language does not specify what type of method to use when sterilizing lyophilizers. AnazaoHealth responded that they left this language open since multiple methods may be used and each machine is different. Ms. Rivera suggested updating the guidelines to reflect that the chosen method must be tested prior to using, which AnazaoHealth agreed with. Mr. Wright expressed concern with requiring too much detail, requiring the rule to be updated every time things change. Ms. Rivera clarified that she wasn't as concerned with detail as she was with ensuring the process is working.

Mr. Flynn suggested that the rule can require a validated sterilization method, which should be documented. Dr. Mikhael agreed with Mr. Flynn and explained that the current Good manufacturing process (cGMP) is the initial validation or qualification of the equipment and process, which requires initial qualification (IQ), operational qualification (OQ), and process qualification (PQ) prior to using equipment. He added that testing prior to manufacturing is missing from the proposed language, which would make him more comfortable with the rule. AnazaoHealth agreed with adding this to the proposed language. Mr. Montgomery reminded the committee that it is important to be as specific as possible in rule because pharmacies may not be properly inspected without reference to what is being inspected.

Mary Crane, senior pharmacist with Inspection Services, agreed that the sterilization of a lyophilizer needs to be validated and added that it should be done annually. She explained that to validate, pharmacies should look for three successful and consecutive runs by using strategically placed biological indicators. Dr. Mikhael asked if requiring PQ annually would meet Ms. Crane's recommendations. She agreed that it would. Ms. Rivera expressed concern with adding something to rule that people cannot do, which would create a financial impact. Dr. Hickman agreed that some pharmacies could have substandard equipment and will have to update them, which board members agreed is not a bad thing but could still impact pharmacies financially.

Dr. Mikhael asked the committee to voice any edits to the proposed language from AnazaoHealth, then suggested including language related to IQ, OQ, PQ and annual validation of the PQ. Mr. Montgomery reiterated that he would be more comfortable with additional detail. Dr. Mikhael reminded the committee of Ms. Rivera's and Mr. Wright's suggestions. He suggested creating a smaller committee, which would include AnazaoHealth and Ms. Crane, to work on language. Dr. Mikhael thanked AnazaoHealth for submitting their proposed language and their assistance with discussion.

Richard Green, nuclear pharmacist for Cardinal Health, referenced four USP chapters: 795, 797, 800, and 825, as a reminder that they will become enforceable as of December 1, 2019. He further informed the committee that Cardinal Health does not have a lyophilizer and only sources lyophilized drugs from FDA-approved drug manufacturers. He explained that this is due to an FDA document titled "When to Register As A Drug Establishment", commonly referred to as the nuclear pharmacist guidelines, which states that establishments using lyophilizers should register as a drug manufacturer. He added that he doesn't believe any radio pharmacy practice should involve the use of a lyophilizer.

Mr. Flynn agreed that radio pharmacies may not require a lyophilizer. He reminded committee members that 503A pharmacies are exempt from getting a new drug application, cGMP, and labeling requirements, otherwise those compounding drugs must register as a drug manufacturer. He added that radio pharmacies are excluded from this 503A exemption. Mr. Flynn pointed out that due to this, the board may have to work with other agencies regarding certain changes they wish to make in this rule. Mr. Wright asked how the rule can be updated without violating federal statute. Mr. Flynn explained how the FDA enforces laws based on how states utilize FDA guidelines, which may lead to federal and state conflicts that the FDA overlooks. Discussion ensued regarding nuclear pharmacies in relation to compounding drugs and lyophilization.

David Barnes, Southeast Regional Pharmacy Director for GE Healthcare, agreed that lyophilizers should stay with drug manufacturers due to risk of producing lyophilized drugs

that haven't met FDA standards. Dr. Mikhael suggested making the rule specific to the process of lyophilization and not focusing on radio pharmaceutical products, which Mr. Flynn agreed with. Discussion ensued regarding the differences between AnazaoHealth and Cardinal Health processes and how the rule would fit radio pharmaceuticals.

Mr. Harris explained that if there is a drug that would need to be created outside of the process defined in the rule, pharmacies may file a petition for variance or waiver from the rule. He further stated that if multiple pharmacies request variances from a particular section of the rule, the board will address the rule language again. Mr. Wright expressed concern with a pharmacy being required to stop a process due to rule change until a petition for variance or waiver is granted. Mr. Green expressed concern with the discussion focusing too much on USP Ch. 797, which he feared would leave USP Ch. 800 and 825 out of the proposed language. Mr. Flynn confirmed the rule would indicate its requirements are in addition to the USP chapters.

Fred Gavas, a representative of Curium Pharmaceuticals, reminded the committee that the FDA guidance may not be legally binding but is based on the FDA's thinking and therefore should be adhered to. He also stated that the guidance for radio pharmaceuticals can be applied to any pharmaceuticals and would be good language to add to the rule. Dr. Mikhael and Mr. Flynn asked whether a product can be safely made using lyophilization if the process has front and back-end validation, to which Mr. Gavas answered yes. Mr. Flynn clarified that the purpose of updating this rule is to ensure the safety points around that process are in language.

Melissa Stefko, a microbiologist with Wells Pharmacy, stated that she felt it was important to understand how a lyophilizer works, which she felt is similar to a biosafety cabinet in that the drug is exposed to both environments. She asked Ms. Crane if the hood would have to also be sterilized if the lyophilizer must be, since both can be sterilized in the same way. Ms. Crane answered that the difference entails air being involved with a hood but not a lyophilizer, which is why a hood should also be sterilized. Ms. Stefko expressed concern with some lyophilizers requiring a custom sterilizer, which pharmacies may not have. She also referred to lyophilizers used by pharmacies that aren't necessarily a machine, which Ms. Crane clarified is what she is concerned with due to taking uncapped products and putting them into a deep freezer. Ms. Rivera agreed that some pharmacies may not have all the processes that a regular manufacturer has. Clarification was made on how container closure integrity is tested by Wells Pharmacy.

Edwin Bayo, Attorney, asked the committee not to forget about smaller 503A pharmacies that use the lyophilization process. He suggested requiring a documented cleaning technique instead of sterilization, due to the inability of sterilizing some equipment. Ms. Stefko proposed showing cleanliness through environmental monitoring. Mr. Harris requested feedback to rule language stating if using the lyophilization process, pharmacies shall have policies and procedures which guarantee x, y, and z, which is certified or proven through documented logs. He asked Ms. Crane whether the language he proposed would be enforceable. Dr. Crane stated that clear rules are needed so the end product has the best chance of being sterile and their main concern is with transport. She added that she did not see how the proposed language would allow her to find violations and tie them back to rule. Mr. Montgomery asked what the risk of contamination is for transferring from an ISO-5 to an ISO-7 room. Ms. Stefko answered that there is a high risk which is why it should all be conducted in a contained room. Mr. Montgomery stated that based on this

answer, transport should be considered in the rule language.

David Joseph stated that he is in support of the direction the board is taking in regulating lyophilization. He asked the board to view this rule as a template for future gadgets and machines that will need to be regulated, referencing dry-heat ovens and autoclaves as requiring the same care.

Yanrisi Valero with APS Pharmacy, stated that if pharmacies have a defined process requiring IQ, OQ, and PQ product testing, they should be able to comply. She expressed concern with requiring sterilization due to the possibility of a pharmacy's equipment not being suitable for sterilization. She added that her pharmacy sanitizes their equipment instead. She also expressed concern with pharmacies being forced to change a process they have in place, they will have to repeat stability studies, which will be costly. Dr. Mikhael agreed that the rule should not create an environment that gives an unfair advantage to certain companies.

Dr. Mikhael stated that the board will conduct a workshop in March to develop the finalized rule. He added that the workgroup will be limited to five or six people, including committee members. He requested for interested participants to submit their contact information to Jennifer Wenhold.

II. Old Business / New Business

III. Public Comment

IV. Adjournment

Meeting adjourned at 3:44 p.m.