

COMMONWEALTH OF MASSACHUSETTS
BOARD OF REGISTRATION IN PHARMACY

MINUTES OF THE PHARMACY ADVISORY COMMITTEE

239 Causeway Street, Fourth Floor ~ Room 417A
Boston, Massachusetts 02114

Friday, March 27, 2015

Advisory Committee Members Present

Monica Bharel, MD, MPH, DPH Commissioner, Chair
Sylvia B. Bartel, RPh (Expert in USP<797>), departed @ 11:35 a.m.
Judith Barr, MEd, ScD, FASHAP (Expert in Pharmacoeconomics)
Caryn D. Belisle, RPh, MBA (Expert in USP<71>)
Karen B. Byers, MS, RBP, CBSP (Expert in Microbiology)
Anthony M. Cundell, PhD (Expert in USP<71>), arrived @ 10:45 a.m.
David H. Farb, PhD (Expert in Clinical Pharmacology)
Rory K. Geyer, PhD (Expert in cGMT)
Michael J. Gonyea, RPh, PharmD, Med, BCPS, FNAP, FCCP (Expert in Clinical Pharmacology)
Eric Kastango, RPh, MBA, FASHP (Expert in USP<797>)
Antoinette Lavino, RPh, BCOP (Expert in USP<797>)
Francis McAteer (Expert in Microbiology)
Michael C. Thomas (Expert in Clinical Pharmacology)
John Walczyk, RPh, PharmD (Expert in USP<795>)

Advisory Committee Members Not Present

Keith B. Thomasset (Pharmacoeconomics)

Support Staff

Deborah Allwes, RN, BS, BSN, MPH, Director, Bureau of Health Care Quality and Safety
James Lavery, JD, Director, Divisions of Health Professions Licensure
David Sencabaugh, RPh, Executive Director, Board of Pharmacy
Heather Engman, JD, MPH, Board of Pharmacy Counsel
Vita Berg, JD, Chief Board Counsel
Jennifer Barrelle, JD, Director of Policy
Timothy St. Laurent, Assistant Director, Divisions of Health Professions Licensure
William Frisch, Jr., RPh, Director of Pharmacy Compliance
Kelly Ann Barnes, RPh, JD, Director of Pharmacy Quality Assurance
David Dunn, RPh, Assistant Executive Director
Samuel Penta, RPh, Investigator
Richard Harris, Administrative Assistant
Joseph Sceppe, RPh, MS, MBA, Pharmacy Consultant

Board of Pharmacy Members

Patrick Gannon, RPh, MS, President
Edward Taglieri, President-Elect
Michael Godek, RPh
Timothy Fensky, RPh

TOPIC:

1. CALL TO ORDER

DISCUSSION: At 10:05 a.m., DPH Commissioner and Advisory Committee Chair, M. BHAREL, MD, called the first meeting of Pharmacy Advisory Committee to order. A quorum was present. She asked if anyone in the audience was recording the meeting; no one indicated that they were recording the meeting. She indicated that the Board was recording the meeting.

Dr. BHAREL briefly described her background, thanked the members for their commitment of time and interest, and asked members to introduce themselves.

Executive Director, D. SENCABAUGH then introduced and thanked those members of the Board of Pharmacy and support staff in attendance.

ACTION: So noted.

TOPIC:

2. APPROVAL OF AGENDA

10:15 a.m.

DISCUSSION: DHPL Director, J. LAVERY, asked if there were any changes to the tentative agenda.

ACTION: Motion by M. THOMAS, seconded by E. KASTANGO, and voted unanimously to approve the agenda with the no changes. A. CUNDELL was not present for the vote.

TOPIC:

3. OVERVIEW OF CHAPTER 159, AN ACT RELATIVE TO PHARMACY PRACTICE IN THE COMMONWEALTH

10:18 a.m.

DISCUSSION: J. LAVERY summarized the State's response to the national fungal meningitis outbreak:

- Creation of a Special Commission on the Oversight of Compounding Pharmacies,
- Initial legislation to address long-term reforms (based on the Commission's recommendations),
- Board's response: Promulgated emergency regulations; created an audit tool; conducted unannounced inspections; addressed reports of abnormal result,
- Chapter 159 of the Acts of 2014 mandated steps to improve pharmacy services in the Commonwealth:
 - Changed the Board's composition from 11 to 13 members, 8 of whom are pharmacists,
 - Mandated USP and NABP training of inspectors,
 - Created additional licensure categories, including a separate license for hospital pharmacies engaged in sterile compounding,
 - Requires annual inspections prior to license renewal,
 - Requires an annual report to the Board,
 - Authorizes a one-time provisional license of not more than 1 year,
 - Authorizes penalties & fines,
 - Mandates reporting of serious adverse drug events (ADEs),
 - Mandates labeling to indicate when a medication is a sterile or non-sterile compounded drug,
 - Increase in CE from 15 to 20 contact hours of which, if appropriate, 5 hours for sterile compounders and/or 3 hours for complex, non-sterile compounders,
 - Creates a Pharmacy Advisory Committee to the Board of Pharmacy.

ACTIONS: So noted. A. CUNDELL was not present for much of the discussion.

TOPIC:

4. PROCEDURAL ISSUES

10:48 a.m.

DISCUSSION: J. LAVERY mentioned that a quorum of 8 is necessary for the 14 member Pharmacy Advisory Committee. A quorum is also necessary for Subcommittee meetings.

ACTION: So noted.

TOPIC:

5. OPEN MEETING LAW OVERVIEW

10:50 a.m.

DISCUSSION: Board Counsel, H. ENGMAN, summarized aspects of the Open Meeting Law (OML) which would be relevant to the Pharmacy Advisory Committee. She indicated that the purpose of the Law was to ensure transparency in government. To that end:

- All committee communication must be done in open meetings,
- Notice of meetings and agenda must be posted on the website at least 48 hours prior to the meeting,
- The Advisory quorum is 8 members. Subcommittees are subject to OML; a reduced quorum (<50%) could be approved by majority vote,
- Members may participate remotely; a quorum must be in the room; votes must be by roll call.

In response to a question, she indicated that a member reaching out to a non-member for information would not be subject to the OML.

She also cautioned members with regards to emails, as they would be subject to the OML.

ACTION: So noted.

TOPIC:

6. COMMUNICATION BETWEEN BOARD AND ADVISORY COMMITTEE **10:57 a.m.**

DISCUSSION:

D. SENCABAUGH recognized the pharmacy students in the audience and thanked the members of the Board who were able to attend.

- a. D. SENCABAUGH described the need to be able to capture ongoing communication between the Board and Advisory Committee in a single document, using a standard numbering format. He distributed a draft of an *Advisory Committee Recommendation Document* that the Board felt would meet the objectives.

ACTION: Motion by M. GONYEAU, seconded by S. BARTEL, and voted unanimously to accept the *Advisory Committee Recommendation Document* format to communicate between the Board and the Advisory Committee.

- b. Board member, T. FENSKY, distributed the first two Advisory Committee Recommendation Documents: Abnormal results (#15-01) and Outsourcing Facilities (#15-02).

ACTION: Motion by J. BARR, seconded by K. BYERS, and voted unanimously to formally accept the Advisory Committee Recommendation Documents #15-01 and 15-02.

BREAK 11:10 – 11:25 a.m.

TOPIC:

7. TOPICS FOR REVIEW/PRESENTATION

11:25 a.m.

DISCUSSION:

Director of Pharmacy Compliance, W. FRISCH introduced K. A. BARNES, Director of Pharmacy

Quality Assurance, who requested input from the Advisory Committee on what to do when reports of abnormal results are received by the Board.

She referred to her March 24, 2015 memo to Board members, *Board Members Request to Advisory Committee Regarding Regulations Pertaining to Above Action Level Environmental Monitoring Results*. Environmental monitoring includes testing for bacterial and fungal contamination. She asked what it meant to be outside the USP <797> action limits.

- EK: Although not required by the USP, he felt that 2 plates (soybean–casein digest medium/(trypticase soy agar/TSA as well as malt extract agar) should be required.
- AC: Occasional microorganisms are observed, even in well-controlled environments.
- FM: Rather than testing with TSA and then, if positive for fungi, testing with malt extract agar, it would be better to initially test with both growth media.
- KB: Indicated that her more conservative approach was to use single TSA plates.

K. BARNES noted that the Board currently recommends resampling if action levels are exceeded and that subsequent sampling be done on a monthly basis.

- AL: Indicated time constraints when a second plate is used only after the results from the first plate have been completed, and then retesting after remediation.
- FM: Viable microbial monitoring of airflow (vs. surface sampling) is a much more definitive scenario if positive tests result.
- EK: Six-month sampling is not enough. In the 2005-2010 USP <797> review cycle, there were 2 distinct opinions; the CDC felt there was no need to monitor and the FDA recommended that monitoring be done daily. The decision to keep the current language was a compromise.

The concept of State of Control could be thought of as a matrix of various testings, etc. with USP <797> iterations; testing monthly for low-risk level and weekly for high-risk level compounding, especially if the compounder is exceeding the USP's BUDs.

- RG: Sampling twice a year is not enough; sampling should be risk based/product based.
- JB: The clinical microbiology lab goes through a similar procedure to test their growth media. The batch is quarantined until the test results have been received.

W. FRISCH noted that if the format for microbiological reports were standardized, they would be easier to review.

J. LAVERY suggested that K. BARNES and W. FRISCH develop a proposal draft for the Advisory Committee.

- RG: To ensure a State of Control it is necessary to review all aspects, from the beginning to the end of a process. Quality needs to be built into each part of the process. The firm should know which operations are high risk, and review them accordingly.
- DF: Is there a compliance officer in each facility?

K. BARNES indicated that the Manager of Record (MOR) is the responsible party. Facilities vary, the larger ones may have a compliance officer. Most testing is done by contract testers (rather than in-house).

- RG: The commercial facilities that the FDA inspects have more structure with respect to individuals responsible for risk management.

W. FRISCH focused the discussion on Response to Actionable Limits Under USP <797>.

- FM: It is important to focus on the location of positive results. If actionable levels are exceeded in the ante room, it is less of a concern than if they were found in an ISO-5 space. In an anteroom that has both positive and negative airflows, contamination may be the result of ongoing contaminated airflow.
- CB: It is important to differentiate between compounding pharmacies and hospital

pharmacies based on the scope of activities and the impact on patient care.

- EK: Every cleanroom is not sterile and the person doing the sampling may inadvertently cause the contamination. The genus of the sampling might be the focus with respect to the contaminates and where to further investigate and remediate. FDA-registered facilities are required to speciate contaminants.

If one CFU is found, investigate, reclean, and retest. Document subsequent results. If contamination continues, escalate to “DEFCON 3”.

- RG: If actionable levels are exceeded, the response should be based on worst case scenario. The firm could continue manufacturing but not release product.

K. BARNES asked when it would be safe to keep compounding.

- EK: It can take from 7 to 10 days to obtain testing results. Unlike FDA-registered firms, pharmacies can’t recall all products.
- JB: Media broth are never used in a microbiology lab until the results of the testing are received.

K. BARNES indicated that holding products until testing results were received was not practical in a hospital, as most compounded IVs are patient-specific, low or medium-risk level products

- AL: Is the Board uncomfortable with the USP <797>: actionable limits?

K. BARNES indicated that the Board’s issue is what to do when actionable limits are met or exceeded.

- JW: Hospitals do not have the luxury to shut down operations based of the results of testing from 7-10 days ago.
- AL: Microbiologists did not agree with the Boards decision to shut down a facility.
- AC: Industry doesn’t give weight to the pathogenicity of an organism; he feels something is sterile or it is not.

J. LAVERY suggested that K. BARNES put together a proposed plan.

K. BARNES indicated that the Board recommends that facilities that meet or exceed USP’s actionable limits should stop compounding, but needs the Committee’s input.

- FM: The onus is on the pharmacy to analyze the testing results and to remediate.
- CB: Can we delineate between surface contamination and the bigger issue of air contamination?
- FM: The problem must be systemic and encompass a series of reports before shutting a facility down.
- KB: We should focus on risk assessment points and specific remediation.
- EK: Suggested that we consider three levels of contamination: Critical Major (involving ISO 5 areas); Major (ISO 7); Minor (Ante Room). Contamination could be due to changes in room pressure. He reminded us that the USP <797> refers to actionable levels, not limits. He also suggested we think about logarithmic levels. He further suggested that we consider the level of contamination (Critical Major, Major, or Minor), investigate, and remediate. The issue may have been bad behavior vs. a true health risk.

S. PENTA indicated that Board inspectors act on results. No trending data has been available.

J. LAVERY acknowledged the need to increase the frequency of testing in order to have trending data.

V. BERG expressed the need for the Board to have an algorithm. Authority to take action rests with the full Board. The law vests discretion with the Board (not Board inspectors). An algorithm is needed to take action that is immediate and consistent.

D. SENCABAUGH feels that we have a plan. Shutting a hospital pharmacy does not make sense.

K.BARNES reminded the group that the Board will be licensing non-resident pharmacies and will

have to work through NABP with respect to remedial actions.

M. BHAREL indicated that we need to communicate with pharmacies as to what will be expected.

- EK: If a pharmacy engages in minimum monitoring and obtains a positive test, it may have to be shut down. A pharmacy with more frequent monitoring that can show trends and a Risk Mitigation Strategy may be able to prove a State of Control.
- JW: Believes that pharmacies will agree to increased testing.
- CB: Noted that many hospitals currently test frequently.
- AC: It is important to focus on the frequency of positive tests in a particular time period. Emphasis on a single species is not the critical issue. High-risk level compounding involves a greater risk of contamination.
- JB: Once a positive test is obtained, more frequent testing should occur.
- AL: Read from the USP <797> which indicated that remediation needs to be immediate; it does not indicate that the pharmacy needs to be shut down.

W. FRISCH: The Board needs a decision tree and an algorithm with multiple variables.

M. BHAREL suggested, and the group agreed, to create a subgroup and bring recommendations back to the full Committee. The following members volunteered to be part of the Subgroup to address issues involving Abnormal Test Results: K. BYERS, A. CUNDELL, D. FARB, R.

GEYER, E. KASTANGO, A. LAVINO, F. McATEE, E. TAGLIERI, J. WALCZAK.

The Subgroup agreed to meet monthly and recommended a quorum of 4 members.

ACTION: Motion by J. WALCZYK, seconded by M. THOMAS, and voted unanimously to create an Abnormal Test Results subcommittee and that 4 members constitute a quorum.

TOPIC:

8. CLOSING REMARKS

12:50 pm

DISCUSSION: J. LAVERY thanked the members for their help and commitment of time. He also recognized the work of staff in preparing for the meeting. Given the Board's need for immediate guidance from the Advisory Committee, he asked if members would consider meeting on a relatively frequent basis.

ACTION: Motion by A. LAVINO, seconded by E. KASTANGO, and voted unanimously to have monthly meetings.

TOPIC:

9. ADJOURNMENT

12:55 pm

DISCUSSION: None.

ACTION: At 12:55 p.m., motion by D. FARB, seconded by M. THOMAS, and voted unanimously to adjourn.

LIST OF EXHIBITS USED DURING THE MEETING

1. Preliminary Agenda for the March 27, 2015 Pharmacy Advisory Committee Meeting
2. Open Meeting Law, Summary for Advisory Committee, March 27, 2015
3. Chapter 159 of the Acts of 2014, Advisory Committee
4. Advisory Committee Recommendation Document Template
5. Advisory Committee Recommendation Document 15-01, Abnormal Results
6. Advisory Committee Recommendation Document 15-02, Outsourcing Facilities
7. Proposed Memo from the Board of Pharmacy to the Advisory Committee: *Board Regulations Pertaining to Above Action Level Environmental Monitoring Results*, March 24, 2015

8. Memo from Kelly Ann Barnes and William Frisch, Jr. to Members of the Board of Registration in Pharmacy: *Board Members Request to Advisory Committee Regarding Regulations Pertaining to Above Action Level Environmental Monitoring Results*, March 24, 2015
9. Specific Questions for Advisory Committee Approval
10. US FDA *Pharmacy Compounding Legislation and Implementation*, March 20, 2014
11. US FDA Guidance for Industry, *Whether to Register As Outsourcing Facility Under 503B*

Respectfully submitted,

Joseph M. Sceppa, RPh, MS, MBA, Secretary Pro Tem