EXPERT DECLARATION OF DR. MICHAELA ALMGREN

I. Background and Qualifications

1. My name is Michaela Almgren, Pharm.D., M.S. I am over the age of eighteen and competent to testify to the truth of the matters contained herein. The factual statements I make here are true and correct to the best of my knowledge. I hold the opinions expressed in this declaration to reasonable degree of scientific certainty.

2. I am a Clinical Associate Professor in the Department of Clinical Pharmacy and Outcomes Sciences at the University of South Carolina College of Pharmacy. I teach principles of sterile compounding per United States Pharmacopeia ("USP") Chapters 797 and 800, aseptic technique in drug compounding[1] and pharmacy regulations applicable in a compounding environment run under Section 503B of the Drug Quality and Security Act of 2013, as well as pharmacokinetics and biopharmaceutics courses. I specialize in sterile compounding, medication safety, and pharmacy laws and regulations that relate to pharmacy compounding practices. I also provide continuing education courses for pharmacists in those topics. I received my Doctor of Pharmacy degree from the University of South Carolina College of Pharmacy in 2010. Additionally, I have a Master's Degree in Pharmaceutical Chemistry from the University of Florida.

3. In conjunction with my academic appointment, I currently maintain a practice site at a 503B[2] outsourcing pharmacy where I perform duties of outsourcing pharmacist, clinical advisor, and pharmacy student preceptor. Previously, I worked in

[1] Aseptic technique in drug compounding refers to specific practices to avoid physical and microbial contamination when preparing sterile medications that are to be used for parenteral applications, such as IV infusion, injection, etc.

[2] 503B Outsourcing Pharmacy is a compounding pharmacy that produces large batches of sterile products and distributes them directly to health systems pharmacies to address drug shortages, as specified in Section 503B of the FD&C Act.

pharmacy operations in a local large teaching hospital as a pharmacist. I have almost 15 years of experience in sterile compounding and aseptic technique. Prior to joining the faculty at the University of South Carolina, I worked for several years in pharmaceutical manufacturing where I was involved in drug formulation, quality assurance, quality control and analytical method development. A copy of my CV is attached as Exhibit A.

II. Referral Questions.

4. I have been asked by the Federal Community Defender Office for the Eastern District of Pennsylvania ("FCDO"), who represent death-sentenced prisoners in the State of Texas, to submit an expert medical and scientific opinion, based on the information and documentation provided to me, about whether Texas is properly extending the Beyond Use Dates ("BUDs") on their lethal injection drugs, or if the drugs are in fact expired. The FCDO further asked me to opine on whether there is a risk of harm that can be caused by administration of compounded pentobarbital past its BUD.

III. Materials Relied Upon.

5. I have reviewed the following documents: Texas Department of Criminal Justice ("TDCJ") Execution Procedure (version published April 2021); order and purchase forms, including DEA Forms 222; and analytical and inventory records reflecting TDCJ's Pentobarbital ordering and storage from December 2018 to November 2022. I have also reviewed an email that TDCJ sent to the FDCO on November 29th, 2022, containing information about the BUDs of pentobarbital currently in the possession of TDCJ.

IV. Background Information.

6. When drugs are commercially manufactured, they undergo extensive quality control testing which assures that they maintain their quality, such as potency and

purity, up to their expiration date. Stability studies are performed to determine if there are any concerns with drug deterioration. Expiration dates are determined using these carefully designed stability studies.

7. Commercially manufactured medications are tested for important quality attributes such as assay, potency, impurities, content uniformity, and other characteristics that are product specific and typically defined for each product in the USP Compendium Monograph for each individual drug. The medications are tested multiple times during the manufacturing process and again when completed and prior to release for sale and distribution using methodologies that are validated according to the USP Compendium Monograph. The manufacturers collect stability data showing that the medications do not degrade before their expiration date. The medication's storage container and the container's closure also undergo extensive integrity testing. Additionally, if these medications are sterile, each batch must undergo extensive sterility testing.

8. When medications are compounded, Active Pharmaceutical Ingredients ("APIs")[3] may be used to prepare them. The compounding is usually done in a pharmacy that specializes in sterile compounding, as specific equipment and personnel training are necessary to prepare the sterile products correctly.

9. Sterile compounding can be performed in a Biological Safety Cabinet or Laminar Airflow Hood and it must follow the strict guidelines of USP Chapter <797>. USP Chapter <797> describes best practices to follow in order to prepare the product aseptically and to keep it sterile, how to sterilize it, how to maintain the compounding environment free

[3] Active Pharmaceutical Ingredient is typically concentrated drug active ingredients in powder form.

from contamination, how to perform training assessments for the personnel handling the medication preparation, how to determine BUDs of sterile compounded products, etc.

10. BUD refers to Beyond Use Date, or expiry of the compounded product. Because compounded products do not undergo the same extensive quality testing as commercially available products, their expiry or BUD is significantly shorter. While commercially produced medications may have expiry dates measured in months and years, compounded products typically have BUDs specified in days, or even just hours. The APIs used are typically not sterile and the product has to be sterilized at the final stage of compounding. It is important to use APIs from sources that guarantee high quality and offer USP or pharmaceutical grade APIs, as those are most likely to meet all USP quality standards.

11. USP is a compendium of quality requirements, quality specifications, practices, and guidelines to achieve the highest pharmaceutical quality for pharmacy practice as well as to set the standards for the pharmaceutical industry. Chapters 1 through 999 are enforceable by the Food and Drug Administration. Individual states' Boards of Pharmacy may also enforce USP. Texas State Board of Pharmacy has codified language from USP Chapter <797> into its regulations regarding compounded sterile products. A compounding pharmacist should be very familiar with USP Chapter <797> guidelines in order to prepare safe and effective sterile compounded products. If USP Chapter <797> guidance is not followed, it can lead to medication contamination which will cause patient harm and unpredictable drug actions.

V. The pentobarbital in TDCJ's possession is expired.

12. It is my understanding that TDCJ intends to execute prisoners by an intravenous ("IV") injection of compounded pentobarbital prepared by an undisclosed compounding pharmacy.

13. According to USP Chapter <797>, sterile medications that are prepared from initially non-sterile components, such as APIs, or using a methodology that potentially causes the preparation to lose sterility, are considered high-risk sterile compounds. The preparation then must be terminally sterilized if it is to be used for parenteral application such as IV bolus injection, or IV infusion.

14. Based on the records I reviewed, it appears that TDCJ is using compounded pentobarbital. Pursuant to USP Chapter<797>, once prepared, this is considered a high-risk sterile compound. All the pentobarbital in TDCJ's possession has already been prepared—meaning that the active ingredient has been compounded and put into a solution for IV injection. If that is the case, all the pentobarbital in TDCJ's possession is expired, as it is far beyond the USP specified BUD.

15. A BUD is defined in USP Chapter <797> as "the date or time after which a compounded sterile product (CSP) shall not be stored or transported." The BUD is determined from the date and time the preparation was compounded. A compounded product's BUD shall be determined as outlined in current USP Chapter <797>, Pharmaceutical Compounding—Sterile Preparations, of the USP/NF 2022 Issue 3. The maximum BUD for high-risk compounded sterile preparations such as the compounded pentobarbital in TDCJ's possession are:

- 24 hours, if stored at room temperature between 20° and 25°C;

- 72 hours, if kept refrigerated at temperature range between 2° and 8°C, or
- 45 days, if kept in a solid, frozen state at temperature range -25° and -10°C.

16. TDCJ receives pentobarbital in two different vials sizes – 50ml and 100ml final volume. It appears that the solution in the vials are of the same concentration – 50mg/ml – regardless of the vial size. Therefore, if prepared as specified, each 50ml vial should contain 2.5 grams of pentobarbital and each 100ml vial should contain 5 grams of pentobarbital.

17. Based on my review of the Huntsville Unit Storage Inventory logs, it appears that TDCJ most recently received 50ml vials of pentobarbital injection solution on March 18, 2021. Those 50ml vials are now (at the time of writing this report, December 2022) more than 630 days old, well over the BUD limit of 24 hours when stored at room temperature as specified in USP Chapter <797> (or 45 days if kept frozen). However, based on the email TDCJ sent on November 29, 2022, those 50ml vials (2.5grams of pentobarbital) have a newly assigned BUD of September 27, 2023.

18. Also, based on my review of the Huntsville Unit Storage Inventory logs, it appears that TDCJ most recently received 100ml vials of pentobarbital injection solution on April 29, 2019. Those 100ml vials are now more than 1,300 days old, well over the BUD limit of 24 hours as specified in USP Chapter <797> (or 45 days if kept frozen). And again, according to the TDCJ email, these 100ml vials (5 grams of pentobarbital) now have a BUD of November 1, 2023. Based on the records I reviewed, the BUDs were extended in contravention of USP.

19. Other preparations in TDCJ's possession may be even older, as the records do not show specific lot numbers, so there is a possibility that some vials in stock could be from previous shipments.

20. A drug that has surpassed its BUD is at risk of stability and sterility failings and may not retain sufficient potency, thus it must not be used. Pharmacological activity of expired medications is unpredictable, but in general the effectiveness will decrease over time. The risk of degradation is even greater if the drug storage conditions are not optimal, as specified in the USP. Some of the drug degradants may have their own pharmacological activity, often times completely different from the original drug action. There is vast evidence in literature pointing to the fact that expired medications should not be used in human patients due to unpredictability of the action, and potential harm, including nausea, vomiting, acute renal failure, and other severe side effects. The FDA also strongly advises against the use of all expired medication. For injectable medications this is even a greater concern, as the pharmacological activity of the drug may decrease significantly when in solution.

VI. TDCJ improperly extended the expiration date (BUD) of its pentobarbital. The "potency" test results TDCJ obtained cannot be used to extend expiry. The true potency of the drug is not known and needs to be determined.

21. I have reviewed a set of documents labeled "Laboratory Report" which appear to show that potency testing of the pentobarbital injection was performed in attempt to extend the BUD or drug expiry. However, this approach to extending BUD is completely unscientific and incorrect, and therefore the results are invalid. A stability study should be performed to establish an extended BUD using completely different methodology. It appears that TDCJ's pentobarbital was tested for potency using the High-Performance

Liquid Chromatography ("HPLC") assay method specified and validated in the USP monograph for pentobarbital injection. This HPLC method is a quantitative test commonly used to determine the amount of the drug in a sample which is freshly prepared/compounded, when there are no concerns about potential degradation. However, this method is not intended to determine stability of pentobarbital, and it may not detect if the drug has deteriorated over time as it is not sufficiently sensitive to detect degradation.

22. The purpose of an assay or potency method listed in the USP Monograph is to verify that the prepared drug contains the correct amount of API, as stated on the drug label, for example 50 milligrams per milliliter. It is appropriate to use this method for quality control purposes, for manufacturing release and product approval when the drug is freshly compounded or manufactured, but not to extend the expiry of the drug. A stability indicating HPLC method needs to be used to determine whether there is any degradation of the drug.

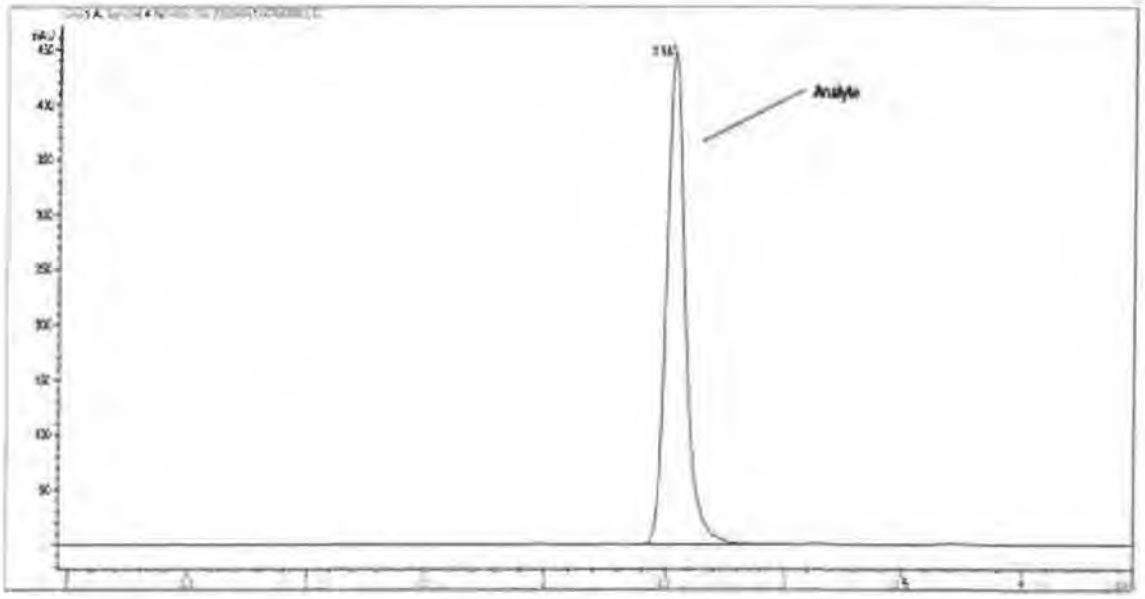
23. The HPLC Assay test method used by the laboratory is not validated for use as a stability-indicating assay. A stability-indicating assay is an analytical method that is capable of separating the API drug peak from degradation residues, which are impurities that form over time. This method is necessary to determine the extent of degradation that happens over time and will show the true potency of the drug. An assay used to release freshly prepared medications does not test for degradation, as there should not be any, thus this type of method is not designed to be sensitive enough to detect any degradants potentially present.

24. Degradation products of the drug can be structurally similar to the drug (API) itself, but their pharmacological action may be completely different. Additionally, the presence of degradants will likely lower the potency of the compounded drug tested (because

some of the drug has degraded), and may change solubility, pH and other parameters of the solution which may also impact the pharmacology and pharmacodynamics of the drug product itself. A change in pH can lead to formation of precipitants and isomers, decrease in drug solubility and other potential changes in the drug's actions.

25. Here is an example of a chromatogram of **non-stability-indicating HPLC** assay method that evaluates the potency of a single API only:

Chromatography Example 1:[4]

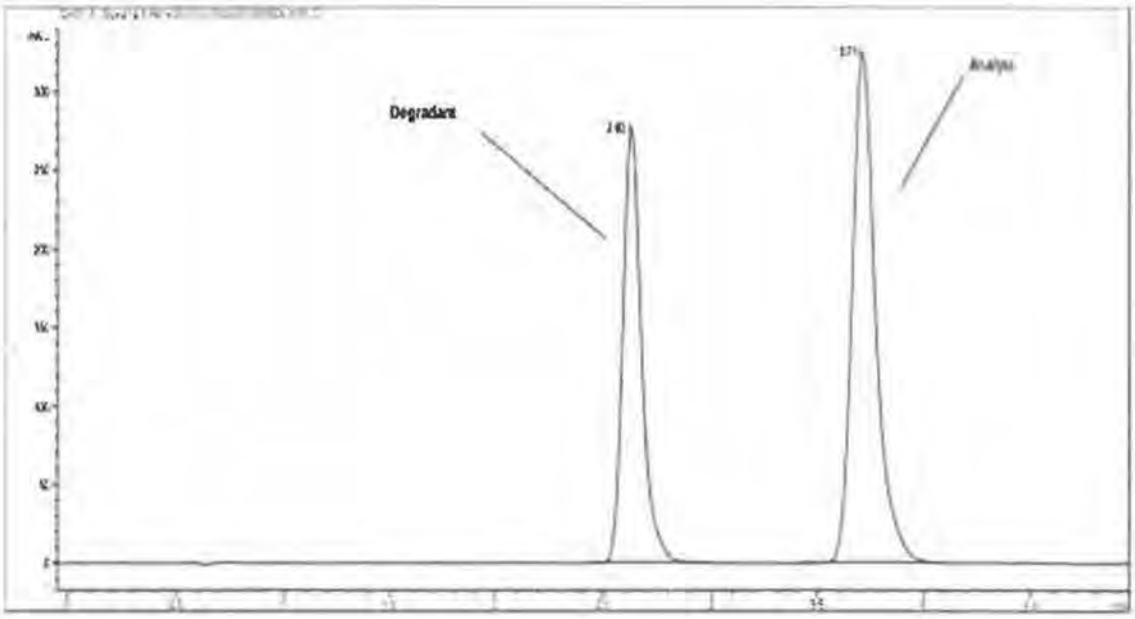


The potency of the drug is calculated based on the area of the peak shown in the chromatography (labeled as Analyte). Due to lower sensitivity of the method only one peak is visible, although other impurities may be present.

26. Here is an example of a chromatogram of the **same drug using stability-indicating method** that shows the presence of degradant in addition to the API (Analyte):

[4] Reference: USP Compounding Expert Committee: Loyd V Allen Jr, PhD, Gus S Bassani, PharmD, Edmund J Elder Jr, PhD, Alan F Parr, PharmD. Strength and Stability Testing for Compounded Preparations.

Chromatography Example 2:[5]



Because the stability-indicating study separated the API peak (labeled Analyte) from the Degradant, the area of the Analyte peak will be smaller and thus the calculated true potency of the drug will be different (lower) in Chromatography Example 2 than the assay result obtained using the less sensitive HPLC assay method in Chromatography Example 1. In other words, the HPLC assay method with lower sensitivity overstates the amount of API present when the sample has degraded over time.

27. Pentobarbital is known to have degradants that form over time. The pentobarbital molecule breaks down into a number of different substances. Pentobarbital's three most commonly identified degradants are: N-(Aminocarbony])-2-ethyl-3-methylhexanamide, 2-Ethyl-2-(1-methylbutyl)propanediamide and 2-Allyl-2-(1-methylbutyl)propanediamide. Pharmacology of these structures is poorly understood, but it

[5] *Id.*

is clear from their chemical structures alone that they do not produce the same pharmacologic effect as pentobarbital. Included below is the chromatography showing stability-indicating assay for pentobarbital:[6]

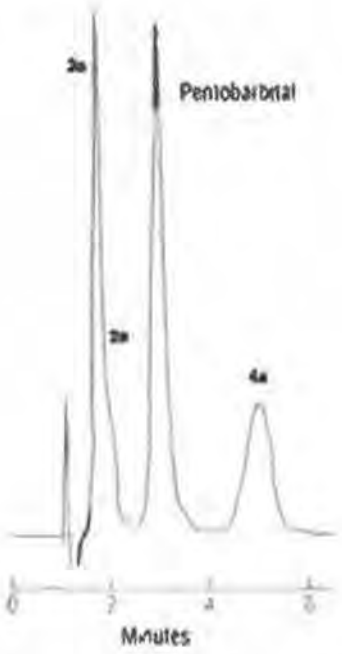


Figure 3—Chromatogram of a synthetic mixture of pentobarbital and its degradation products. Compound 2a is N-(aminocarbonyl)-2-carboxy-2-ethyl-3-methylhexanamide; 3a is 2-ethyl-2-(1-methylbutyl)propanediamide; 4a is N-(aminocarbonyl)-2-ethyl-3-methylhexanamide.

25. Strength and assay testing is designed to determine how much API is in the product, while stability testing is required to extend BUD and to determine the true expiry of the product. The assay test used to assess TDCJ's pentobarbital is unable to detect if degradation of the API has occurred.

26. A stability study is required to properly extend the BUD. Stability studies are used to determine if there are any concerns with drug deterioration over time and are used to establish extended expiry for compounded drugs, beyond the BUD as established in

[6] Reif VD, Kaufmann KL, DeAngelis NJ, Frankhouser MC. Liquid chromatographic assays for barbiturate injections. J Pharm Sci. 1986 Jul;75(7):714-6.

the USP Chapter <797>. Stability studies must be performed to determine if expiry of the drug can be extended beyond the BUD limits specified in USP Chapter <797>. Without performing the adequate stability studies, it is unknown if the compounded drug will perform pharmacologically as expected once it is past its assigned BUD.

27. Stability study requirements are listed and explained in FDA guidance documents and mentioned in USP Chapter <797>. Under the proper FDA protocol, the drug substances are stored in their final containers inside of stability chambers with specified storage conditions (for example 25 degrees C with 60% relative humidity, or 40 degrees C with 75% relative humidity for accelerated studies). Regular testing according to USP specified parameters, which will also include the stability-indicating assay, must be performed to determine if any significant changes in drug quality had occurred. If such changes occur, it signals that the drug is expired, and its pharmacological action cannot be guaranteed. These studies are typically done using multiple samples from multiple batches to assure reproducibility. A stability study determines a proper expiration period. It is completely wrong to test the medication and to predict what the expiry is based on the current data without any stability study results. Additionally, each strength, formulation, and type of container used to store the drug needs to have a separate stability study performed to extend the BUD correctly.

28. TDCJ tests a single vial of pentobarbital for potency and then assumes that the results of that test apply to every vial from a particular batch. Such an assumption is faulty. Even if potency testing were a sufficient basis to extend BUD, which it is not, extending the BUD for all vials based on the test results of a single vial is unscientific and further violates USP requirements.

29. TDCJ also appears to test a single vial of pentobarbital from a 50ml batch and then assume that the results of that test apply to every vial from a different 100ml batch. Such an assumption is also faulty. Extending the BUD for 100ml vials based on testing results from a single 50ml vial of an unrelated batch is likewise unscientific and further violates USP requirements.

30. The process of compounding pentobarbital is rather complex because this drug is not water soluble. Additional ingredients with poor stability profiles such as propylene glycol and alcohol are utilized, and sodium hydroxide and hydrochloric acid are used to adjust pH. The presence of these additional ingredients is a concern as they effect the stability of the solution, play a role in the rate of the API degradation, and thus impact the BUD.

VII. Not all quality testing as specified by USP Monograph for Pentobarbital Injection was performed.

31. The USP Monograph, which lists quality attributes for pentobarbital injection, specifies that pH should be tested and be in the range between 9.0 and 10.5. However, none of the analytical reports contain this information. This test result is also important, as the pH can shift over time and impact stability and BUD of the product, as well as solubility of the API. The changes in pH can lead to formation of precipitant. Also, exposure of pentobarbital to pH outside of the acceptable range can lead to quicker breakdown of the pentobarbital molecule itself, producing further degradation, leading to decrease in potency. Additionally, based on the records I reviewed, it does not appear that visual inspection as per USP Chapter <790> has been performed, thus it is not certain that the drug is free and clear of particulate matter.

VIII. Sterility testing was performed using incorrect methodology and the sterility results are therefore unreliable.

32. According to the analytical reports I reviewed, ScanRDI technology was used to determine if TDCJ's pentobarbital is contaminated by microorganisms and thus not sterile. But this method for sterility testing is not acceptable by USP as USP <71> is the correct method to be used for sterility testing. Rapid sterility test methods, such as ScanRDI, may not detect all microorganisms that a traditional USP <71> sterility test method would detect. Bacterial contamination of sterile preparations to be used in parenteral applications is an unacceptable practice that can lead to severe harm.

IX. Questionable recordkeeping and concerning pattern of samples shipping and returning into the stock inventory.

33. The Huntsville Unit Storage logs raise serious concerns about TDCJ's inventory practices. From the records it appears that the drug vials are occasionally removed from the inventory, shipped out for testing, and then the samples are shipped back from the laboratory and returned to TDCJ's inventory.

34. For example, it appears that a sample (a 100ml vial) was removed from TDCJ's inventory and shipped back to the supplier on September 8, 2020. A lab report indicates that testing was performed on this sample between September 18, 2020, and September 24, 2020. On January 21, 2021, a "Return" is noted in the records showing that a 100ml vial was returned back to the stock. It is not certain where the vial came from and there is a possibility that the vial was used for testing and the remainder of the drug was placed back into the inventory. This practice is completely unacceptable. Once a drug vial is opened to get a sufficient amount of the liquid out for testing, it is considered adulterated and misbranded, as defined in the FD&C Act. When a sterile container is opened in the

laboratory to perform any kind of test, the reminder of the vial must be wasted, as there is a potential for chemical and microbial contamination, decrease in total volume leading to an incomplete dose, and potential for tampering with the drug.

35. A similar situation occurred on November 2, 2020, when a 50ml vial was returned to supplier, followed by the removal of seven additional 50ml vials from the stock. It is not clear why these vials were removed, leaving just one 50ml vial in the inventory. On February 23, 2021, one 50ml vial was received from the supplier and entered onto the inventory.

36. There is also a question about the BUD and how the expired drugs are removed from the inventory. For example, a single 100ml vial was removed from the inventory on May 6, 2020, and labeled as "expired," but the rest of the 100ml vials were kept in stock. If these vials were all made on the same date, they all should be expired and removed at the same time.

37. The recordkeeping of the pentobarbital inventory lacks fundamental information such as expiry, lot numbers for traceability, explanations for removal and replacement of each vial, and an accounting of who handled the drug vials, in addition to the storage conditions monitoring, which should also be performed on a regular basis.

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

Executed on this 12th day of December 2022.

Michaela M. Almgren

Michaela M. Almgren, PharmD, MS

EXHIBIT A

Michaela M. Almgren, PharmD, MS

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Lexington, SC 29072
almgren@cop.sc.edu
(803) 622-5231

EDUCATION

Doctor of Pharmacy, 2010 *Magna Cum Laude*
South Carolina College of Pharmacy, University of South Carolina, Columbia, SC

Master of Science in Pharmacy, 2010 *Magna Cum Laude*
Pharmaceutical Chemistry (Industrial Pharmacy focus)
University of Florida, Gainesville, FL

Bachelor of Science, 1997 *Magna Cum Laude, Graduated with Honors*
Major: Biology, Chemistry
Columbia College of South Carolina, Columbia, SC

EMPLOYMENT HISTORY AND EXPERIENCE

Clinical Associate Professor
University of South Carolina, College of Pharmacy, Columbia, SC
August 2013 – present

- Teach pharmacokinetics and biopharmaceutics lectures.
- Teach pharmacy law and ethics lectures and moderate in-class discussions, including ethics debates .
- Lectures at USC School of Medicine on natural medicine, pain management pharmacology, opioid and non-opioid as well as multimodal analgesia.
- Teach in USC School of Medicine PA program lectures on women's health.
- As a former Institutional Lab Course coordinator taught basic and advanced institutional pharmacy practice focused laboratory courses with focus on sterile compounding and aseptic technique to students in the second year of pharmacy education. Typical class size is 110 students.
- Developed, completely designed and implemented training course content for basic sterile compounding training with focus on USP chapters 797 and 800, and introduction to current institutional pharmacy practice.
- Developed and implemented 6-hour module for student training in 503A versus 503B environment regulations to emphasize critical differences in cGMP (per 21 CFR 210 and 211) versus USP standard requirements.
- Implemented practical assessment criteria for student competency of performing basic sterile compounding procedures according to USP 797 and 800 guidelines to demonstrate and document preparedness for IPPEs and APPEs.

- Revised course content and objectives for the laboratories to meet the ASHP-ACPE Task Force guidelines for entry-level competencies needed for pharmacy practice in hospital and health-systems.
- Enhanced and updated the content of advanced sterile compounding course PHMY 791, including TPN compounding, neonatal TPN formulation and compounding, chemotherapy and hazardous drug compounding, and IV access line introduction and maintenance.
- Introduced hazardous drug handling guidelines and USP 800, with emphasis on student training in utilization of all closed system transfer devices currently available in the U.S.
- Provided competency testing and certification for students to be able to participate in institutional pharmacy practice site sterile compounding activities (media fill testing, fingertip testing).
- Consulting pharmacist, performing duties of a permit holder (Non-dispensing pharmacy permit # 4956) and fully responsible for maintaining the facility, inventory control and daily operations.
- Mentor students in research offering variety of independent study projects.
- Clinical seminar evaluator and student advisor.
- Developed and implemented ACPE accredited course titled *Basic Aseptic Technique* for Kennedy Pharmacy Innovation Center, offering pharmacists and pharmacy technicians 23.5 hours of continuing education credit composed of two-day live hands-on course as well as home study.

Outsourcing Pharmacist and Clinical Specialist
Preceptor for University of South Carolina College of Pharmacy APPE Program
Nephron Pharmaceuticals Company, West Columbia SC
September 2018 - present

- Lead number of innovative and research-oriented projects (Yaskawa, Straubli, SteraMist) for manufacturing and outsourcing facility.
- Oversee formulation and filling operations for 503B outsourcing pharmacy.
- Perform product development including scale-ups for product development for outsourcing pharmacy.
- Troubleshoot quality events to develop safe solutions and set clinical limits for quality excursions.
- Develop new standard operating procedures and train staff as needed.
- Provide research information about new products, develop support materials for marketing purposes.
- Answer clinical questions when customers reah out for product guidance.
- Developed and maintain APPE site for 4th year pharmacy students, precepting record numbers of students yearly.
- ACTO app (training platform for sales force) management—review of content, provide training information about products.
- Assist with FDA quality inquiry investigations and management.
- Provide information for product development and production planning.
- Provide important information on labeling guidance for new products.
- Provide DocMatter clinician Q and A website support.
- Training of sales force via live lectures, seminars and pre-recorded lectures.

Hospital Staff Pharmacist
Palmetto Health Richland Hospital Pharmacy, Columbia SC
August 2013 – September 2018

- Performed duties of staff pharmacist—review orders, medication utilization review, order entry.
- Preparation and checking of sterile and non-sterile medication compounds.
- Medication history pharmacist—collect medication history via patient interviews, perform medication reconciliation, clinical consultations, patient education, medication use evaluation, and medication history consults.
- Maintained USC College of Pharmacy practice site.

Assistant Professor of Clinical and Pharmaceutical Sciences
South University School of Pharmacy, Columbia, SC
May 2010 -- August 2013

- Taught lectures in large number of courses in pharmaceutical sciences as well as pharmacy practice in distance education setting, managing two classrooms and collaborating with faculty members located in Savannah, GA. Typical class size was 80 students in the Columbia campus classroom, with 90 additional students at the distant site in Savannah.
- Completely redesigned Pharmaceutical Calculations course structure to flipped classroom model in order to increase effectiveness of teaching, significantly reducing the number of students needing remediation and improving overall test scores in the capstone course.
- Applied several active learning teaching techniques and team-based learning to traditionally taught courses to enhance student learning.
- Developed laboratory exercises to increase student understanding by applying learned material to practice using hands-on experiments.
- Developed and delivered elective course on animal envenomation pharmacology, medicinal chemistry and drug management.
- Taught majority of hospital-related lab coursework including TPN compounding, IV and chemotherapy preparation, and USP<797> training.
- Provided competency testing and certification for students to be able to participate in institutional pharmacy practice site sterile compounding activities (media fill testing, fingertip testing).
- Evaluated student performance of Objectively Structured Clinical Examination (OSCEs).
- Provided APhA certified immunization training for pharmacy students.
- Initiated student chapter of Student Society of Health Systems Pharmacists and guided students to the ASHP national recognition of the chapter.
- Served as faculty advisor for Rho Chi chapter.
- Academic advisor to 30 students per year.
- Faculty advisor to Student Society of Health Systems Pharmacists chapter.
- Research interests: use of complementary medicine in treatment of chronic disease states, smoking cessation and electronic cigarette utilization, new and engaging teaching methods in pharmacy education.
- Precepted Advanced Pharmacy Practice Experience students in elective academia setting.

Adjunct Faculty, University of Florida Graduate Distance Programs
University of Florida, School of Pharmacy
January 2011-- May 2014

- Supported distance education learning for UF Masters and Doctorate degree programs.
- Met with students on-line in small group setting as well as large discussion groups.
- Led chat sessions, communicate via email.
- Graded assignments, tests and presentations.

Consulting/Dispensing Pharmacist PRN
United Healthcare, Lexington, SC
August 2010 - August 2012

- Performed patient medical chart reviews, clinical monitoring, and managed appropriate drug therapy in accordance with federal and state regulations.
- Evaluated physician medication orders regarding dosage, appropriateness of drug, potential interactions, stability and route of administration.
- Analyzed, retrospectively and prospectively, drug utilization for the institutional drug formulary maintenance.
- Reviewed and checked technician prepared orders for delivery and dispensing.
- Consulted with advanced practitioners, healthcare professionals and managers of pharmaceutical services to develop and implement best working practices.

Hospital Pharmacy Student Intern
Lexington Medical Center, West Columbia, SC
June 2008 - May 2010

- Prepared IV compounded medications, interpreted and prepared orders per medications orders in CPOE.
- Ensured proper control and dispensing of narcotics.
- Interacted with clinical pharmacists, physicians, and nurses regarding drug therapy.
- Compounded a wide variety of specialty preparations including chemotherapy and TPN.

Retail Pharmacy Student Intern
Rite Aid Pharmacy, Columbia, SC
September 2006 – May 2010

- Accurately interpreted, processed, and filled prescriptions.
- Effectively communicated with physicians' offices and insurance companies regarding patients' pharmacy needs.
- Counseled and answered patients' questions concerning their prescriptions, OTC medications, nutritional supplements, and herbal products.
- Assisted with appropriate recordkeeping to assure compliance with federal and state laws.
- Maintained pharmacy inventory and supplies.
- Provided excellent customer support and follow up.

Senior Pharmaceutical Formulation Scientist
Pfizer Inc., December 2004 – August 2006

- Worked with formulation team in determining of yields (actual and theoretical), performed batch production record verification, ingredient review, and conditional quality releases, all per company's SOPs (standard operating procedures) and following guidance of cGMPs.
- Performed OOS (Out-Of-Specifications) investigations and reported process deviations on products not meeting all quality criteria set by QC department (for example, content uniformity, particle size and other quality issues.)
- Collaborated with drug formulation research team in development of new products and their test methods, with focus on natural products, supplements, and vitamins.
- Assisted with development of new medication delivery system of liquid drug products (Licaps), assisting with taking the products through ANDA process.

- Developed and validated methods for analytical testing of raw materials and finished products for QC department to test for identity, purity and strength to meet quality standards set by FDA and USP.
- Assisted with improvements in stability studies, including utilizing USP 71 guidance in new products.
- Supported all activities involving new product transfers, compliance, testing and various manufacturing process validations.
- Authored, updated and edited SOPs for training of new employees, changes in process control as well as laboratory manuals, then trained personnel to assure proper understanding of the methodology and troubleshooting.
- Comfortable with regulatory environment as set by cGMPs per 21CFR 210 and 211, USP, BP, EP, ISO, ICH and FDA regulations.
- Assisted with management of five laboratory technician team.
- Certified emergency responder.

OTHER PROFESSIONAL ACTIVITIES

Sterile Compounding Committee Volunteer Expert
SC Board of Pharmacy, Columbia SC
August 2019-present

- Provide expertise on sterile compounding practices to the Board of Pharmacy members to help with updating of the assessment forms for inspections of pharmacy facilities.
- Consult members of state legislature on options in regulatory areas of pharmacy practice, specifically in the area of compounding.

Expert Witness

- Area of expertise includes sterile compounding, compounding, pharmacy, pharmacokinetics, USP 797, drug preparation.
- Provide medicolegal consulting for state and federal court cases.
- Analyze evidence provided and consult the legal team with options for further actions.
- Prepare testimony statements, depositions, testify in court.

Lexington School District 1 Health Sciences Advisory Committee Member

- Provide guidance and recommendations on development of health and science related courses in the district's curriculum for high school students.

Lexington School District 2 Health Sciences Advisory Committee Member

- Provide guidance and recommendations on how to initiate and develop health and science related courses in the district's curriculum for high school students.

Member of South Carolina Pharmacy Practice Act (SC PPA) Revision taskforce

- Chair of the committee on compounding section revision: lead a group of professionals to update SC PPA section of steile and non-sterile compounding
- Memmber of the group aligning the SC PPA with NABP's Model pharmacy act
- Member of the taskforce working on pharmacy practice expansion

FACULTY APPOINTMENTS AND TEACHING EXPERIENCE

DIDACTIC TEACHING EXPERIENCE

Clinical Assistant Professor in Department of Clinical Pharmacy and Outcomes Sciences, University of South Carolina, Columbia SC
August 2013 to present

- PHMY 885: Pharmacy Law and Ethics (3 credit hours, course coordinator)
- PHMY 790: Pharmacy Skills Laboratory III: Introduction to Health-Systems Pharmacy I (1 credit laboratory course, course coordinator)
- PHMY 791: Pharmacy Skills Laboratory IV: Advanced Health System Pharmacy Practice (1 credit laboratory course, course coordinator)
- PHAR 401: Introduction to Pharmacy as a Profession
- PHMY 710: Biopharmaceutics, Pharmaceutics and Pharmacokinetics (3 credit hours)
- PHMY 999: Clinical Seminar
- PHMY 757: Independent Study

KPIC Master instructor, University of South Carolina, Columbia SC
August 2014 to March 2015

- Basic Aseptic Technique course, 23.5 hours of CE, Master instructor
- Advanced Aseptic Technique course 16 live hours of CE, Master instructor

Assistant Professor of Pharmacy
South University School of Pharmacy, Columbia SC,
May 2010 to August 2013

- PHA 4367 Integrated Sequence IV Autonomic Nervous System (Pharmacology and Pharmacotherapy lectures), 8 credit hours
- PHA 3159 Introduction to Integrated Sequence: Basic Pharmacology Modules, Medicinal Chemistry, 6 credit hours
- PHA 3107 Pharmaceutical Calculations (use of pre-recorded lectures and in-class hands-on exercises), 3 credit hours (course coordinator)
- PHA 3113 Pathophysiology I (topics include geriatrics, inflammation, cancer, HIV, immune response), 4 credit hours (course coordinator)
- PHA 3114 Pathophysiology II (topics include autonomic nervous system, wound healing, gout, RA), 4 credit hours
- PHA 3109 Microbiology and Immunology (lectures in immunology, virology), 5 credit hours
- PHA 5335 Animal Venoms and Poisons (developed and implemented this elective), 3 credit hours (course coordinator)
- PHA 5332 Applied Pharmaceutical Care II (topics including, OA, RA, BPH, ED), 4 credit hours
- PHA 4265 Integrated Sequence III Inflammation (Pharmacology and Pharmacotherapy of osteoarthritis, rheumatoid arthritis, gout, would healing, lupus), 6 credit hours
- PHA 3162 Integrated Sequence I: Introductory Pharmacology and Medicinal Chemistry, 5 credit hours
- PHA 4212 Pharmacokinetics I (Implemented team-based learning), 4 credit hours

- PHA 4228 Pharmacokinetics II (Implemented team-based learning), 4 credit hours
- PHA 3135 Integrated Pharmacy Skills Lab I, 3 credit hours
- PHA 3136 Integrated Pharmacy Skills Lab II, 3 credit hours
- PHA 3137 Integrated Pharmacy Skills Lab III, 3 credit hours
- PHA 4238 Integrated Pharmacy Skills Lab IV, 3 credit hours
- Longitudinal Pharmacy Practice Experiences I – V: PHA 3135, 3163, 4266, 4369, 5330, 1 credit hour, course coordinator

Adjunct Faculty, UFL Graduate Distance Programs
University of Florida, School of Pharmacy, January 2012—April 2016
- Medicinal Chemistry I
- Fundamentals of Medicinal Chemistry, course coordinator
- Herbal and Dietary Supplements

EXPERIENTIALTEACHING EXPERIENCE
Advanced Pharmacy Practice Experience (APPE) Elective INDUSTRY—University of South Carolina College of Pharmacy, Preceptor for PharmD students**.**

Advanced Pharmacy Practice Experience (APPE) Academic Rotation—South Carolina College of Pharmacy, Preceptor for PharmD students.

Advanced Pharmacy Practice Experience (APPE) Academic Rotation—South University School of Pharmacy, Preceptor for PharmD students.

COLLEGE OF PHARMACY COMITTEES
- South University SOP Curriculum Committee, member, chair 2013
- South University SOP Curriculum Subcommittee for Pharmaceutical Calculations course advisory member, 2010-2012
- South University SOP Committee for Professional Outreach, member 2011-2013
- South University SOP Technology Committee, member 2010-2013
- South University SOP ACPE Self-Study and Assessment Committee, member 2012-2013
- South University SOP Admissions Committee, member 2012-2013
- University of South Carolina COP Continuing Education Committee, member 2013-2016
- University of South Carolina COP Search Committee for Lab assistant, chair, 2014-2016
- University of South Carolina COP Curriculum Committee, member 2017-2019
- University of South Carolina COP Admissions Committee, member 2019-present

AWARDS
2018: SC College of Pharmacy CPOS Department Service Award
2020: SC College of Pharmacy CPOS Department Service Award
2022: University of South Carolina Clinical Teaching Award

INVITED LECTURES AND PRESENTATIONS

Almgren M. Mitigation Strategies of COVID-19 in the Workplace. Palmetto Business Forum. Presented Webinar September 13, 2021.

Almgren M. CDB: Exploring Regulations, Trends and a Potential role in Opioid Epidemic. Annual Continuing Education Conference. Presented live April 21st, 2021.

Emelia Beam PharmD, Michaela Almgren, PharmD, MS. Update on COVID19 Vaccines. Nephron Pharmaceuticals, May 3, 2021.

Almgren, M., COVID-19 Prevention Myth vs. Fact: Assessment of Complementary Therapies as Preventative Measures for Safety and Efficacy. SCSHP Fall 2020 Meeting, Columbia, SC, October 2020.

2020 Immunization Update. 1.0 ACPE accredited CE presentation at Nephron Pharmaceuticals, October 2020.

COVID 19 Prevention: Myth versus Fact. 1.0 credit hour ACPE accredited presentation at Nephron Pharmaceuticals Inc., West Columbia, SC June 8th, 2020.

Update on COVID19 Vaccines. 1.0 credit hour ACPE accredited presentation at Nephron Pharmaceuticals Inc., West Columbia SC, May 3rd, 2021.

M. Almgren. My Path to Pharmacy. CAPPS USC student chapter speaker, February 4th, 2021.

USP Updates in Sterile Compounding. 1.0 credit hour ACPE accredited presentation at Nephron Pharmaceuticals Inc., West Columbia, SC, April 13th and 15th, 2020.

Multimodal Analgesia Basics. 1.0 credit hour ACPE accredited presentation at Nephron Pharmaceuticals Inc., West Columbia SC, April 1st and April 3rd, 2020.

COVID19—Separating Facts from Fiction. SC Palmetto Business Forum Quarterly Meeting in Columbia SC, March 9th, 2020.

New Approaches to Pain Management: Multimodal Opioid Free Analgesia. 1.0 credit hour ACPE accredited presentation at UofSC COP CE Conference, February 1st, 2020.

Medication Safety of Hazardous Drugs: Can We All Be Safe? 1.0 credit hour ACPE accredited CE presentation at SCSHP Fall Meeting in Columbia SC, October 17th 2018.

Review of Sterile Compounding per USP 797. 1.0 credit hour ACPE accredited CE presentation at SCSHP Fall Meeting in Columbia SC, October 17th 2018.

M. Almgren. Current Status and Future Trends in Sterile Compounding as Defined by USP Chapters 797 and 800. 1.0 ACPE Live CE accreditation awarded. SCSHP Annual Meeting March 11-13, 2018, Hilton Head Island, SC.

M. Almgren. Who wants to be a pharmacist? CAPPS USC student chapter speaker, April 11th, 2018.

M. Almgren. Importance of unification of performance protocols for CSTD testing per NIOSH. November 7, 2016, Cincinnati, OH. NIOSH Public Comment meeting, invited speaker.

M. Almgren. Important role of CSTD utilization in compounding of hazardous materials to enhance protection of the compounder. 2016 ASHP Midyear, Las Vegas. Hazardous Drug Task Force speaker for USP 800 implementation.

M. Almgren. Sterile Compounding and Implementation of USP Chapter 797: Where we came from, where we are and where we might be headed. 1.0 ACPE Live CE accreditation awarded. SCSHP Annual Meeting, March 2015, Hilton Head Island, SC.

M. Almgren. Pharmacy school pathways. CAPPS USC student chapter speaker, April 2015.

PEER-REVIEWED PUBLICATIONS

Almgren M., Cooper C., Maxwell W., Baker J. Instruction on compounded sterile preparations at U.S. schools of pharmacy—a ten year follow up study. American Journal of Health-System Pharmacy, Volume 75, Issue 12, 15 June 2018 Pages 845-847, https://doi.org/10.2146/ajhp170641

Textbook chapter: Khazan M., Phillips C., **Almgren M**. "Pharmaceutical Calculations" In: Sutton S. Scott. McGraw Hill's NAPLEX Review Guide. 3rd Edition, McGraw Hill 2018

Textbook chapter: **Almgren M**. "Sterile Compounding Regulations" In: Sutton S. Scott. *McGraw Hill's NAPLEX Review Guide*. 3rd Edition.

Karyn I. Cotta, Samit Shah, PhD, RPh, MBA, **Michaela M. Almgren**, PharmD, MS, Lilia Z. Macías-Moriarity, PhD, MPH, Vicky Mody. Effectiveness of flipped classroom instructional model in teaching pharmaceutical calculations. *Currents in Pharmacy Teaching and Learning*. 2016. Volume 8, Issue 5, Pages 646–653. https://doi.org/10.1016/j.cptl.2016.06.011

Braga S, **Almgren M**. Complementary Therapies in Cystic Fibrosis: nutritional supplements and herbal products. *Journal of Pharmacy Practice*. 2013 Feb;26(1):14-7.

Wynn W, **Almgren M**, Stroman R, Clark K. Pharmacist's Toolbox for Smoking Cessation. *Journal of Pharmacy Practice.* 2012 Dec;25(6):591-9.

POSTERS WITH ABSTRACTS

Rachel Lehn, BS, PharmD Candidate; Kayla Hutto, BS, PharmD Candidate; Nikki Chen, PharmD Candidate; Lauren Caines, PharmD Candidate; **Michaela Almgren, PharmD, MS**. Comparison of Impact of Facial Coverings Mandate as Mitigation Strategy on Positivity Rates of COVID-19 in a Workplace versus Community Rates Prior to Vaccine Availability. December 2021 ASHP Midyear Virtual Clinical Meeting.

Kara Taylor, PharmD Candidate; Lauren Caines, PharmD Candidate; Cole Colemander, PharmD Candidate; Zach Altenberg, PharmD Candidate; **Michela Almgren, PharmD, MS**.

Safety Evaluation of a New Container Closure System Design of a Blow Fill Seal Type of IV Bottles. December 2021 ASHP Midyear Virtual Clinical Meeting.

Lauren Caines, PharmD Candidate; Kara Taylor, PharmD Candidate; **Michaela Almgren, PharmD, MS**. Impact of Implementation of Mandatory Facial Coverings as Mitigation Strategy on Rates of Positive Cases of COVID19 in a Workplace Prior to Vaccine Availability. December 2021 ASHP Midyear Virtual Clinical Meeting.

Petscavage Katie, PharmD Candidate; **Almgren Michaela, PharmD, MS**. Assessment of complementary therapies as preventive measures for COVID-19 for safety and efficacy. December 2020 ASHP Midyear Virtual Clinical Meeting. Poster #SP-243.

Aya Ahmed PharmD Candidate; **Michaela Almgren PharmD, MS**; Ryan McCormick PharmD Candidate; Carolyn McNamara PharmD Candidate; Robert Singleton PhD. Establishing a Coronavirus (COVID-19) Testing Lab in 40 Days. December 2020 ASHP Midyear Virtual Clinical Meeting.

Ryan McCormick PharmD Candidate; **Michaela Almgren, PharmD, MS**; Sarah Arnold PharmD Candidate, Madeline Dean PharmD Candidate, Marianna Vinson, PharmD Candidate. Process improvements and validation of a syringe-filling robot though collaboration between pharmacy and engineering student teams. December 2020 ASHP Midyear Virtual Clinical Meeting.

Alexis Caronis, PharmD Candidate 2021; **Michaela Almgren, PharmD, MS**; Samantha Lindeman, PharmD Candidate 2021; Kristen Kilby, PharmD Candidate 2021. Evaluation of medication safety effectiveness training in a workplace environment. 2020 APHA Annual Meeting, Baltimore MD, March 2020.

Caroline Hansen PharmD Candidate; **Michaela Almgren PharmD, MS**; Kristen Kilby PharmD Candidate; Alexis Caronis PharmD Candidate; Ryan McCormick PharmD Candidate; Benjamin Tabor PharmD Candidate. College of Pharmacy and School of Engineering Student Teams' collaboration to design pharmacy compounding system using robotic arm to perform aseptic syringe filling. 2020 SCSHP Annual Meeting, Charleston SC, March 2020.

Alexis Caronis, PharmD Candidate 2021; **Michaela Almgren, PharmD, MS**; Kristen Kilby, PharmD Candidate 2021; Caroline Hansen, PharmD Candidate 2021; Benjamin Tabor, PharmD Candidate 2021; Ryan McCormick, PharmD Candidate 2022. Development of the Masterflex L/S peristaltic pump process validation in a 503B outsourcing pharmacy. 2019 ASHP Midyear Clinical Meeting, Las Vegas, December 2019. Poster #3-445.

Ashton Holley, PharmD Candidate**; Michaela Almgren, PharmD, M.S**.; Normando Sandoval, PharmD Candidate; Priya Patel, PharmD Candidate; Xiaoxia Wang, PharmD Candidate; Lauren Moran, PharmD Candidate. Evaluation of cleaning effectiveness of 7.8% ionized hydrogen peroxide mist versus 7.8% hydrogen peroxide mist in a cleanroom environment. 2019 ASHP Midyear Clinical Meeting, Las Vegas, December 2019. Poster #3-449.

Caroline Hansen PharmD Candidate; **Michaela Almgren PharmD, MS**; Kristen Kilby PharmD Candidate; Alexis Caronis PharmD Candidate; Ryan McCormick PharmD Candidate; Benjamin Tabor PharmD Candidate. College of Pharmacy and School of Engineering Student Teams' collaboration to design pharmacy compounding system using robotic arm to perform aseptic

syringe filling. 2019 ASHP Midyear Clinical Meeting, Las Vegas, December 2019. Poster #3-432.

Kristen Kilby PharmD Candidate**; Michaela Almgren PharmD, MS**; Alexis Caronis PharmD Candidate; Caroline Hansen PharmD Candidate; Ryan McCormick PharmD Candidate, Benjamin Tabor PharmD Candidate, Noah Smith MBA, PharmD Candidate**.** Performance comparison of the Baxter repeater pump and the Masterflex peristaltic pump using high flow tubing set L/S 24. 2019 ASHP Midyear Clinical Meeting, Las Vegas, December 2019. Poster #3-446.

Samantha Lindeman, PharmD Candidate 2021; **Michaela Almgren, PharmD, MS**; Alexis Caronis, PharmD Candidate 2021; Kristen Kilby, PharmD Candidate 2021; Noah Smith, Pharm D Candidate 2020; Caroline Hansen, PharmD Candidate 2021; Ashton Holley, PharmD Candidate 2021; Priya Patel, PharmD Candidate 2021. Evaluation of naloxone safety effectiveness training in a workplace environment. 2019 ASHP Midyear Clinical Meeting, Las Vegas, December 2019. Poster #3-440.

Tristan Gore, PharmD Candidate 2022. Noah Smith, PharmD Candidate 2020. Dana Nelson, PharmD Candidate 2020. **Michaela Almgren, PharmD, MS**. Incidence and clinical impact of particulate matter in injectable drug products. 2019 ASHP Midyear Clinical Meeting, Las Vegas, December 2019. Poster #3-422.

Almgren M, Maxwell W, Grant A, Hembree H, Shah A. Disability and Accommodations in Pharmacy Practice and Education. 2019 AACP Annual Meeting, Chicago 2019. Abstract #53.

Cooper C., **Almgren M.**, Maxwell W., Baker J. Instruction on compounded sterile preparations at US pharmacy schools. 2018 SCSHP Annual Meeting poster session, Hilton Head Island, SC.

Cooper C., **Almgren M**. Maxwell W., Baker J. Instruction on compounded sterile preparations at US pharmacy schools. Poster presentation at 2017 ASHP Midyear in Orlando, FL, poster # 368.

Parth Parikh, PharmD. Candidate; Paul Philavong, PharmD Candidate, Sam McCallum, PharmD Candidate, Nhung Nguyen, PharmD Candidate; **Michaela Almgren, PharmD, MS**. Assessing Microbial Growth Rates of Sterile Versus Non-Sterile Gloves Used During Sterile Compounding. 2017 SCSHP Annual Meeting Hilton Head, SC, poster session.

Cotta K**, Almgren M**. "Effectiveness of Blended Teaching Method for Pharmaceutical Calculations." Poster presentation at 2012 AACP Annual meeting in Kissimmee FL.

Almgren M., Clark K. "Laboratory Exercise to Enhance Integration and Application of Basic Sciences to Pharmacy Practice in Students." Poster presentation at 2012 AACP Annual meeting in Kissimmee FL**.**

Peer Review/Editorial Boards/Editorships for Journals

Reviewer for AJPE
Reviewed: Prerequisite Courses: Barriers to Pharmacy Admission or the Keys to Student Success?

Reviewer for Currents in Pharmacy Teaching and Learning.

Reviewed: Book review of the Handbook on Injectable Drugs

Reviewer for AJHP
Reviewed: Commentary: Impact of revised USP 797 guidance and how we might mitigate risk: A real-world example

Reviewer for AJHP
Reviewed: Third Consensus Development Conference on the Safety of Intravenous Drug Delivery Systems – 2018

Peer Reviewer for The Joint Commission Journal on Quality and Patient Safety
Reviewer and member of editorial board of Alternative Medicine Studies Journal
Reviewer for Journal of Dietary Supplements
Reviewer for Natural Standard Research Collaboration
Reviewer for Currents in Pharmacy Teaching and Learning
Reviewer for AACP Annual Meeting Research/Education Abstracts for Poster Session

PROFESSIONAL AFFILIATIONS

American Pharmacist Association (APhA), 2006-2018

American Society of Consultant Pharmacists (ASCP), 2008-2013

American Society of Health-System Pharmacists (ASHP), 2008-present
- Pain management SIG 2011-2013

SC Pharmacist Association (SCPhA), member 2006-2018
- Professional Affairs committee 2010-2011, 2017-2018
- Legislative Affairs Committee 2011-2012

SC Society of Health Systems Pharmacists member (SCSHP) 2008-present
- Education Committee 2014-2016
- Professional Affairs Committee 2015-2016
- Legislative Committee 2017-2018

American Association of College of Pharmacy (AACP), member 2010-present
- AACP Pharmacy Practice Strategic Plan, Bylaws, and Resolutions Committee member 2018-2020
- Member of the Scholarship Committee of the Curriculum SIG for AACP 2018-2020
- AACP Audit Committee member 2018-present
- House of Delegates representative for USC College of Pharmacy 2017-2018
- AACP Pharmacy Practice Strategic Plan, Bylaws, and Resolutions Committee member 2018-2019
- Lyman Award Committee Member 2012-2013

Parenteral Drug Association Member (PDA) 2019-2022

ADDENDUM TO THE EXPERT REPORT OF DR. MICHAELA ALMGREN

1. The attorneys who represent death-sentenced prisoner Brent Brewer asked me to submit an expert medical and scientific opinion in this case. I offered an initial expert report on December 12th, 2022. I am now further supplementing the opinions that I offered in that initial report based on my review of additional pharmacy related documents—September 14, 2023 Huntsville Fire Department report and analytical testing report received October 5, 2023.

2. My experience, qualifications, testimony in prior cases, and fee schedule for this case are set forth in my initial report.

3. More documents, studies, and other pertinent information may become available to me at a later date, and I reserve the right to take such materials into account and to modify or supplement my opinions accordingly. I may also be present at hearings or at trial and may consider any testimony or other evidence related to my opinions and modify or supplement my opinions accordingly.

I. The area where lethal injection chemicals are stored in the Huntsville facility was exposed to fire leading to major concerns with environmental control of drug storage conditions.

4. According to the report from Huntsville Fire department the Walls Unit building experienced major fire on August 25, 2023. The pharmacy is located on third floor which was completely overtaken by the fire and where some of the heaviest damage had occurred. The report from the fire department states that there was an attempt made to check on the status of pharmacy but due to heavy fire it was unsafe to enter that area. Large quantity of water (1,500 gallons of water per minute over 4 to 5 hours) had to be used to eventually extinguish the fire in the building, which included the pharmacy. It appears that the third-floor area suffered severe damage. The medications stored in this area had to be exposed to uncontrolled temperatures and moisture.

II. Medications exposed to extreme temperatures will undergo degradation and loss of effectiveness. USP Guidelines do not allow for medications to be used if exposed to extreme environmental conditions.

5. All medications have specific storage conditions identified by their manufacturer under which they are assessed, and their effectiveness can only be guaranteed if they are stored according to those requirements. USP Chapter 659[1] titled Packaging and Storage Requirements further defines specific storage conditions for medications, including temperature, humidity, and light exposure. These conditions are critical to maintaining the stability and effectiveness of medications. While USP Chapter 659 provides guidance on how medications can be stored briefly outside of those conditions without compromising their quality and effectiveness, it limits transient excursions in room temperature to not more than 40 degrees C (104 degrees F). The temperatures during the fire without any doubt exceeded this limit.

6. Compounded medications must be stored according to USP Chapter 797 within a specific temperature range to maintain their effectiveness and stability. Vials containing compounded pentobarbital could be stored either in controlled room temperature at 20-25 degrees C, refrigerator at 2-8 degrees C, or freezer at -25 to -10 degrees C (temperature limits defined by USP Chapter 659). When exposed to uncontrolled temperatures, such as during a fire, the integrity of these medications will be compromised and the medications should be discarded. Extreme heat will lead to chemical changes, degradation of active ingredients, and alterations in the medication's composition.

[1] USP Chapter 659 from USP-NF 2023 issue 1.

7. Furthermore, in the study performed by Ajemni et al[2] degradation of liquid pentobarbital was studied under various stress conditions. The study demonstrated that when pentobarbital is exposed to high temperature, it has a tendency to degrade. Considering the narrative from the fire department's report describing the efforts to put the fire out, it is very apparent that the temperatures in the heavily damaged third floor areas likely exceeded 105 degrees C for four to five hours. This would lead to drug deterioration rendering the medication less effective.

III. Humidity and light are also shown to have impact on compounded drug quality.

8. The study by Ajemni et al mentioned previously also examined the effects of light and moisture exposure on liquid pentobarbital. Both factors also cause the medication to change its chemical composition resulting in the reduction of drug's potency. The drug vials stored in the facility were likely exposed to excessive moisture and humidity, as there is possibility that due to high amounts of water in the storage area the vials ended up getting wet. High temperatures caused by the fire likely resulted in the loss of vial cap seal compromising the integrity of the closures and allowing the water to infiltrate the vials. When water enters medication vials, it can initiate chemical reactions with the active ingredients. These reactions can alter the composition of the medication, rendering it less effective. The study by Ajemni also documents pentobarbital's loss of potency due to water and light exposure.

IV. Testing a few vials to confirm potency of all vials involved in the fire does not guarantee that the rest of the drug vials are unaffected.

[2] Ajemni M, Balde IB, Kabiche S, Carret S, Fontan JE, Cisternino S, Schlatter J. Stability-Indicating Assay for the Determination of Pentobarbital Sodium in Liquid Formulations. Int J Anal Chem. 2015;2015:697937. doi: 10.1155/2015/697937. Epub 2015 Oct 12. PMID: 26543481; PMCID: PMC4620273.

9. In a fire, the exposure to heat, water and smoke is often not uniform across all vials or batches of medications stored in the same area. Some vials may be closer to the source of heat, water or smoke than others, resulting in varying levels of exposure. This heterogeneous exposure will result in varying levels of damages to vials stored in the affected area with unpredictable outcomes. Thus it cannot be assumed that passing results for potency of some of the drug vials means that all vials are unaffected. Testing one vial may provide some information about that specific vial's condition, but it cannot guarantee the safety or effectiveness of the entire batch or other vials that were exposed to the fire.

10. Interestingly, the vials tested and submitted in the analytical repost show significant variability of results, ranging from 94.2% to 100% potency. This further supports the above concern that inconsistent exposure to heat during a fire leads to different levels of breakdown in the samples. This variability can be attributed to several factors related to the fire and the conditions experienced by the samples during the fire such as temperature gradients. Fires can have varying temperature gradients, with different parts of a structure or materials experiencing different levels of heat exposure. This can result in some samples being subjected to higher temperatures for longer durations while others experience milder conditions. Also heat distribution within a fire can be uneven. Certain areas may be exposed to direct flames and intense heat, while others may experience indirect or less intense heat. This can lead to differences in the breakdown of materials. Another concern is fire dynamics, as fire behaviour including factors like ventilation, fuel load, and fire growth, can influence the overall heat distribution within a structure and, consequently, the breakdown of materials. All of these considerations lead to conclusion that the sample potency may vary greatly due all of the above mentioned factors.

V. When drugs are exposed to a fire, they are likely to be compromised and should be discarded.

11. Sometimes the damage caused by fire may not be immediately visible. However, these hidden changes will affect the potency and safety of the medications. In such situations, it is essential to exercise extreme caution and discard all medication.

VI. Analytical testing performed on medication samples is inadequate.

12. According to the monograph for pentobarbital injection listed in the current USP Compendium which provides standards of testing and quality control for all medications, the following additional parameters must be tested: pH and visual inspection. The acceptable result for pH is between 9.0 and 10.5. If pH is found to be outside of the specified range the medication must not be used, as it is unsafe causing unpredictable effects, and not meeting USP quality requirements. All vials also should undergo visual inspection making sure that no change of color is noted and there is no precipitant present, as those are the most common signs of drug degradation. Injectable drugs should not contain precipitates because precipitates can pose serious risks to patient safety. Precipitates are solid particles that can cause occlusion of blood vessels, embolism and reduced drug efficacy, as the precipitates will not dissolve properly in the bloodstream leading to suboptimal effect of the drug. The report submitted only shows testing for potency (only via HPLC assay), sterility (using ScanRDI) and bacterial endotoxin. However, the missing tests may provide more insight into the status of the compounded medication.

13. From the analytical report it appears that the sterility test was not performed according to the USP Chapter 71 as required in the USP Monograph, rather using Scan RDI. As stated previously Rapid Sterility test methods, such as ScanRDI, may not detect all microorganisms that a traditional USP Chapter 71 sterility test method would detect. This methodology is deemed

inappropriate and inadequate by FDA unless the lab performing the testing has performed proper validation and demonstrated the methodology to be equal or better that the compendial method USP 71.

VII. The incorrect analytical method is used for testing of potency.

14. As I previously explained in my expert statement from 12-12-2022, a stability-indicating assay should be used to test the potency of the drug exposed to extreme conditions, such as high temperatures and humidity. This method is necessary to determine the extent of degradation and will show the true potency of the drug ensuring that degradation products are detected and quantified. The HPLC assay method with lower sensitivity which was used to test the two medication vials most likely overstates the amount of API present. When there is a chance that the sample has degraded, a stability-indicating method is crucial for accurately assessing the stability and potency of a drug product by detecting and quantifying degradation products. Regular assays with lower sensitivity alone are not suitable for this purpose and may lead to an overestimation of drug potency.

Executed on this 10th day of October 2023.

Michaela M. Almgren

Michaela M. Almgren, PharmD, MS