CASE STUDY

Environmental Monitoring Matters: Going Beyond the USP <797> Standard

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Erin Patton
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Erin received her Bachelor of Science degree in biology from Xavier University and her Master of Science degree in cell and molecular biology from the University of Illinois, Urbana-Champaign. Erin has over 15 years' experience in molecular biology research, microbiology QC, and regulatory compliance. As a Senior Product Specialist for Charles River's Microbial Solutions division, Erin provides innovative rapid micro solutions for endotoxin testing, microbial identification, and microbial detection (Celsis® rapid bioburden and sterility testing).

PRIMARY INTENDED OUTCOME

Compounded sterile products (CSPs) are individually made medications that are administered via injection, and include vaccines and epidural anesthesia. Chapter <797> of the United States Pharmacopeia (USP) outlines the facility and operational requirements for compounding sterile drugs and specifically calls for the collection and monitoring of environmental data through air and surface sampling. These standards aim to ensure patient safety and reduce the real risks of contamination, infection, or incorrect dosing.

Charles River provides a range of environmental and product sterility testing that meets and exceeds compliance with USP regulations. Their laboratory services support drug manufacturing, monitoring, and testing, and can be tailored to a facility's specific needs to ensure patient safety.

THE CHALLENGE

Drug compounding creates relatively small batches of medications that are tailored to the needs of special populations, including patients with allergies or those who require nonstandard doses, such as children or the elderly. The compounding process is carried out under the oversight of state pharmacy boards, and enforcement of standards differs from state to state. Importantly, some compounded drugs are not regulated by the United States Food and Drug Administration for safety, effectiveness, or manufacturing quality. Serious adverse events have occurred, including a fungal meningitis outbreak in 2012, which was caused by a contaminated injectable drug. The facility that manufactured the drug was not in compliance with USP guidelines.

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"Sterility testing of finished drug products is important but is not sufficient to completely ensure patient safety", says Erin Patton, Senior Product Specialist at Charles River. "Final product sterility testing uses such a small sample that, statistically, the product would have to be grossly contaminated to fail. Our model is process testing, which includes the facility, the ingredients, and the operators, even in products that pass sterility testing. This is a better way to ensure quality and safety of compounded drugs."

USP <797> is currently in an extended revision process. The updated standard is expected to be published on June 1, 2019 and will become official on December 1, 2019.

THE DECISION

Environmental monitoring involves collection of numerous facility surface and air samples and analysis of resulting sample data relating to enumeration and identification of flora captured during sampling. It measures the microbiological cleanliness of a drug-production process, documents the state of control of the facility, and, ideally, exposes any trends in loss of control that could lead to contamination. This level of data collection is a powerful tool that can provide early warning of serious issues, but only if used optimally. One of Patton's concerns is the currently required frequency of monitoring.

"Right now, for surface sampling in hoods or compounding areas, the proposed USP <797> draft requirement is only one time per month," Patton said. "This is just not enough. The key to sampling and identification is to look at the data to understand the story they tell. Monitoring once a month only provides a snapshot."

Similarly, Patton believes the required level of microbial identification called for by the existing draft standard needs to be more specific. "If an investigation is required, the guidelines currently say you must identify the microbe to the genus level," Patton said. "This is not good enough. We test to the species level. You can know the general group of bugs, but sometimes you find a genus that contains both routine microbes and problematic ones." Without species-level testing, a facility may unnecessarily decide to destroy an entire lot of expensive drugs or – worse – take a risk with patient safety.

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ESTABLISH ALERT LIMITS

The existing version of USP <797> contains tables that provide what are called "action limits," specifying the number of colony-forming units (CFUs) that indicate the acceptable cleanliness of a space. If a sample is found to exceed those limits, a facility is required to conduct an investigation.

"You don't have to wait until things get to that level," Patton said. "You can take action sooner than that." Many companies set their own "alert limits" that fall below action limits. "Say an action limit is 10 CFUs," Patton said. "Many would establish an alert limit of 5 CFUs, which essentially gives the opportunity to catch a problem well before it starts."

THE RESULTS

Charles River offers a number of testing services that evaluate a facility's entire environmental picture. "We always promote that it is better to have data from multiple perspectives – the room, the ingredients, the operator," Patton said. "If you are not doing enough sampling, there is not enough granularity to tell the whole story of your facility."

The USP <797> requirements also apply to storage and testing of finished drug preparations. If a product fails a final sterility test, there is an obligation to test further and identify the contaminating organism. Additional testing can be time-consuming and may pose a financial burden for compounders.

Charles River's MALDI-TOF testing provides microbial identification results efficiently and affordably. "This is one of the biggest ways we support our customers," Patton said. "We make this new technology affordable and accessible to compounders so that they may do more critical environmental monitoring work while keeping within the same budget."

Rapid sterility testing is available through Charles River's Celsis® line, which delivers bioburden testing results in 18 to 24 hours and sterility testing results in four to six days. These shorter turnaround times are beneficial in final product testing, but are also an advantage in process testing. "It can be frustrating to take the time to test raw materials before you even start compounding," Patton said. "Our Celsis® instruments allow faster, confident testing along the way."

THE CONCLUSION

When environmental data are tracked and reviewed regularly, negative trends can be identified early and contamination can be caught and reversed before a problem occurs. Proposed revisions to the USP <797> standards place a greater emphasis on the requirement for conducting investigations and implementing corrective actions, but may still fall short of optimal procedures.

Going beyond minimum recommendations for in-process testing is the best way to protect patient safety from the start. "Compounders are so close to the patient. I feel very passionately about improved testing beyond the standard," Patton said. "I believe it will make a difference to patients and can help a compounding facility stand out from the competition."

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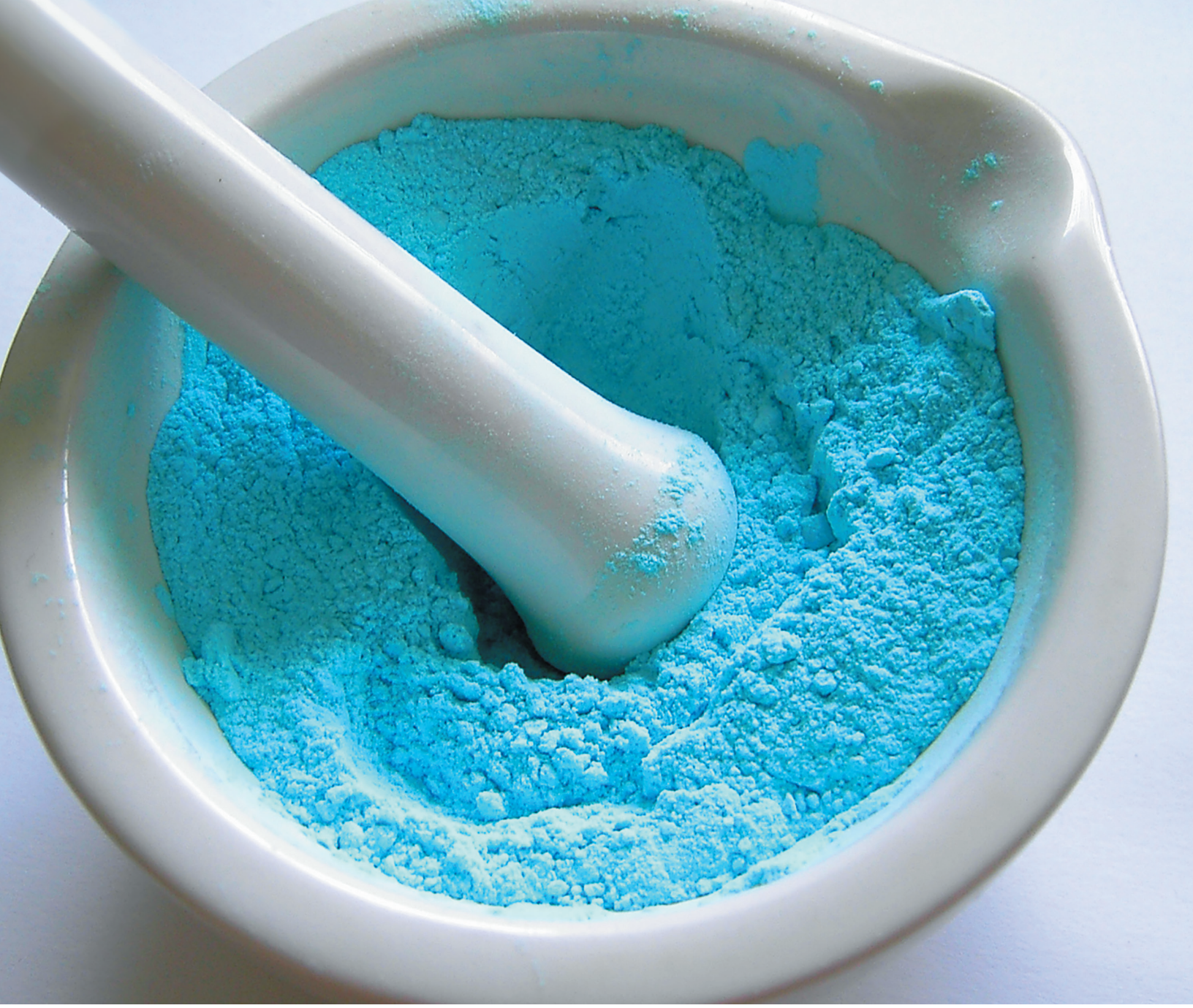

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