Environmental Monitoring for Nonsterile Manufacturing

Radha Tirumalai, *U.S. Pharmacopeial Convention*

As indicated in a recent article in the November-December 2009 issue of the PDA Letter, USP is in the process of developing a new General Information Chapter (numbered over 1000) proposal on "Control Programs for Nonsterile Product Manufacturing".

Microbiological monitoring and control programs for non-sterile drug products, unlike those for sterile drug products, are not well defined by either compendia or regulatory guidelines. This void, and requests from the industry, justifies the need for such a general information chapter in the USP-NF.

A major consideration during routine manufacturing is the exclusion of microorganisms from our drug substances, excipients, and drug products to prevent product degradation and improve patient safety. Non-sterile product manufacturing generally lacks the rigorous microbiological control elements of sterile product manufacturing. As a consequence there are more factors that can result in the introduction of microorganisms. Although the presence of intrinsic microbiological contaminants is permissible in non-sterile products, the numbers and types of microorganisms must be controlled. In order to control these microorganisms, an in-depth knowledge of the ingredients, products and manufacturing process is essential. This knowledge is developed through microbial risk assessment and microbiological monitoring.

The proposed chapter will enumerate the factors that influence contamination of nonsterile product manufacturing, including the facility, equipment, active pharmaceutical ingredients, excipients, water, and personnel, and discuss measures to minimize potential contamination

Environmental monitoring is typically used to demonstrate sustained process and environmental control, so instituting an environmental monitoring program may be beneficial. The sampling methods and practices utilized for aseptic facilities may be utilized; however the contamination rates for Control and Monitoring of Aseptic Processing Environments are excessively restrictive for nonsterile products. In selecting sites for monitoring, a risk-based approach may be used that more frequently selects sites close to those operations were the product would be exposed to the manufacturing environment and areas of high personnel activity. The frequency of periodic monitoring should reflect the potential risk of infection of the dosage form. For example, tablet manufacturing areas may be monitored infrequently, while, manufacturing areas for inhalant products may be monitored frequently. Isolates should be evaluated for their ability to grow in the product, overcome preservative systems, deteriorate the product, and potentially cause infection in the patient. Based on the identity and possible origin **of** the organisms, specific corrective actions may be developed.

The draft chapter is yet to be finalized and is being targeted for publication in the Pharmacopeial Forum in the summer of 2010. Based on the interest in response to the PDA letter article, USP will consider posting the approved draft proposal on the USP website for early access by interested parties.