Chapter 28

Environmental Quality and Control

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Introduction and Requirements

A high quality management program seeks to identify problems before they occur. Although there are several critical elements to consider when working in or managing a sterile compounding operation, historically environmental sampling has received minimal consideration in pharmacy practice. In other industries, great attention is placed on the influence and impact that the operating environment has on the quality of the product.[1] It is widely accepted in the pharmaceutical industry that production facility design, environment, and personnel have a direct effect on the sterility of aseptically prepared products.[2]

As such, it is essential to ensure that quality be built into compounded sterile preparations (CSPs) before they are distributed. This system is known as quality by design. The characteristics of a quality-by-design system include the following:

- The preparation is designed to meet patient requirements.
- The process is designed to consistently meet preparation critical quality attributes.
- The impact of formulation components and process parameters on preparation quality is understood.
- Critical sources of process variability are identified and controlled.

The process is continually monitored and updated to ensure consistent quality over time.[3] Proper sterile compounding requires "a strict design regime, not only on the process area, but on the interactions with surrounding areas and the movement of people, materials and equipment so as not to compromise the aseptic conditions."[4] Quality must be built into CSPs. The environment where sterile preparations are compounded must be suitable for its intended purposes.[5] One intended purpose of a properly designed, constructed, and operating compounding environment is to minimize the impact of human and process generated contamination that can affect sterility or stability. There are several intercon-

Note: The author acknowledges Eric S. Kastango who authored this chapter in the previous edition.

nected and dynamic variables that form the foundation of a solid environmental monitoring program (**Figure 28-1**). Failing to understand, maintain, and monitor the compounding environment and the personnel working in these areas has resulted in significant patient injury and death.[6-15] Primary and secondary engineering controls (PECs and SECs) are used to prevent, reduce, and control potential contaminants from being introduced into CSPs and to support environmental control programs (Chapters 9 and 25). They can, however, be thwarted by inappropriate personnel work practices.

An equally important area is the contribution and influence of the employee, hand hygiene and garbing practices on the sterility of CSPs. In 1982, a study was published that demonstrated that there is an excellent correlation between the bacterial contamination on hands and contaminated vials.[16] Several other studies have confirmed the significant contribution of employee technique and touch contamination to contaminated vials.[17-19]

USP Chapter <797> Pharmaceutical Compounding—Sterile Preparations requires each organization to have a written environmental quality and control plan. Common problem areas for compounding locations that received Food and Drug Administration (FDA) warnings for violating good practices include the following[20]:

- Lack of or not following policies and procedures
- Lack of environmental monitoring that is robust enough to detect trends
- Media fill testing not reflecting the most complex CSP mixed
- Insufficient cleaning
- Not reacting to sterility test results or not using the correct methods to justify extended beyond-use dates (BUDs)
- Poor technique

In recent years, most healthcare providers have been affected by drug shortages and discontinu-

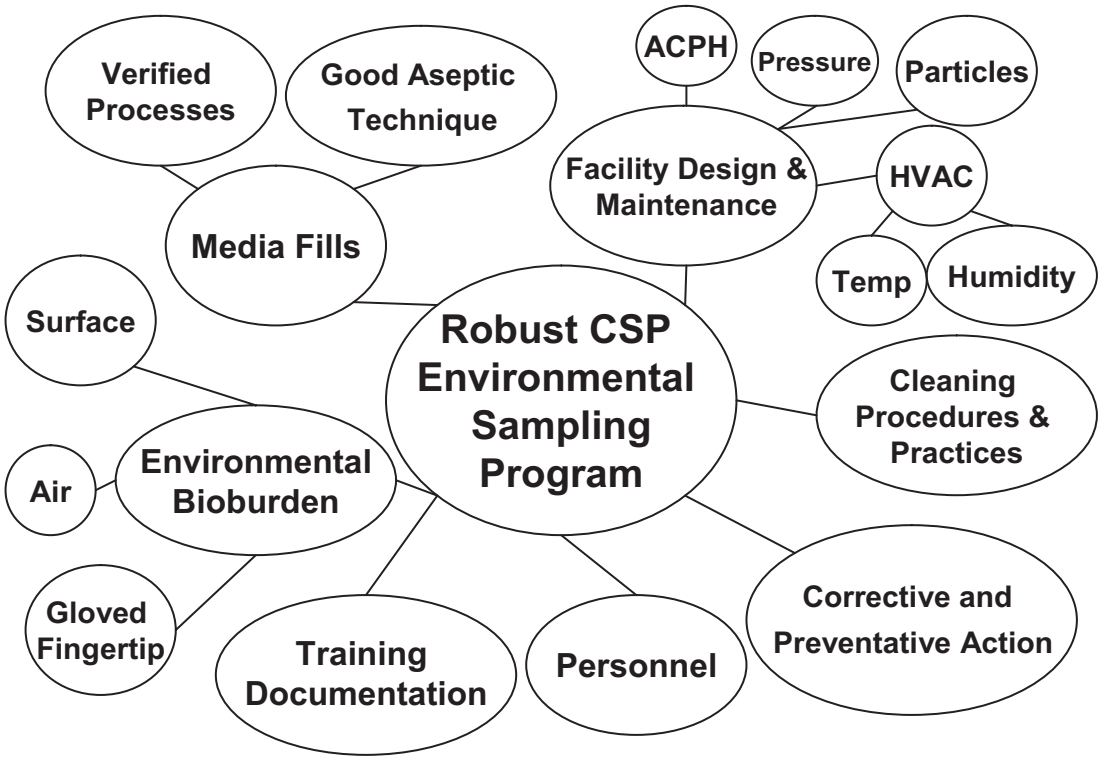

Figure 28-1. Elements of robust environmental monitoring quality program. *Source:* Used with permission from Clinical IQ, LLC, 2017.

ACPH = air changes per hour; CSP = compounded sterile preparation; HVAC = heating, venting, and air-conditioning.