



Pharmacy Compounding Urban Legends

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Abstract

This article reviews and clarifies a small sampling of the myths, or urban legends, about compounding. Included are comments on *United States Pharmacopeia (USP)* Chapter <797>, environmental issues related to sterile compounding, and suggested resources for clarification of some of these myths. This article recommends a knowledge-based partnership between compounding pharmacists and pharmaceutical manufacturers to improve compounding activities and quality assurance methods to ensure that compounded medications are safe.

Introduction

As pharmacists and technicians redouble and focus their effort and attention on the “science of compounding,” there are a number of myths—and corresponding truths—on this topic that need to be addressed. This article reviews many of the myths, or urban legends, about compounding that are widely believed and need to be clarified. An urban legend is a short tale that is told and retold as truth, although it usually has little or no basis in reality or science, and can’t be confirmed one way or another. Whether we know it or not, we’ve all heard them. Usually it is something “we have always done” or understand as an absolute truth because of the way we were trained. The problem comes when these urban legends are challenged through information found in some of the newer training programs, videos, CDs, and articles. This challenge can cause some employees to be very resistant to change because their “intellectual universe” and self-esteem come under attack and seemingly may collapse. There may be a realization that everything they have known to be true is not. Knowledge is power, but it is the intelligent use of knowledge, that is genius.

Compounding Myths

■ *USP Chapter <797> is not enforceable, nor is it law.* The practice of pharmacy draws its regulations from several sources. They include local, state, and federal requirements. *USP* Chapter <797> is drawn from the general test and assay chapters within the *United*

States Pharmacopeia (USP). The 1938 US Food, Drug, and Cosmetic Act (FFDCA) assigned the US Food and Drug Administration (FDA) legal authority to enforce standards in the *United States Pharmacopeia–National Formulary (USP–NF)*. The *USP* “General Notices and Requirements,” drug monographs or articles, and chapters numbered <1> to <999> contain FDA-enforceable standards, whereas chapters numbered <1000> and higher contain information considered interpretive.^{1,2} Most, if not all, of the pharmacy practice acts and regulations make reference to the FFDCA and admonish pharmacists to comply with all local, state, and federal laws. This makes *USP* Chapter <797> enforceable (and law) and, more importantly, the standard of practice for pharmacy compounding in the United States. *USP* standards have been successfully applied in lawsuits.

- *USP Chapter <797> is a static document and not subject to change.* This chapter and any chapter within the *USP–NF* is subject to constant review and change. Pharmacists and technicians must be vigilant about staying aware of changes in this chapter, other *USP* chapters, and all other laws or regulations that affect pharmacy practice. The United States Pharmacopeial Convention recently released the *USP Pharmacists’ Pharmacopeia*, specifically designed to provide pharmacists and technicians with the *USP* content that is specific to the practice of pharmacy.³ This reference book is significantly less expensive than the *USP–NF* and should be in every pharmacy library. Official *USP–NF* content in the *USP Pharmacists’ Pharmacopeia* includes the following:
 - More than 120 official compounding monographs
 - General chapters specific to compounding:
 - ◆ General Chapter <797> Pharmaceutical Compounding—Sterile Preparations
 - ◆ General Chapter <795> Pharmaceutical Compounding—Nonsterile Preparations
 - ◆ General Chapter <1075> Good Compounding Practices
 - ◆ General Chapter <1160> Pharmaceutical Calculations in Prescription Compounding
 - General chapters relating to weighing and measuring; containers, packaging, and storage; labeling; dosage forms; sterility and pyrogen testing; analytical tests and procedures; and other topics

- *USP Chapter <797> will be repealed and is not an issue worth considering.* It is important to understand that this chapter will not be going away, repealed, or “dumbed-down.” In fact, unless the profession of pharmacy gets serious about complying with this chapter and others, it is not outside of the realm of possibility that more onerous regulations will be promulgated regarding the professional activities of pharmacists and technicians, including requirements for board certification and/or specialized licensing or accreditation of “sterile compounding pharmacies.” The practice of pharmacy in some other countries in the world (England, Belgium, and Brazil) has standards that resemble FDA Good Manufacturing Practice standards and are being met.
- *Cleanrooms or International Organization for Standardization (ISO) Class 7 controlled environments are not required for pharmacies that prepare only low-risk level compounded sterile preparations (CSPs).* Despite what you may have heard, all CSPs, regardless of risk level, are required to be prepared within an ISO Class 5 environment (laminar airflow workstation [LAFW], biological safety cabinet [BSC], or barrier isolator), which is located in an ISO Class 8 buffer zone or cleanroom. The air cleanliness requirement for cleanrooms will be changing to ISO Class 7 in the next version of USP Chapter <797>.
- *High-efficiency particulate air (HEPA) filters prevent vapors and gases from escaping into the environment.* Prevention of vapor and gas escape is important, especially when working with hazardous drugs. In October 2004, the National Institute of Occupational Safety and Health (NIOSH) released *Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings*.⁴ This publication must be mastered by all employees (pharmacists, technicians and others) who handle, prepare, or administer hazardous drugs. A number of articles have shown the extent of hazardous drug contamination in areas outside of the pharmacy, identified vials of antineoplastics as a source, and demonstrated the possibility of volatilization of these drugs.⁵ Many older BSCs recirculate a percentage of HEPA-filtered air directly back into the cleanroom. It has been demonstrated that cyclophosphamide may evaporate and form a gas phase during normal handling, and thus is able to pass through a HEPA filter.⁶ The current NIOSH recommendations call for BSCs to be exhausted totally outside of the building whenever feasible.⁴
- *Cleanroom HEPA filters never need to be changed.* Remember that no HEPA filter is immortal. HEPA filters are made of boron silicate fibers and a binder. Sooner or later every HEPA filter needs to be replaced. The two factors that dictate the need to change a HEPA filter are (1) a decrease in the filter’s air volume/velocity capacity due to high pressure drops caused by dirt loading, or (2) deterioration of the HEPA filter because of age. The components of a HEPA filter are subject to mechanical and chemical attack over time. HEPA filters can last a very long time if protected by upstream prefilters. Most HEPA filters can have a normal service life of 8 to 10 years depending upon their application. It is prudent management to test HEPA filters for airflow capacity and leak tightness on a regular basis. By doing so, their service life can

be determined well before they fail, thereby preserving the integrity of your controlled environment (James T. Wagner, personal communication, May 2005).

- *The vial septum under the cap is sterile and does not have to be disinfected with 70% isopropyl alcohol prior to use.* The flip-off caps on vials are only dust protectors, and the vial septum cannot and should not be considered sterile. The manufacturers do not guarantee that the surfaces between the flip cap and rubber septum or stopper are sterile.⁷ During the manufacturing process, the capping of vials typically occurs outside an ISO Class 5 area and generally in an ISO Class 7 environment. If the vial septum is not sanitized, there is a risk that the contents of the vial could become contaminated. The vial septum should be disinfected by wiping a sterile 70% isopropyl alcohol prep across the top of the septum in a unidirectional sweeping motion at least three times. The residual alcohol should then be allowed to air dry. This procedure has two critical and separate functions: (1) the wiping action mechanically removes any contaminants, and (2) the drying alcohol disinfects the septum.
- *The protective grille in front of the HEPA filter cannot be cleaned.* As long as the filter is not sprayed or splashed with the cleaning

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agent, the HEPA filter grille can be cleaned. It is important to maintain the cleanliness of the grille, since it interacts directly with the filtered air coming off the HEPA filter face. A grille that has been splashed with dextrose or some other solution may become a nutrient source for microorganisms, especially if the primary engineering control (LAFW, BSC, or barrier isolator) is not left running continuously (James T. Wagner, personal communication, May 2005). Care should be exercised when cleaning the protective grille in front of the HEPA filter to avoid damaging the filter.

- *After donning sterile or nonsterile gloves, the gloves should be washed with soap and water prior to compounding.* Washing of gloves can cause micropunctures. Micropunctures can cause a condition known as “wicking,” which may allow liquids to penetrate through undetected holes in the gloves. For that reason, washing of gloves is not recommended. In addition to the risk of wicking, water is an excellent source of microbial contamination. There have been several reported cases of CSP contamination with *Pseudomonas aeruginosa* and with *Burkholderia (Pseudomonas) cepacia*, which is widely distributed in soil, water, sewage, and plants and is a common human intestinal bacterium. Upon donning gloves, the gloves should be sanitized with isopropyl alcohol and carefully inspected for holes or tears.⁸
- *The cleanroom meets ISO 7 requirements because the particle count is within the limits.* It is important to consider that a room cannot be considered a cleanroom just on a particle count alone. There are four other performance criteria that must be met relative to certification testing for a room to be classified as a cleanroom, as follows:
 - HEPA-filtered air: A cleanroom is a compounding environment that is supplied with HEPA or HEPA-filtered air that meets ISO Class 7.
 - Room air exchanges: At minimum, room air should be exchanged at least 50 times per hour (air changes per hour [ACPH]), but the cleanroom manufacturer should specify ACPH.
 - Room pressurization: A minimum positive pressure differential of 0.05 column inches of water shall be maintained from a classified noncontainment room to an unclassified space or a room of lesser classification.
 - Temperature and humidity: All rooms must maintain a temperature range of 66 to 72 degrees Fahrenheit and a relative humidity range of 35% to 60%.

Summary

This list of compounding legends is only a small sampling of the many bits of misinformation that circulate among pharmacy workers. It is time that pharmacists and technicians look to reputable, reliable, and verifiable resources such as the *International Journal of Pharmaceutical Compounding*, *American Society of Health-System Pharmacists*, and even the Parenteral Drug Association, a nonprofit international association of more than 10,500 scientists involved in the development, manufacture, quality control, and regulation of phar-

maceuticals, biopharmaceuticals, and related products. Many of the compounding activities and quality assurance methods that are needed to ensure that our compounded medications are safe can be learned from our colleagues in pharmaceutical manufacturing. Knowledge is power only if it is used intelligently.

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