

Kap 27.11 Positions-dokument CSP - USP 797

USP <797> Position Paper

Classification of Ambulatory Pain Pumps as Compounded Sterile Preparations

Some manufacturers of ambulatory pain pumps have recently taken the position that their products are not considered compounded sterile preparations as defined in USP 28/NF 23 <797> “Pharmaceutical Compounding—Sterile Preparations” when filled with drug products in accordance with a licensed practitioner’s prescription.

These manufacturers have attempted to use examples provided in USP 28 <1075> “Good Compounding Practices” to defend their position that these devices need not be handled in accordance with <797>. According to <1075>, four examples of compounding include: (1) pharmaceuticals that are prepared in anticipation of a prescription order, (2) prescription orders that require the reconstitution of two or more ingredients, (3) manipulated commercial products that may require the addition of one or more ingredients, and (4) drugs and devices prepared for the purposes of, or as an incident to, research, teaching, or chemical analysis. The manufacturers assert that if a device is not included on this list, then it is not compounded. This position is shortsighted and does not meet either the content of USP <1075> or the spirit.

The four examples of compounding listed above and in <1075> are not all inclusive. USP <1075> defines compounding as “the preparation, mixing, assembling, packaging, and labeling of a drug or device in accordance with a licensed practitioner’s prescription....”

The preparation of an ambulatory pain pump involves: preparation of the pump; adding or mixing of multiple small-volume parenteral vials of drug to fill the pump; potential packaging of the pump for transport to the surgical area; and proper labeling of the pump.

These processes are clearly defined in USP <1075> as “compounding.” Support for this position is found in the section of <1075> entitled Levels of Compounding. In this section, an example is listed under level 4 that describes the preparation of simple sterile injections reconstituted for immediate use. This section does not require that only products reconstituted with more than one ingredient qualify as compounded products. Additionally, when defining the requirements of compounded sterile devices (CSPs), USP <1075> refers the reader to USP <797>. USP <797> provides detailed instructions for the preparation of CSPs and presents examples of CSPs that undoubtedly describe ambulatory pain pumps.

At the heart of USP <797> and <1075> is the importance of evaluating and controlling the risk of microbial contamination. The reconstitution of several vials of different drug products is no higher risk than the combination of multiple vials of the same drug product. The underlying principle is that multiple vials have to be accessed with sterile transfer equipment and that the risk of contamination increases the more times this occurs.

USP <797> classifies the following examples of compounding as a medium risk for contamination: “Filling of reservoirs of injection and infusion devices with volumes of sterile drug solutions that will be administered over several days at ambient temperatures between 25°C and 40°C” and “Transfer of volumes from multiple ampuls or vials into a single, final sterile container or product.” Both of these examples clearly apply to pain pumps, which provide continuous infusion of a local anesthetic directly into an intra-operative site at ambient temperature over several days for postoperative pain relief. Multiple vials of drug product are combined to achieve a sufficient volume to meet the needs of several days of infusion.

There are two key factors in the microbial risk assessment: First, multiple vials have been accessed, thereby increasing the risk of a break in aseptic transfer. Second, the drug products will be maintained at 25° and 40° for several days. If a break in sterility did occur during the transfer process, bacteria would have a chance to multiply since the drug container is at a growth supporting temperature. These examples in USP <797> are very specific and apply directly to the use of pain infusion devices.

Supporting this is a document that predates USP <797>: the ASHP guideline on Quality Assurance for Pharmacy Prepared Sterile Products. This document provided much of the content for the USP chapter. In the ASHP guideline, a microbial risk level 2 is assigned to “preparing portable pump reservoirs for multi-day (i.e. ambient temperature) administration.”

USP <1075> and <797> are in complete agreement that ambulatory pain pumps, when filled with multiple vials of drug product, are classified as compounded sterile preparations. Guidelines from the pharmacy industry are also in agreement with this assessment. Manufacturers of these devices must manufacture in accordance with the applicable rules and regulations of the U.S. Food and Drug Administration. However, once the device is delivered to a healthcare facility and a licensed practitioner prescribes the use of the device filled with a drug product, the requirements of USP <1075> and <797> apply. USP <797> states that the contents of the chapter apply to CSPs that include “preparations prepared according to the manufacturer’s labeled instructions and other manipulations when manufacturing sterile products that expose the original contents to potential contamination.” Manufacturers have a duty to provide healthcare facilities with proper information on the use of their products and methods for reducing the risk of microbial contamination when manipulating the product.

More information on policies and procedures concerning proper filling techniques, protocols, sterility testing and training is available by contacting I-Flow at (800) 448-3569. For questions concerning this document or other materials concerning USP <797>, please contact Julie Schneider at (949) 206-2678.