Briefly, What exactly is involved in compliance with USP Chapter <797> *Pharmaceutical Compounding: Sterile Preparations* ?

USP 797 does not require sophisticated cleanrooms to be installed. What the guideline does require is environmental controls – specifically, a separate area for compounding that meets a defined level of cleanliness, and monitoring to ensure that control is maintained. A brief explanation of standards clarifies the actual USP 797 cleanroom requirements. First, there are six levels of ISO (International Organization for Standardization) cleanrooms from ISO Class 3 to ISO Class 8. Three of these are:

- ***ISO Class 3 – equivalent to the former Class 1 designation, allows a maximum of one particle (over 0.5 microns in size for all classes) per cubic foot. This cleanliness level is suitable for the ultimate cleanroom application such as microchip manufacturing, but is not required for pharmaceutical manufacturing or sterile compounding.***
- ***ISO Class 5 – (formerly Class 100), allows a maximum of 100 particles per cubic foot; which is the level for the typical laminar airflow hood that is required by USP 797 for the actual mixing area. Mixing IVs in a hood is nothing new in US pharmacies.***
- ***ISO Class 8 – (formerly Class 100,000), allows a maximum of 100,000 particles per cubic foot. This level is required for an IV preparation area/IV room.***

There are other recommendations, but the Class 100,000 mixing area is the primary environmental control requirement. Implementing the most basic steps of straightening up an IV room, coupled with a positive pressure air system, will result in a room with less than 10,000 particles per cubic foot. Getting an IV room to less than 100,000 particles per cubic foot is achievable by following simple USP 797 facility suggestions.

The first step is getting a baseline on your existing facility to determine what remediation steps, or facility and procedural redesign, will be required to meet the environmental controls above. The net result of the USP 797 guidelines is that sterile mixing take place in a properly maintained laminar airflow hood (ISO Class 5) situated in a relatively clean room (ISO Class 8). For most pharmacies, this is neither difficult or unreasonable. In some cases, individual interpretations of this requirement have made it seem more onerous.

Is A Cleanroom Necessary?

Since the publication of USP 797 in 2004, facilities that compound sterile preparations (CSPs) have been trying to find the best and most cost-effective way to comply with the new regulations. USP 797 deals with policies and practices for CSPs, and is the first official and enforceable requirement for CSPs.

One issue USP 797 addresses is standards and requirements for reducing CSP contamination caused by an unclean environment. Air quality and cleanliness affects the likelihood of microbial contamination. Dust, dirt, pollen, skin flakes, lint, and cosmetics can all introduce contamination.

Anyplace where CSPs are prepared must meet USP 797 requirements. The goal as a facility that prepares CSPs is to create an aseptic or sterile environment which can

control the risk of microbial contamination and cross-contamination of admixtures or compounds.

A cleanroom, with its HEPA filters and low dust levels, is certainly an alternative - possibly the best alternative - to achieving this environment. However, with the cost of installing a cleanroom starting at $150/square foot, their cost can be prohibitively expensive. In addition, cleanrooms have high operating costs and take up valuable floor space.

What is the Alternative to a Cleanroom?
As an alternative to cleanrooms, USP 797 specifically defines the use of barrier isolators :

> ***Compounding Aseptic Isolator (CAI)***
> *A form of isolator specifically designed for compounding pharmaceutical ingredients or preparations. It is designed to maintain an aseptic compounding environment within the isolator through the compounding and material transfer processes. Air exchange into the isolator from the surrounding environment should not occur unless the air first passes through a microbial retentive filter (HEPA minimum).*

Barrier isolators can take the place of a cleanroom by providing cleanroom conditions within a contained workspace. It provides the same level of air quality a cleanroom does, while taking up less space and being more cost-effective to operate. Barrier isolators offer several advantages:

- ***Workers have no direct contact with the work area. Instead, they access the work area via sealed gloves. This isolation eliminates the largest source of contamination in compounding – PEOPLE .***
- ***Barrier isolators take up far less valuable floor space than do cleanrooms.***
- ***Workers do not have to fully gown before they begin work, which can save significant work time.***
- ***Decontamination is easier in the small, contained environment of the barrier isolator.***

Where Can An Isolator Be Placed ?
The location of the isolator is very important. USP 797 doesn't require that the barrier isolator is located within a buffer area or cleanroom that maintains at least an ISO Class 8 environment. However, this environment must be kept as clean and sterile as possible. Any contamination that could occur as products are transferred into and out of the barrier isolator must be minimized. Pharmacy Isolators address this issue by including a transfer chamber that acts as an air lock. When materials are placed in this chamber, the ventilation system cleans the air in the background chamber up to class 100 quality.

Other options for improving cleanliness levels include:

- ***Installing HEPA filters in the ceiling tiles***
- ***Replacing ceiling tiles with "cleanroom grade" tiles***
- ***Removing refrigerators, computers, and printers from the compounding area***

- ***Replacing flooring with seamless vinyl floor covering***
- ***Implementing proper housekeeping procedures for cleaning and sanitizing***