Table 19: Is There a Problem Using Closed System Transfer Devices with Biological Products?

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SCOPE:

Closed System Transfer Devices (CSTDs) have been designed to protect healthcare workers from accidental exposure of hazardous drugs during clinical preparation, compounding, and patient administration of intravenous infusion products. However, the potential impact of the use of the large variety of such devices on product quality, compatibility, and hold-up volume, specifically for biological drug products, has not been generally well characterized to date. This Roundtable session will discuss and identify the most pertinent CSTD challenges across stakeholders, including device and drug manufacturers, regulatory authorities, and pharmacies implementing USP <800>. We hope to also drive a shared appreciation and understanding across stakeholders and agree upon the highest priority issues to resolve going forward, given that CSTDs may be implemented in hospitals regardless of whether a biologic is classified as a NIOSH hazardous drug or not.

QUESTIONS FOR DISCUSSION:

1. What makes biologics unique in terms of use with CSTDs?
2. What is the potential impact of CSTD use, USP <800> and NIOSH hazardous drug classification on biological product development?
   Pharmacies are using CTSD in general without checking whether they are listed in NIOSH or not. Maybe classify in manual pharmacy that the drug is not hazardous or toxic. How do determine or support such statement
3. What are the expectations from the manufacturers, regulatory authorities, and hospital pharmacies for CSTD use with biological products, and how do we work together?
4. How do drug manufacturers accommodate compatibility and hold-up volume testing across a wide variety of CSTD formats from different manufacturers?

DISCUSSION NOTES:

CSTDs are being used by Health Care Practitioners (HCPs) for not only administering hazardous drugs eg, cytotoxins and oncology drugs intravenously (IV), but also for subcutaneous (SQ) and invasive intravitreal injection (IVT) administrations.

Certain hospitals typically commit to a system, so specifying a type of CSTD in the label might not be practical. Some hospitals use CTSDs regardless of whether the drug is hazardous or not.

HCPs are typically aware of usability challenges, but perhaps not aware of challenges related to drug compatibility.

List of the different consortia working on position statements for use of CSTD with biologics: APS, IMI, PQRI, IQ, BPOG.

Some of CSTDs Challenges:

Hospitals/pharmacy sites might have their own SOPs for describing practices which may or not include the use of a particular CSTD. These practices may also change overtime invalidating the previous in use condition that were tested for a particular CSTD.

How to label product and account for overfill?

- Overfill maybe one of the biggest challenges to CSTDs as the hold-up volume is design-dependent and could vary among different devices.
- 0.1-0.7 mL or larger is typically the hold-up volume. Will depend on the dose and the actual geometry of the container closure.
- Volume transfer and hold-up volume could significantly impact accuracy of delivered dose.
- There is FDA guidance on volume requirement to minimize overfill to prevent potential over-dose. Difficult to accommodate both CSTD and standard (disposable) syringe with a single overfill volume.
- Excluding certain brands of CSTDs due to incompatibility in a commercial drug label might be challenging (finger pointing to a particular brand). Could we link incompatibility to material of construction (MOC) instead of a specific brand? May not be possible if the incompatibility from the device design (type of lubricant) rather than MOC. Also, the MOC of a particular device may not be readily available from a manufacturer.

Misconception that CSTD can be used for microbial control causing potential inappropriate claim of extended in-use time

- CSTDs manufacturers do claim microbial challenges studies can support sterility; however, would that be enough to allow longer in-use time?

Silicone oil or other lubricants like flurosilicone oil may interact with the product causing product incompatibility due to particles formation. Visible and sub-visible particles can also increase from lubricant like silicone droplets.

- Filters in infusion lines are typically used as a mitigation for particles. Filters themselves can cause shedding and particles formation. What level of particles pre-filtration would be acceptable?

Some of the attributes to examine when developing a CSTD:

Sub-visible, visible particles, HMW species, leachables, stopper intrusion, stopper coring (another factor contributing to particles, deliverable volume, opalescence and turbidity.

There is a need to drive consistency across CSTDs by developing device ISO standard for consistency.