Table 17: Opportunities for Engagement and Collaboration to Achieve Stakeholder Alignment on Closed System Transfer Devices (CSTDs)

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Scope:

As per NIOSH definition, Closed System Transfer Devices (CSTDs) are intended to mechanically prohibit the transfer of environmental contaminants to the drug product while also prevent the escape of potentially hazardous vapors to the environment. CSTDs are supplemental engineering controls that are meant to offer protection to healthcare professionals against harmful exposure of hazardous drugs during compounding and administration. CSTDs are Class II medical devices subject to the 510(k) regulatory requirements. The impending deployment of USP <800>, which references the NIOSH List of Hazardous Drugs, has resulted in more widespread use of CSTDs. As a result, several compatibility concerns have come to the forefront, especially with respect to the use of CSTDs with biological products. Furthermore, a lack of clarity around the requirements of USP <797>, which governs sterile compounding, has resulted in confusion amongst many stakeholders about requirements and/or recommendations for using CSTDs. The scope of this roundtable discussion is to highlight the biologic drug product compatibility challenges when CSTDs are used and to address the interplay between biologic manufacturers, health care professionals, CSTD manufacturers and regulatory agencies.

Discussion Notes:

Background:

- Team briefly talked about CSTD background info and challenges (CSTD dose preparation and administration, clinical site communications etc.).
- Suggestions for communication with clinical sites/HCPs about CSTDs
- Reach out to clinical sites ahead of time to understand a clinical site's strategy for CSTD use.
- Align with internal teams and start a dialogue with clinical site regarding why a CSTD is not needed for a (non-ADC) biologic.
- Include the nursing/pharmacy staff (this has been the hardest audience to reach) along with hospital/clinical staff management to ensure the alignment with the right stakeholders to get real time feedback on CSTD use
- Understand the clinical site policy and documentation that needs to be provided for not using a CSTD at a clinical site for a (non-ADC) biologic, since not using a CSTD can be a deviation from a clinical site protocol.
- It is recommended to include references (specifically relating to exposure of modalities through a specific route of administration) when requesting a clinical site not to use a CSTD in the pharmacy manual.

- Internal teams to understand clinical practices around the globe (US, Europe, Asia etc.)
- Provide data if available to the clinical site (if need be) regarding compatibility of your biologic with CSTD(s)/component(s).

CSTD testing, risk level assessments and inquiries into regulatory expectations

- Should CSTD testing be a part of in-use studies or stand alone? It is recommended to keep the CSTD testing studies separate studies as it is better to have a baseline understanding of in-use compatibility. Helps with troubleshooting compatibility challenges or finding a path forward with clinical sites.
- Inquiries into what are regulatory expectations. Not all sponsors are capturing CSTD compatibility testing data in IND filing (in part because it is not always known what CSTDs will be used at time of filing & also a product will fall in to the combination device space if paired with a specific CSTD – note regulatory requirements are different for combination products).
- Studies may be executed post filing. However, teams recommended to follow good documentation practices in case data is requested by health care agencies.
- Teams recommended to capture lot #s as well as part #s when testing CSTDs. This helps in case of process changes from CSTD manufacturers.
- Teams recommended to use a two prong approach: CSTD testing ("well behaved" molecules that are otherwise safe may show incompatibilities with CSTD that are unexpected) and a risk based assessment. Some companies may have a lot more prior knowledge with certain components of CSTDs. Administration components are less complex (less risky) than dose prep components.

Further engagement for CSTD alignment

- Need public/private partnership to engage with agencies and come to alignment.
- HCP, industry/biologic manufacturers, CSTD manufacturers & regulatory agencies (CDER, CDRH) collaborate to make sure we are doing the right thing for the patients.