Review of Closed System Transfer Devices (CSTD) and Compliance to USP <800>
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Disclosure Information

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- I have the following financial relationships to disclose:
  - Consultant for: Wolters Kluwer
  - Grant/Research support from: BD Medical, Equashield, and Braun (past client)
  - Principal of: Clinical IQ, and CriticalPoint, LLC

- I will not discuss off label use and/or investigational use in my presentation.
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Acknowledgements

Thanks to Fred Massoomi, Luci Power, Kate Douglass, and Patti Kienle for the use of slides/information presented in this slide deck!
At the completion of this activity, you will be able to:

• Discuss the FDA medical device classifications of CSTD and “microbial ingress” claim

• Describe the chapter position of the use of a CSTD for compounding and administration

• Explain the differences in CSTD design and its ability to contain vapors according to the 2015 Draft NIOSH Vapor Containment Protocol

- List References here
History of CSTDs

• FDA classifies medical devices based on the risks associated with the device. Devices are classified into one of three categories—Class I, Class II, and Class III.

• CSTDs are designated by the US Food and Drug Administration as Class II medical device via 510(k) process
  • Two approval pathways
    • “Approved” – Premarket Approval (PMA) – First to market
    • “Cleared” – Substantially equivalent
  • 1998 First FDA approved CSTD (PhaSeal-Carmel Pharm) Intravascular catheter
  • PhaSeal CSTD is predicate device for all others

According to the National Institute for Occupational Safety and Health (2004 NIOSH), a closed-system transfer device (CSTD) is “a drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor concentrations outside the system.”

- Intent: Nothing in and Nothing Out!
- No testing procedures are described to prove this point
In addition to preventing transfer of environmental contaminants (e.g., bacteria) into vials in which parenteral medications are prepared, CSTDs serve the important function of protecting health care professionals compounding and administering hazardous drugs (HD) from the occupational hazard of chronic, low-level exposure to carcinogenic and/or teratogenic medications.

• Microbial Ingress Testing
  • Expected Testing – Not clearly defined by FDA
  • Many CSTD manufacturers have tested their product
History of CSTD Definition

• 2004 NIOSH Alert Defines CSTD

• 2015 NIOSH publishes or comment NIOSH Alcohol Vapor protocol

• 2016 NIOSH creates new Vapor test with new substrates based on feedback – Substrates mimic hazardous drugs – Comment period through June 2017

• 2016 NIOSH Town Hall Meeting CSTD Testing Protocol

• Present: NO standardized tests for CSTDs
Sec. 880.5440 Intravascular administration set.

(a) Identification. An intravascular administration set is a device used to administer fluids from a container to a patient's vascular system through a needle or catheter inserted into a vein. The device may include the needle or catheter, tubing, a flow regulator, a drip chamber, an infusion line filter, an I.V. set stopcock, fluid delivery tubing, connectors between parts of the set, a side tube with a cap to serve as an injection site, and a hollow spike to penetrate and connect the tubing to an I.V. bag or other infusion fluid container.

(b) Classification. Class II (special controls). The special control for pharmacy compounding systems within this classification is the FDA guidance document entitled "Class II Special Controls Guidance Document: Pharmacy Compounding Systems; Final Guidance for Industry and FDA Reviewers." Pharmacy compounding systems classified within the intravascular administration set are exempt from the premarket notification procedures in subpart E of this part and subject to the limitations in 880.9.

Many of the devices marketed and used for HD compounding are not CSTDs by definition and may not be appropriate for HD use.

- Dispensing pins, etc.

- FDA ONB, specifically for a closed antineoplastic and HD reconstitution and transfer system.

- More stringent

- Use ONB classification as factor as acceptance criteria

FDA ONB Definition

Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH). Product code classification database. Product code ONB.

Summary of CSTDs Regulation

- NIOSH recommending body for best practices - CDC and OSHA
- CSTD defined as part of 2004 NIOSH Alert “A drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor outside the system”
- FDA for clearance and 510K process
  - Medical Devices – CDRH branch of FDA
- FDA for ONB designation as a CSTD
- NO Regulatory Oversight
### Summary of CSTDs Regulation

<table>
<thead>
<tr>
<th>Device</th>
<th>Manufacturer</th>
<th>FDA Cleared</th>
</tr>
</thead>
<tbody>
<tr>
<td>BD Phaseal™ System</td>
<td>Becton Dickinson and Company; Camol Pharma, Inc. (original)</td>
<td>1998</td>
</tr>
<tr>
<td>Spiros®</td>
<td>ICU Medical, Inc.</td>
<td>2005</td>
</tr>
<tr>
<td>Texium™ with SmartSite™</td>
<td>Becton Dickinson and Company; CareFusion, Inc. (original)</td>
<td>2006</td>
</tr>
<tr>
<td>OnGuard® with Tevadaptor®</td>
<td>B. Braun Medical Inc. (U.S. distributor) TEVA Medical, Ltd. (manufacturer)</td>
<td>2006</td>
</tr>
<tr>
<td>ChemoClave®</td>
<td>ICU Medical, Inc.</td>
<td>2006</td>
</tr>
<tr>
<td>Equashield®</td>
<td>Equashield, LLC; Plastmed, Ltd. (original)</td>
<td>2008</td>
</tr>
<tr>
<td>ChemoLock®</td>
<td>ICU Medical, Inc.</td>
<td>2013</td>
</tr>
<tr>
<td>ChemoSafety</td>
<td>Becton, Dickinson and Company; CareFusion, Inc. (original)</td>
<td>2013</td>
</tr>
<tr>
<td>EquaShield II®</td>
<td>Equashield, LLC</td>
<td>2014</td>
</tr>
<tr>
<td>Halo®</td>
<td>Corvida Medical</td>
<td>2015</td>
</tr>
<tr>
<td>Arisuro®</td>
<td>Baxter</td>
<td>2017</td>
</tr>
</tbody>
</table>

The FDA leaves no such opening. “FDA has not assessed any data demonstrating sterility assurance or chemical stability of the drug product for extended [BUD] dating when CSTDs are used,” the agency noted in a statement sent to *Pharmacy Practice News*. “FDA clearance of these devices should not be interpreted as modifying, extending or superseding a drug manufacturer’s labeling recommendation for storage and expiration dating.”

Source: Pharmacy Practice News; 2018 June 8
“based on feedback received directly from the FDA, the extension of a beyond use date beyond 6 hours for a single-dose vial has not been approved as an indication.”

**IMPORTANT** to keep in mind some US States may not allow DVO programs

Source: Pharmacy Practice News; 2018 June 8
The use of CSTDs in the HD Life Cycle

HD Lifecycle
- Receive
- Transport to Intermediate storage
- Store
- Compound
- Transport to Patient
- Administer
- Discard

www.ivpnsymposium.org
Skin contact

- Workers from 6 Canadian hospitals sampled
- Wiped front and back of hands
- Analyzed for cyclophosphamide
- 44/225 (20%) had levels above the limit of detection
- A number of workers from various job categories had contaminated hands
  - Volunteer, oncologist, aide and dietician
  - Pharmacist, pharmacy technician, pharmacy receiver, nurse, transporter

Contamination of drug vials

• The exterior of many drug vials are contaminated with their contents
• The contamination is not the result of breakage during transportation
• Some facilities pre-clean the exterior of the vials before use

What can we conclude from surface contamination with hazardous drugs?

- Surface contamination is common in pharmacy and nursing areas and where drugs are handled.
- It has been well documented with ~5% of drugs in use.
- Status of other 95% is unknown.
- Uptake of several drugs has been documented in healthcare workers.
HD Compounding Strategies: Negative Pressure

• Negative pressure compounding techniques ensure that the pressure within the drug container is always maintained at a slight negative pressure

• Too much negative pressure can cause fluid to leak from the needle when withdrawn

• Positive pressure can cause the HD to spray out around the needle or through the needle hole

• Always use a syringe that is 25% larger in volume than the total volume to be withdrawn
HD Compounding Strategies: Use of CSTDs

• USP 800 uses the term supplemental engineering controls
  • Must be used in containment primary engineering control (BSC or CACI)
• These devices are adjunct controls that may be used with C-PECs and C-SECs to offer additional levels of protection (containment)
• Facilitate enhanced occupational protection especially during drug administration
• Closed System Drug-Transfer Devices are the only kind of Containment Supplemental Engineering Control available at this time
• Two types of CSTDs
  • Capture vapors
  • Filters
Engineering Controls for Containment: Definitions

Containment Primary Engineering Control (C-PEC)
- Ventilated device to minimize worker and environmental exposure
- For sterile compounding, also provides product protection

Containment Secondary Engineering Control (C-SEC)
- The room in which the C-PEC is placed

Containment Supplemental Engineering Controls
- Adjunct controls to offer additional levels of protection
- Closed System Drug-Transfer Devices (CSTDs)
HD Compounding Strategies: Use of CSTDs

- Many devices are marketed as CSTDs however until recently there was no published performance criteria.

- In 2015 NIOSH published “A Vapor Containment Performance Protocol for Closed System Transfer Devices Used During Pharmacy Compounding and Administration of Hazardous Drugs.”

- For this protocol, NIOSH settled upon 70% isopropyl alcohol (IPA) as a tracer compound due to its propensity to generate vapor at room temperature, its ubiquity, and the availability of equipment to reliably measure concentrations of IPA within a test environment using a gas analyzer.
  
  - (The Miran SaphIRe detector, which reports IPA concentrations in parts per million once per second).8,9

HD Compounding Strategies: Use of CSTDs

- The 2015 Draft NIOSH Vapor Containment document provides testing criteria for CSTD manufacturers to use (for systems that use vapor capture technology).
- An alternative NIOSH
- Vendors need to be held accountable for their claims so that objective evaluations of CSTD performance can be done against a performance standard
- CSTDs differ in many ways and each organization must review the offerings to see which system is best for them
HD Compounding Strategies: Use of CSTDs

• Key CSTD Features
  • Containment
    • Performance Testing Criteria – VAPOR
    • Performance Testing Criteria – Microbial Ingress Testing (Container Closure Integrity Testing)
  • User & Design interface
  • Integration
  • Workflow
  • Repetitive strain reduction
  • Pre-bonded components

Source: Massoomi. Pharmacy Purchasing Products 2015; February S1-S12  www.ivpnsymposium.org
Ongoing surface contamination with HDs (Table 1-3) presents a risk to workers who are inadvertently exposed to these drugs, including workers who are not involved with compounding or administration.

- Negative-pressure technique is difficult to use
- Dry-connections and pressure equalization are key performance elements
- More critical for nurse and patient than pharmacy, but important consideration for pharmacy based on vapor study results
HD Compounding Strategies: Use of CSTDs

• Provides additional safeguards to prevent occupational exposure to nursing and other staff who administer these drugs

• Provides additional safeguards to patients, families and organizational environments by reducing risk of exposure to HDs

• Increased operational cost associated with CSTD use
  • Reimbursement isn’t routinely available

Remember, CSTDs still can’t prevent damage or spills from poor handling or transport!
Performance of CSTDs – Caveat Emptor

• CSTDs have shown ability to limit (not prevent) the potential of generating aerosols and reduce (not eliminate) HD contamination in the workplace.
• Not all marketed CSTDs have been studied
• Capture technology appears to perform better than other technologies

https://giphy.com/
Key Points

• An efficiency study\(^1\) that actually has shown that using a CSTD actually decreases the amount of time from preparation to administration

• Improves compounding efficiency since negative pressure compounding techniques significantly increase the length of sterile compounding

• Reduces HD contamination inside the C-PEC thereby reducing the amount of HD contamination available for migration out of the C-PEC into the C-SEC and C-SCA

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Any Closed system drug-transfer devices (CSTDs) needs to reduce HD leaks and spills during compounding and administration, thereby reducing overall surface contamination in work areas.

Published peer-reviewed studies of individual CSTDs are needed to adequately evaluate the effectiveness of these devices in reducing surface contamination and vapor containment is claimed.
Resources


- Centers for Disease Control and Prevention. Occupational exposure to antineoplastic agents and other hazardous drugs. CDC website. www.cdc.gov/niosh/topics/antineoplastic/pubs.html

- Forshay CM, Streeter SO, Salch SA, and Eckel SF. Application of the 2015 proposed NIOSH vapor containment performance protocol for closed system transfer devices used during pharmacy compounding and administration of hazardous drugs. J Oncol Pharm Practice 2018; 0(0) 1–7.

Questions?
FDA designates CSTDs as what class of medical device?

a. Class I  
b. Class II  
c. Class III  
d. none of the above
Which of the following statements is **FALSE**?

a. CSTDs provide additional safeguards to prevent exposure to staff that are administering these drugs

b. CSTDs provide additional safeguards to patients and families that may be at risk of exposure to hazardous drugs

c. **CSTDs have decreased operational cost**

d. CSTDs still can’t prevent damage or spills form poor handling or transport
True or False? Too much negative pressure can cause fluid to leak out from needle upon withdraw, but positive pressure can cause the HD to spray around the needle or through the hole.

• True
• False
If a total volume of 9.6ml of HD must be withdrawn from a vial, what the minimum size syringe should be used?

a. 30mL
b. 20mL
c. 10mL
d. 5mL