It is very clear that occupational exposure to hazardous drugs is a serious concern for healthcare professionals.1, 2 Guidelines to minimize this exposure have been in existence since 1981.3 Since that time, pharmacy and nursing practitioners have continued to explore opportunities to minimize exposure through the use of personal protective equipment (PPE), compounding techniques and drug administration practices. These practices have been summarized in two key practice guidelines—the National Institute for Occupational Safety and Health (NIOSH) health alert to employers Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings and the American Society of Health-system Pharmacists (ASHP) Guidelines on Handling Hazardous Drugs.4, 5

Fluorescence studies demonstrate that compounding hazardous drugs using traditional vial-to-syringe technique is one of the riskiest points of occupational exposure due to vial over-pressurization, which can lead to spraying and leakage (Fig 1). Without the aid of fluorescence, these sprays and spills go unnoticed and may lead to exposure for staff and for patients from the contaminated finished product. The best practice approach to managing these hazardous products is to treat every hazardous drug as if it is contaminated during each step of the distribution process—from receiving through disposal—and follow the recommended precautions outlined in the NIOSH Alert and the ASHP Guidelines to minimize occupational exposure (Fig 2).

Closed System Transfer Devices
Both the NIOSH and ASHP documents recommend that you consider

![Figure 1. Fluorescence Studies](image1)

Compounding hazardous drugs using the vial-to-syringe method can lead to spraying and leakage, as evidenced in fluorescence studies.

![Figure 2](image2)

Throughout the distribution process, treat every hazardous drug as if it is contaminated to minimize occupational exposure.
using a closed system drug transfer device (CSTD) to minimize occupational exposure to hazardous drugs. These devices aid compounding personnel in the reconstitution and mechanical transfer of hazardous drugs from the drug manufacturer’s container to the patient-specific product, and aid drug administration personnel with the safe administration to patients.

A closed system transfer device is defined within the NIOSH Alert as “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.” These criteria for a CSTD simply mean nothing should enter and nothing should exit the vial transfer device. While vented, filtered devices may reduce the release of drug aerosols, their design allows the device to be transferred from one vial to another, which creates the opportunity for environmental and product contamination. As such, they may not be considered CSTDs per the NIOSH Alert.

Vial Transfer Devices on the Market
Since the 1998 introduction of the first Food and Drug Administration cleared CSTD, PhaSeal, three additional vial transfer devices have been cleared with more anticipated to enter the market in the near future (Table 1). To be considered CSTDs under the NIOSH definition and ASHP guidelines, these devices must demonstrate containment of spills and leakage as well as aerosols and vapors. In addition, they should demonstrate their effectiveness in independent studies. It is important to note that the guidelines also state that the CSTDs should be used within a ventilated cabinet while following appropriate PPE and work practices.

Establishing Best Practices
At Nebraska Methodist Hospital, we are committed to reducing the risk of occupational exposures for our staff. While implementing any system that reduces employee exposure to hazardous drugs is laudable and better than simply using a needle and vial during compounding, our goal was to establish best practices based on the NIOSH and ASHP guidelines. Therefore, when compounding hazardous drugs, our staff is required to use a closed system transfer device within a compounding aseptic containment isolator (CACI) while being properly garbed in chemo-rated PPE.

We found it challenging to evaluate the CSTDs available in the market, as little independent, published clinical data is available to assess each device’s containment ability. In fact, the published tests simply affirm a device’s containment, they do not quantify degrees of control. To aid us in our decision, we conducted simple tests in-house to evaluate the containment ability of CSTDs. I recommend first conducting these tests with your current method of compounding hazardous drugs and then test the vial transfer systems you are considering. Have multiple staff members trial the devices so you can evaluate the effect of technique on the consistency of the results.

### Simplified Leakage Containment Test
A simplified test to examine the spill/leakage containment of a vial transfer device involves the use of a solution with a low pH (i.e., sodium bicarbonate or ordinary lemon juice) in combination with pH paper (urine dip sticks or litmus paper). This test is quick, repeatable and easy to perform.

Simply fill a 10 mL syringe with the low pH solution and using the vial transfer device, perform the preparation and administration manipulations as usual, transferring 1 ml of solution between the syringe and the vial. To determine the presence of leakage, disconnect and press the connection point of each component against your pH indicator (i.e., litmus or urine dip sticks). Blue litmus paper signifies liquid is present, indicating leakage. Repeat this transfer process as many times as normally seen in the compounding process.

### Table 1. Devices on the Market

<table>
<thead>
<tr>
<th>Device</th>
<th>Manufacturer</th>
<th>FDA Cleared*</th>
</tr>
</thead>
<tbody>
<tr>
<td>PhaSeal</td>
<td>Carmel Pharma</td>
<td>1998</td>
</tr>
<tr>
<td>Texium with Smart Site</td>
<td>Cardinal Health</td>
<td>2006</td>
</tr>
<tr>
<td>OnGuard with Tevadaptor</td>
<td>Teva Medical</td>
<td>2006</td>
</tr>
<tr>
<td></td>
<td>B. Braun (distributor)</td>
<td></td>
</tr>
<tr>
<td>Genie with Spiros</td>
<td>ICU Medical</td>
<td>2008</td>
</tr>
<tr>
<td></td>
<td>Hospira (distributor)</td>
<td></td>
</tr>
</tbody>
</table>

*denotes date total system cleared, specific parts of the system may have had prior FDA clearance

CSTDs aid compounding and drug administration personnel in minimizing occupational exposure to hazardous drugs.
to ensure the device maintains a dry connection during multiple manipulations. Containment can be assumed if the blue litmus paper does not demonstrate leakage.

**Simplified Vapor Containment Test**

Only one study has been peer-reviewed and published on aerosol and vapor containment and it involved the use of titanium tetrachloride. This test is not easy to repeat, however it does provide visual confirmation of aerosol and vapor containment (Fig 3). A quick visual test for this containment can be performed using a vial transfer device, air, an empty vial, and water. It is important to note that this test has not been peer-reviewed and is not intended to be referenced in lieu of published clinical data; however it can be used as another method of assessment as it is quick, inexpensive, and easy to perform.

Fill a 10 mL syringe with air; connect it to the syringe component of the vial transfer device; attach the vial adaptor of the transfer device to an empty vial or vial of saline; engage the syringe device onto the transfer device’s vial adaptor; submerge the connected device into a clear container full of water and large enough to cover the engaged device; transfer as much of the air from the syringe into the vial and aspirate back into the syringe, repeat the transfer of the air into and out of the syringe in a manner that would simulate the practice of compounding. Containment can be assumed if bubbles are not present during the transfer process, however it is not completely conclusive, due to the unique characteristics drugs possess as they form vapors.

Figure 3. Titanium Tetrachloride Tests

Titanium tetrachloride tests demonstrate aerosol and vapor leakage using the traditional vial-to-syringe method.
Vial Transfer Systems in Use
Consistent, proper usage of these systems is paramount to ensuring containment. Staff members should be observed regularly while they are using the devices. If they do not understand the process or if they find a particular step to be cumbersome, they may not follow proper procedures. We have assigned a super-user who provides the initial training and then assesses the staff users annually. Additionally, it is important that all users, including those in pharmacy and nursing, are instructed to report any failures the system may have so they can be promptly reported to the manufacturer.

Remember that nursing is also an end-user and as such, should join pharmacy in the assessment and training processes. If nursing does not like the product that is selected, you run the risk of it not being used properly, thus losing the value of a closed system.

Conclusions
Closed system transfer devices provide important protection to both hospital staff and patients and should be given serious consideration in any facility where hazardous drugs are compounded. A comprehensive safe handling hazardous drug program requires a continuous review of all transfer devices; available independent, peer-reviewed, published clinical data; and practice standards to be effective.

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Critical CSTDs Assessment Steps
1. CSTDs should be considered as part of a comprehensive hazardous drug safety program.
2. Conduct an assessment of all devices used for compounding hazardous drugs in comparison to current practice.
3. Request a demo product from the sales representative to test the vial transfer device’s containment properties.
4. Have compounding staff test the devices in conditions that mirror how they will be using them in practice.
5. In addition to reviewing independent, published, peer-reviewed clinical data, compounding staff should review the device for ease of use, number of pieces required for compounding and administration, and consistency in compounding technique by multiple staff members.
6. Continually assess new vial transfer devices as they are cleared by the FDA.

References