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FEATURED ARTICLE

Contamination Comparison of Transfer Devices Intended for Handling Hazardous Drugs

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Abstract

Purpose: Heightened awareness of hazardous drug contamination in the workplace has increased the number of marketed, closed-system drug transfer devices (CSTDs). Currently, no official specifications for a closed-system device are available. Therefore, it is important to validate each system against the recommendations given by International Society of Oncology Pharmacy Practitioners and the National Institute for Occupational Safety and Health to make the best decision for an institution.

Summary: Titanium tetrachloride was selected to simulate the escape of vapor from each product. The second evaluation concentrated on the "dry connections" between the vial and syringe during drug preparation and between the syringe and access port during administration. Fluorescein sodium was selected to simulate contamination with the dry connections between the vial and syringe and between the syringe and access port.

Conclusion: The 2 studies found that only 1 of the 5 devices tested met the criteria or definition of a CSTD.

Key Words—closed-system device, fluorescein, hazardous drug, titanium tetrachloride

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Many procedures used in the preparation and administration of hazardous drugs have the potential for leakage and accidental spills, thus putting health care workers and those within the environment of care—including patients and family members—at risk for exposure to these agents. There are numerous published reports of surface and personnel contamination with these hazardous drugs.[1,2] As a variety of health care disciplines, professional organizations, and regulatory agencies give increasing attention to this subject, it is becoming clear that exposure to cytotoxic agents is a real heath hazard that must be addressed within the workplace.

Multiple reputable, peer-reviewed publications—including the 2004 National Institute for Occupational Safety and Health (NIOSH) Alert—have reported the impact hazardous drug exposure has on reproductive systems and the developing fetus, including significantly higher rates of spontaneous abortion, infertility, still birth, low birth weight, and congenital malformations and abnormalities.[3]

The International Agency for Research on Cancer (IARC) has established 10 different drugs and 2 combination therapies as group 1, known human carcinogens. Given enough exposure, these products will cause cancer in humans. In addition, IARC has listed 9 drugs as probable carcinogens and 10 drugs as possible carcinogens.[4] Published reports of increased cancer rates in health care workers seem to support these IARC data.[5]

Based on all available information, the prudent course of action is the establishment of workplace procedures by health care professionals that result in no exposure to hazardous medications.

In terms of safety procedures, efforts to reduce hazardous drug exposure can be divided into a hierarchy of responses. At the most basic level are isolation controls, which include closed-system drug

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transfer devices (CSTD). Both the International Society of Oncology Pharmacy Practitioners (ISOPP) and NIOSH recommend the use of a CSTD for protection against exposure.[6,7] They define a CSTD as "a drug transfer device which mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor concentrations outside the system." ISOPP distinguishes that a system cannot be "semiclosed"; it is either closed or it is not. ISOPP further stipulates that a system must be "leak proof and airtight." The first CSTD on the market was the *PhaSeal* System by Carmel Pharma. There are numerous published studies demonstrating the effectiveness of this system in reducing exposure to hazardous drugs.[8,9]

There are a variety of drug preparation and administration systems available today; however, before using any products, it is important to make sure—as recommended by ISOPP and the American Society of Health-System Pharmacists (ASHP)—that peer-reviewed, independent studies can be provided for each component of the system to validate its effectiveness.[7-10]

ISOPP stipulates that all manufacturers of transfer and administration devices for chemotherapy should disclose 3 important pieces of information to potential users of these products. First, the manufacturer must disclose whether the device covers all steps in the preparation process and in which routes of administration the containment is guaranteed. If the device covers only some of the steps, the manufacturer should clearly indicate where the closed properties are not retained. Second, the manufacturer must disclose the studies that show that the device eliminates or reduces contamination in daily practice. The studies must also demonstrate that the device can retain its closed characteristics when more than 1 preparation or administration is performed and to what degree. Third, a product described as a *closed system* must be a leak-proof and airtight system.[7]

It is important to note that exposure from preparation and administration are not the only potential routes of exposure, so a CSTD should be considered a necessary, but not the sole, component of a comprehensive safety program.[11]

OBJECTIVE

The purpose of this study was to examine several commercially available systems or devices to ascertain which meet the NIOSH and ISOPP definitions of *closed system*. Two different tests were designed to determine if the products were airtight and leak proof, both in preparation and administration practice. The first test evaluated the preparation components of the systems to determine which device prevents the escape of vapor. The second test evaluated the dry connections between the vial and the syringe in pharmacy preparations and then between the syringe and the port in nursing administration.

METHODS

Five systems were evaluated in the first test, which was conducted by James Jorgenson et al. at the University of Utah: the *Tevadaptor* vial adaptor system by Teva Medical, Ltd. (currently marketed in the United States by B. Braun as the *OnGuard* system), the *Alaris Smart Site* vented vial access device by Cardinal Health, the *PhaSeal* protector 50 & injector luer lock by Carmel Pharma, the *Chemoprotect Spike* by Codan US Corporation, and the *Chemo Mini-Spike Plus* dispensing pin by B. Braun Medical, Inc. Titanium tetrachloride, which generates a visible smoke when it comes into contact with moisture in the air, was selected to simulate the escape of vapor from each product. To fully comprehend the results of the study, it is important to understand the actual mechanics of the smoke. Titanium tetrachloride reacts with moisture in the air to form hydrochloric gas and titanium dioxide. These components formed the visible smoke. However, the particle size of this smoke generally exceeds the size of the pores in a 0.22-micron filter. Thus, it was not the observed smoke from the vials that was escaping; the actual titanium tetrachloride particles are generally *smaller* than the 0.22-micron filter pores, and these particles escaped from the filter-based systems in the study. The particles then reacted with external air to form the smoke observed outside the vials.

Three milliliters of titanium tetrachloride were delivered into a glass vial, and then the vial was sealed with a 20-mm crimp seal and a *Fermpress* H-207 aluminum crimper. The products were assembled, and each device was spiked into its own vial containing titanium tetrachloride. A 60 mL syringe filled with 50 mL of air was attached to each device. The plunger of the syringe was compressed at a constant rate over 10 seconds. Photographs and a video were taken to document any escape of titanium from each product. It was ensured that the filters themselves were not damaged in any way by exposure to the hydrochloric gas or titanium dioxide. To confirm the test methodology and the filter integrity, the test was reproduced by an independent

Figure 1. ***PhaSeal*** **with no release of titanium smoke.**

Figure 2. ***OnGuard Tevadaptor*** **with release of titanium smoke.**

Figure 3. ***Alaris Smart Site*** **with release of titanium smoke.**

Figure 4. **Codan** ***Chemoprotect Spike*** **with release of titanium smoke.**

Figure 5. ***Chemo Mini-Spike Plus*** **with release of titanium smoke.**

testing laboratory, the Pharmasel laboratory at the SP National Testing and Research Institute in Borås, Sweden. All products performed exactly as originally observed when the experiment was repeated by the independent laboratory. After the titanium tetrachloride tests were completed, the filters were carefully removed and dried. They were then coated with gold and viewed under electron microscopy for any evidence of damage that might contribute to the escape of the titanium tetrachloride particles. All filters were determined intact by the independent laboratory, with no observable damage that could have contributed to the escape of the titanium.

For the second test, the *PhaSeal* system, *Tevadaptor* (*OnGuard*) system, and *Alaris* system (*Smart Site* vented vial access and *Texium* male luer) were tested for dry connections between the vial and syringe and between the syringe and access port. This test was conducted by Susan Spivey and Howard Ritter at the University of Texas M.D. Anderson Cancer Center.

Fluorescein sodium, a fluorescent indicator, was prepared as a 0.05% solution, and 15 mL was added to empty 20 mL drug vials; then a rubber stopper and vial cap were added. The devices were used as specified by manufacturer instructions, and each device was tested once, with the steps of the test repeated 15 times. Each phase of the manipulation was photographed using ultraviolet (UV) light to visualize fluorescein leaks and spills. The procedures included pulling back 5 mL of fluorescein into the syringe and then reinjecting 1 mL from the syringe into the vial for a final volume of 4 mL, replicating the preparation phase. In addition, an intravenous (IV) push of 7 mL of fluorescein was given using the syringe adaptor and IV port device for each product, replicating the administration phase. During both procedures, the vial adaptor and syringe components were disengaged, observed, and photographed under UV light and then touched to a 4 × 4 gauze pad. The visual and touch inspections were used to determine presence of contamination.

RESULTS

This study examined several commercially available systems or devices to determine which were closed systems, as defined by NIOSH and ISOPP. The evaluation focused on the prevention of vapor escape and the ability to maintain a dry connection.

In the first test, only the *PhaSeal* system prevented the release of titanium and, therefore, met the NIOSH and ISOPP definition of *closed* (see Figure 1). The other 4 products had visible smoke emitting from their systems (see Figures 2 through 5).

Results of the second test validated that only the *PhaSeal* system contained the drug throughout all preparation and administration manipulations (see Figures 6 and 7). The other systems showed visible fluorescein leaks on the outside of each component during both preparation and administration manipula-

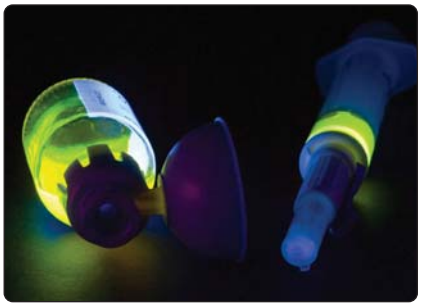

Figure 6. *PhaSeal* with no release of fluorescein.

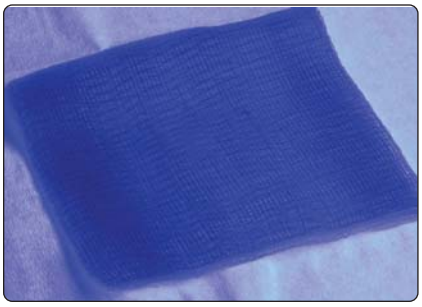

Figure 7. *PhaSeal* touch test results showing no fluorescein exposure.

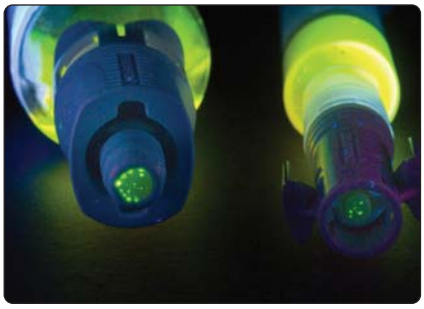

Figure 8. *OnGuard Tevadaptor* system with release of fluorescein droplets.

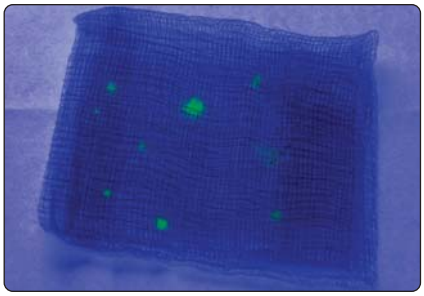

Figure 9. *OnGuard Tevadaptor* system touch test results showing fluorescein exposure.

Figure 10. *Alaris Smart Site* with release of fluorescein droplets.

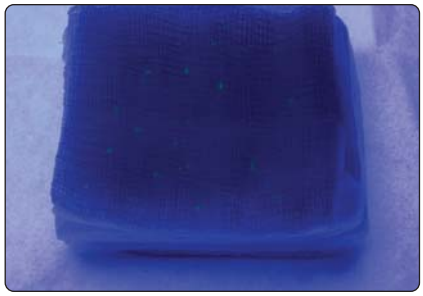

Figure 11. *Alaris Smart Site* touch test results show fluorescein exposure.

tions (see Figures 8 through 11), hence demonstrating the potential to release drug solutions into the work environment and pose health risks to the worker and those within the environment of care.

During the preparation phase, touch testing the *Tevadaptor* (*OnGuard*) system components resulted in visible fluorescein leaks ranging in size from less than 1 to 10 mm in diameter. A 6-mm fluorescein drop flew back onto the mat when disengaging the syringes. Visual contamination was observed in 67% (10/15) of the *Tevadaptor* vial adapter, 47% (7/15) of the *Tevadaptor* syringe adapter, and 80% (12/15) of the touch test. Touch testing the *Texium* components resulted in visible fluorescein leaks in sizes less than or equal to 1 mm in diameter. Visual contamination was observed in 87% (13/15) of the *Smart Site* vented vial access device, 87% (13/15) of the *Texium* closed male luer syringe adapter, and 93% (14/15) of the touch test. During the preparation phase, no visual leakage was observed with the *PhaSeal* system.

During the administration phase, visual contamination was observed in 60% (9/15) of the *Tevadaptor* syringe adapter, 60% (9/15) of the *Tevadaptor* port adapter, and 60% (9/15) of the touch test. Visual contamination was observed in 100% (15/15) of the *Texium* closed male luer syringe adapter, 80% (12/15) of the *Texium* port adapter, and 100% (15/15) of the touch test. During the administration phase, the tests of the *PhaSeal* system resulted in no observed leakage.

CONCLUSION

Filter products, such as the *Tevadaptor* (*OnGuard*) system and the *Alaris* system, which rely on a 0.22-micron filter, did not retain the titanium particles and, therefore, could not meet the NIOSH and ISOPP definitions of a CSTD. They were clearly not airtight or leak proof. These systems also showed visible leakage of fluorescein at the dry connections and, therefore, cannot be considered closed from this perspective either.

Only the *PhaSeal* system met the NIOSH and ISOPP definitions of a CSTD.

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