

How closed is a closed system?

Cytotoxic drugs have been associated with reproductive and developmental toxicity in health care workers and there is limited evidence for increased cancer rates in healthcare workers exposed to cytotoxic drugs

A study has shown that several of the closed-system drug transfer devices that are currently marketed may not prevent the release of drug vapours. The study, which was showcased at the ASHP Midyear Clinical Meeting in Anaheim, California in December, was conducted by James Jorgenson (Director of Pharmacy, University of Utah Hospital and Adjunct Associate Professor, University of Utah Health Sciences Center, Salt Lake City, Utah, USA) and his team.

When cytotoxic doses are reconstituted, an overpressure is often generated in the vial and this sometimes results in the escape of aerosols or vapours as pressures are equalised. Closed system drug-transfer devices are recommended by the National Institute for Occupational Safety and Health (NIOSH) for the preparation of cytotoxic doses to contain aerosols and vapours and thereby to minimise the chances of occupational exposure of pharmacy and nursing personnel.

Mr Jorgenson and his colleagues undertook a study to determine how effectively the available drug-transfer devices contained vapours. They tested five devices:

- Tevadaptor Vial Adaptor System (Teva Medical Ltd).
- Chemo Mini-Spike Plus Dispensing Pin (B. Braun Medical Inc).
- Alaris Smart Site (Cardinal Health).
- Chemoprotect Spike (Codan US Corporation).
- PhaSeal Protector 50 and Injector Luer Lock (Carmel Pharma).

In order to simulate the effects of drug vapour, titanium tetrachloride ($TiCl_4$) was placed in glass drug vials. This substance generates dense smoke



and expands greatly when in contact with moisture in the air. The drug transfer devices were fitted and moist air was injected. The results were not only observed but were also filmed. All the devices except PhaSeal allowed smoke to escape. Real-time filming suggested that the smoke was escaping through the devices rather than from a faulty connection with the vial.

Mr Jorgenson commented that one of the reasons for choosing titanium tetrachloride is that its molecular weight is of the same order as many commonly used cytotoxic drugs. (molecular weights for $TiCl_4$, 5-fluorouracil and cyclophosphamide are 190, 130 and 261, respectively). Smoke particles of $TiCl_4$ have a diameter of 0.48nm.

As the PhaSeal product was the only one that prevented the release of titanium smoke, the authors concluded that this was the only device that satisfies the definition of a closed system drug-transfer device.

A full report of the study will be published in 2007

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for increased cancer rates in healthcare workers exposed to cytotoxic drugs, Thomas Connor (Research Biologist at the National Institute for Occupational Safety and Health [NIOSH], Cincinnati, Ohio, USA) told the audience in a session devoted to handling of hazardous drugs. A systematic review had identified two significant studies concerned with spontaneous abortions and two concerned with fetal malformations. No studies concerned with stillbirths had been identified. There were no recent studies of cancer caused by occupational exposure to cytotoxic agents and no studies of this type had been conducted in the USA. ■

Resources

NIOSH Alert: Preventing Occupational Exposures to Antineoplastic and other Hazardous Drugs in Health Care Settings [DHHS (NIOSH) Publication No. 2004-165]. Available from: <http://www.cdc.gov/NIOSH>

Dranitsaris G, Johnson M, Poirier S, et al. Are health care providers who work with cancer drugs at an increased risk for toxic events? A systematic review and meta-analysis of the literature. *J Oncol Pharm Practice* 2005;11:69-78.