Preventing Exposure to Hazardous Drugs:

Engineering-Control Recommendations in the NIOSH Alert

By Duane Hammond and Kenneth R. Mead, MS, PE

IN 2004, NIOSH PUBLISHED AN ALERT TITLED "PREVENTING OCCUPATIONAL Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings," with the purpose of increasing awareness of the health risks posed by working with hazardous drugs, and of providing employers and health care workers with preliminary recommendations to reduce the potential for occupational exposures. The need for an alert developed following an increase in published data documenting workplace contamination and/or health effects to workers who were exposed to hazardous drugs. The published data reveals evidence of health effects such as skin rashes, developmental and reproductive effects (including infertility, spontaneous abortions, and congenital malformations), and possibly cancer. Furthermore, the published studies provide evidence that workers are being exposed to hazardous drugs and are experiencing serious health effects despite current work-practice guidelines. The recommendations section in the alert provides information on how to reduce worker exposures, beginning when hazardous drugs enter a health care facility, through preparation, administration, and post-administration. The alert highlights the importance of using ventilated cabinets, such as biological safety cabinets (BSCs) and barrier isolators, designed to protect workers from exposure to hazardous drugs in health care facilities.

Ventilated Cabinet Recommendations

The NIOSH alert defines a ventilated cabinet as:

> A type of engineering control designed for purposes of worker protection. These devices are designed to minimize worker exposures by controlling emissions of airborne contaminants through the following:
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> - The full or partial enclosure of a potential contaminant source
> - The use of airflow capture velocities to capture and remove airborne contaminants near their point of generation
> - The use of air pressure relationships that define the direction of airflow into the cabinet

The *Ventilated Cabinets* section of the alert lists engineering control recommendations identified to reduce the potential for worker exposures and discusses the importance of protecting workers from occupational exposures to hazardous drugs, while acknowledging that many of these drugs must be compounded within aseptic environments. The alert points out that drug containment and aseptic compounding are not mutually exclusive objectives. When aseptic technique is required or recommended for a hazardous drug, health care facilities should provide a work environment that protects both the worker and the hazardous drug from contamination by following recommendations from the NIOSH alert, as well as the applicable regulations from USP Chapter <797> and individual state boards of pharmacy. The ventilated cabinet design options identified to provide both aseptic technique and aerosolized drug containment include Class II BSCs, Class III BSCs, and aseptic-containment isolators. Horizontal laminar airflow workbenches should never be used for the preparation of a hazardous drug.

The alert recommends that hazardous drugs be prepared within a dedicated area devoted solely to preparing hazardous drugs, and that access to this area should be restricted to authorized personnel. The alert also recommends that the ventilated cabinet's exhaust be HEPA filtered and directed to the outdoors whenever possible—well away from

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Biological safety cabinets and barrier isolators can protect pharmacy workers from exposure to hazardous drugs.

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windows, doors, and other air intake locations. Proper cabinet performance is also emphasized; the performance of ventilated cabinets should be field certified every six months, consistent with OSHA's requirements for Class II BSCs. Certifications should be done in accordance with applicable published testing standards such as the American Glovebox Society's AGS 2001 Guidelines for Gloveboxes or NSF International's Standard NSF/ANSI 49 Class II (laminar flow) biosafety cabinetry.[1]

For more information on particle vapor interactions consult the 9th edition of *American Conference of Governmental Industrial Hygienists Air Sampling Instruments*, chapter four.

NIOSH provides an annually updated list of drugs considered hazardous: http://www.cdc.gov/niosh/docs/2004-165/2004-165d.html

To view the NIOSH alert, visit: http://www.cdc.gov/niosh/docs/2004-165/

Closed-System Drug Transfer Devices

The NIOSH alert discusses the use of closed-system drug transfer devices and documents studies that have shown a decrease in contaminants inside of a Class II BSC, as well as reduced concentrations of common hazardous drugs in the urine of health care workers when a closed-system drug transfer device is used. NIOSH warns, however, that a closed-system drug transfer device should not be used as a substitute for a ventilated cabinet during compounding processes where hazardous drugs are used. It is also important to use appropriate work practices and personal protective equipment (PPE), including double gloves and protective gowns, even when using a closed-system device.

Particle Vapor Interactions from Hazardous Drugs

The traditional design practice for ventilated cabinets involved with hazardous drug preparation has been to filter the contaminated air-stream with HEPA filters then return all or a portion of the air back into the cabinet and/or pharmacy, while exhausting the rest (if any) to the outdoors. HEPA filters only capture aerosols, not gases or vapors. The most common hazardous drugs are aqueous injections capable of generating liquid aerosol during the drug preparation process. These aerosols may pose an inhalation risk depending on whether vaporization, sublimation, filter bypass, or premature filter failure occurs. Antineoplastic and other hazardous drugs generally have low vapor pressures and are not traditionally considered to pose a vapor-inhalation risk. However, two studies have demonstrated the vaporization potential of at least five common antineoplastic drugs.[2,3]

For most hazardous drugs, there is generally insufficient information from the drug manufacturers or published literature to know if vaporization or sublimation of an aerosol generated from a compounding process will occur, especially when the particles are exposed to the extreme conditions encountered at the face of a filter. Without such information, pharmacies compounding hazardous drugs within cabinets that re-circulate HEPA-filtered air will not know if they are successfully containing the aerosolized drug, or if the contaminated filter is functioning as a hazardous-drug vapor generator as the captured aerosol slowly changes to a vapor state and flows out into the pharmacy.

With the continuous development of bioengineered drugs and drugs that incorporate nanotechnology, it is extremely difficult to determine that a ventilated cabinet with HEPA-filtered, re-circulated air will offer sufficient exposure protection from every hazardous drug that will ever be compounded within it. The cabinet's adequacy will depend on the hazardous drug's occupational exposure limit, the amount of ambient aerosol generated from the process, the frequency of the process, and various physical characteristics of the aerosol. Because vaporization has been shown to occur from some hazardous drugs, and information about safe exposure limits is typically not available to pharmacies, the NIOSH alert recommends not using a ventilated cabinet that re-circulates air inside the cabinet or that exhausts air back into the room environment. Exceptions to this recommendation include those circumstances in which the only hazardous drugs to be used in that cabinet are known not to volatilize (evaporate) during compounding or after capture by the HEPA filter, or in the case of partial within-cabinet recirculation, when the process frequency, aerosol-generation rates, and air-dilution rates within the cabinet can be demonstrated to sufficiently prevent exposure through vapor inhalation or through surface contamination on the finished product. The drug manufacturer should supply volatilization information, preferably in the drug package insert, in the material safety data sheet (MSDS), or by air-sampling data.

Information Gaps and Recommended Research

Information gaps exist regarding occupational exposures to hazardous drugs, such as dose-response relationships, interpretation of exposure-monitoring results, and other important occupational health information. Identification and adoption of uniform sampling procedures and analytical methods are needed for many hazardous drugs. However, as analytical chemists develop techniques that yield lower detection limits, employers are faced with difficult decisions about how to handle positive air-sampling, wipe-sampling, or urine-sample results when the level is detectable but extremely low. In the absence of other sources, employers are encouraged to request information from the drug manufacturers/suppliers regarding safe levels for occupational exposure to their hazardous drugs.

Knowledge gaps involving engineering controls also exist, such as uncertainties related to decontamination agent selection, effectiveness for various hazardous drugs, the incorporation of uniform nomenclature, and performance criteria and testing standards for containment isolators and closed-system transfer devices. NIOSH is conducting ongoing research activities to address many of these gaps and is involved in a new industry-manufacturer partnership that hopes to address the equipment-related issues. P&P

Duane Hammond, a mechanical engineer for NIOSH in Cincinnati, Ohio, has been conducting occupational health research at NIOSH for three years, focusing on evaluating the effectiveness of engineering controls in preventing hazardous occupational exposures.

Kenneth R. Mead, MS, PE, has been a mechanical engineer at NIOSH for more than 12 years. His primary responsibilities include conducting laboratory and field research on the design, evaluation, and recommendation of engineering controls to reduce hazardous exposures in occupational settings. He has written several articles on expedient patient isolation, building vulnerabilities, and other engineering topics.

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