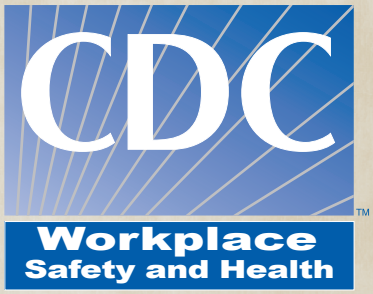

Chemotherapy Drug Evaluation at a Medical Laboratory – Pennsylvania

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Health Hazard Evaluation Report
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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
NIOSH *National Institute for Occupational Safety and Health*

The employer shall post a copy of this report for a period of 30 calendar days at or near the workplace(s) of affected employees. The employer shall take steps to insure that the posted determinations are not altered, defaced, or covered by other material during such period. [37 FR 23640, November 7, 1972, as amended at 45 FR 2653, January 14, 1980].

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Abbreviations

ACGIH®	American Conference of Governmental Industrial Hygienists
BSC	Biological safety cabinet
CFR	Code of Federal Regulations
cm	Centimeter
cm^2	Centimeter squared
HHE	Health hazard evaluation
IARC	International Agency for Research on Cancer
LOD	Limit of detection
LOQ	Limit of quantification
NAICS	North American Industry Classification System
ng	Nanogram
$ng/100\,cm^2$	Nanograms per one hundred centimeters squared
NIOSH	National Institute for Occupational Safety and Health
OEL	Occupational exposure limit
OSHA	Occupational Safety and Health Administration
PEL	Permissible exposure limit
PPE	Personal protective equipment
REL	Recommended exposure limit
STEL	Short-term exposure limit
TLV®	Threshold limit value
TWA	Time-weighted average
WEEL™	Workplace environmental exposure level

Highlights of the NIOSH Health Hazard Evaluation

The National Institute for Occupational Safety and Health (NIOSH) received an employee request for a health hazard evaluation at a medical laboratory in Pennsylvania. Employees were concerned with potential adverse health effects associated with working with a wide range of chemotherapy drugs.

What NIOSH Did

- We visited the medical laboratory in March 2011.
- We watched employees work and interviewed them about their work practices and health concerns.
- We reviewed employee training on handling chemotherapy drugs and the health effects that could occur as a result.
- We tested work surfaces for cyclophosphamide, a chemotherapy drug.

What NIOSH Found

- We did not find cyclophosphamide on any work surfaces.
- We found the work practices for handling chemotherapy drugs to be appropriate.
- The employee chemotherapy drug and health effects training should be more specific to the work being done at the laboratory.
- None of the employees whom we interviewed reported chronic health problems that were related to their work.

What Managers Can Do

- Include information in the chemotherapy drug and health effects training that is pertinent to the job tasks that employees will perform.
- Provide employees with information about chemotherapy drugs and reproductive health.

What Employees Can Do

- Follow recommended work practices and personal protective equipment procedures.
- Continue to learn how to work with chemotherapy drugs safely.

Summary

NIOSH evaluated potential exposures to chemotherapy drugs among employees of a medical laboratory. We did not detect cyclophosphamide, a chemotherapy drug commonly used at the laboratory, on any work surfaces. Employees were observed using safe work practices and wearing appropriate protective equipment. We also found no adverse medical symptoms among employees that can be linked to occupational exposures at the laboratory.

In June 2010, NIOSH received an HHE request from employees who were concerned about their potential exposure to chemotherapy drugs at a medical laboratory in Pennsylvania. The chemotherapy drugs were used to treat biological specimens to help determine which chemotherapy drug protocol would potentially benefit the patient the most. Employees were concerned with reproductive problems and adverse health effects associated with these drugs.

We visited the medical laboratory on March 22–23, 2011. We observed work processes, practices, and conditions. We interviewed 51 employees about their health and their concerns related to chemotherapy drugs and collected surface wipe samples for cyclophosphamide, one of several chemotherapy drugs used at the medical laboratory.

We detected no cyclophosphamide on work surfaces. While most of the 51 interviewed employees at the laboratory reported handling chemotherapy drugs during the course of their work, none reported chronic health effects associated with their work, and three reported experiencing acute symptoms during their work. Employees were aware of the potential risks from exposure to chemotherapy drugs and closely followed administrative procedures and PPE recommendations.

We recommended that the medical laboratory continue to control exposures to chemotherapy drugs to levels as low as are reasonably achievable because the facility uses drugs that are considered hazardous [NIOSH 2010]. Control of these exposures can be validated by routine surface sampling for chemotherapy drugs used at the facility.

Keywords: NAICS 621511(Medical Laboratories), chemotherapy drugs, oncology, antineoplastic drugs, cancer research

In June 2010, NIOSH received an HHE request from employees at a medical laboratory in Pennsylvania. The employees were concerned about potential reproductive effects (miscarriages and irregular menstrual cycles), acute health effects (rash and cough), and chronic health effects (hair thinning, premature graying, and allergies) that they believed were related to their exposure to chemotherapy drugs.

Because of an ongoing OSHA investigation, the NIOSH evaluation of the medical laboratory was delayed until March 22–23, 2011, when we observed work processes, practices, and conditions. We spoke with employees about health and workplace concerns related to chemotherapy drugs. We also collected surface wipe samples for cyclophosphamide, one of several chemotherapy drugs used at the medical laboratory. An interim letter containing the results from the surface wipe samples was sent to the medical laboratory management, an employee representative, and the HHE requestors in June 2011.

Process Description

The medical laboratory consisted of clinical laboratories, research laboratories, and administrative areas. The company employed more than 250 people, including approximately 50 clinical laboratory employees.

The medical laboratory received biological specimens and treated them with chemotherapy drugs as directed by the ordering physician or on the basis of the type of cancer to identify the most effective chemotherapy drug(s) for treating the patient's tumor or specimen. The biological specimen could consist of tissue biopsies or ascitic (pleural) fluid. The specimen was minimally processed by the ordering physician and shipped to the medical laboratory where it was manually plated onto growth media and placed into an incubator. After sufficient growth had occurred and the number of cells on the plate were counted and recorded, the specimen was ready for treatment with chemotherapy drugs. Chemotherapy drugs used at the medical laboratory included cyclophosphamide, doxorubicin, cisplatin, carboplatin, vincristine, paclitaxel, and many others. Cyclophosphamide is classified as a Group 1 Carcinogen by IARC, which means that the drug is a known human carcinogen [IARC 1998]. See the Appendix for more information on the health effects related to chemotherapy drugs. Figure 1 illustrates three employees applying chemotherapy drugs.

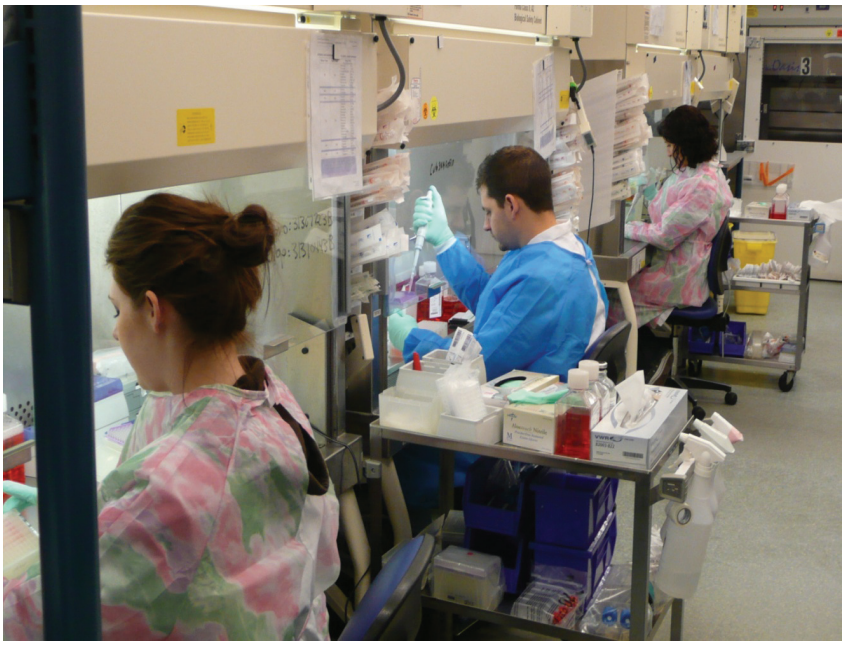

Figure 1. Clinical laboratory technicians working with chemotherapy drugs and patient biological specimens inside BSCs.

A wide range of chemotherapy drugs as described by the ordering physician were prepared by clinical laboratory technicians in various dilutions and then administered to the specimen in assorted combinations. The amount of the chemotherapy drug applied to the biological specimen was approximately 100 – 1,000 times lower than the amount of the drug used in patient treatment. Employees administered chemotherapy drugs to the specimens with automated pipettes or with a proprietary, fully automated computer-controlled system that distributed the chemotherapy drugs into wells containing a patient's cells. After dispensing the drugs, the automated system discarded the tip into a chemotherapy waste receptacle. The chemotherapy waste receptacle was located below the automated system's working surface and was emptied by employees at least daily.

Once treated, the specimen plates were incubated to allow the drug to stay in contact with the patient's cells. After a predetermined amount of time the plates were retrieved and the chemotherapy drug treatment was evaluated for effectiveness (via cell count, morphology, etc.). The report from the laboratory to the ordering physician described the effectiveness of the chemotherapy drug as responsive, intermediate response, or nonresponsive.

Exposure Assessment

We collected cyclophosphamide surface wipe samples throughout the medical laboratory including the clinical laboratory areas, chemotherapy drug storage areas, research and development areas, and general office space. Although sampling methods exist for several drugs (e.g., cisplatin, doxorubicin, and ifosfamide), we sampled for cyclophosphamide because it was used extensively at the facility, a surface sampling method was available for this agent, and we believed that the results for this drug would be indicative of potential exposures to the other drugs.

The samples were collected on Alpha® Texwipe swabs moistened with an extraction solvent comprised of 50% acetonitrile and 50% deionized water. A 10 cm x 10 cm disposable square template was used to outline a 100 cm^2 sampling area. Wipe samples were analyzed for cyclophosphamide by high performance liquid chromatography/mass spectrometry with an LOD of 2.0 ng cyclophosphamide per sample and an LOQ of 6.7 ng of cyclophosphamide per sample. All media and field blanks were below the LOD. The sampling method is an internal procedure developed by Bureau Veritas North America, the NIOSH contract laboratory used for this HHE. Figure 2 illustrates two sample locations and the use of the sample templates. In areas where the template could not be used, a 100 cm^2 sampling area was estimated.

We observed employees handling chemotherapy drugs from the beginning of the process through drug disposal. We also reviewed written and video training materials for employees about handling chemotherapy drugs and the potential health effects related to these drugs. Clinical laboratory technicians are required to watch the training video on hire and annually. Upon completion of the training, they are required to pass a written exam to demonstrate competency.

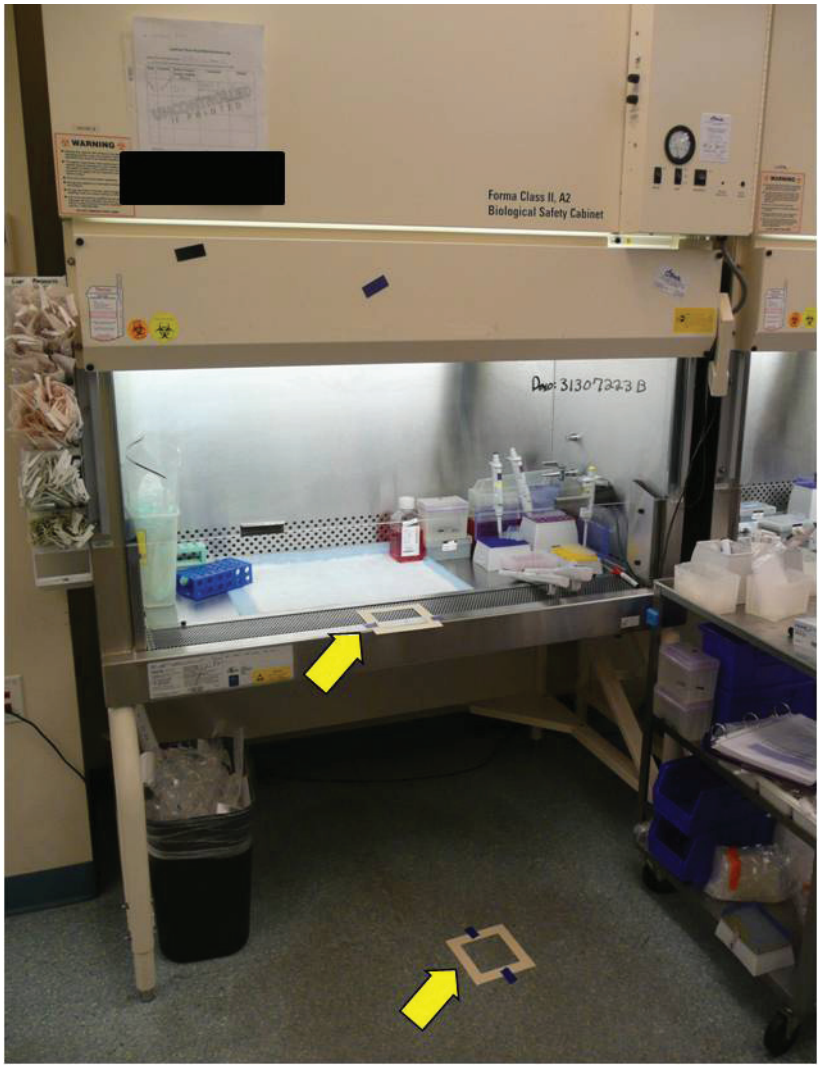

Figure 2. A BSC containing a sample template on the airfoil of the BSC and a sample template on the floor directly in front of the BSC.

Medical Assessment

We held confidential interviews with clinical laboratory technicians and laboratory supervisors to discuss their work practices, medical (including pertinent reproductive) history, and symptoms experienced in the course of their employment. Symptoms asked about included constitutional, dermatologic, respiratory, and gastrointestinal symptoms. We interviewed employees in person and by telephone. After the visit we obtained additional employee information by telephone and pertinent medical records. All 51 clinical laboratory technicians and laboratory supervisors on the first and second shifts participated in the interviews.

We observed all employees wearing two pairs of chemotherapy protective gloves and removing their outer gloves properly when removing their hands from the BSC. Double gloving appeared consistent throughout the clinical laboratory areas. We also observed employees properly disposing chemotherapy drugs and chemotherapy drug contaminated equipment.

We noted that the doors to the automated dispensing machines could be lifted while the robotic head was still moving within the work envelope. Employees could enter into the work envelope to place or remove trays while the robotic head was still active. No electrical interlocks were installed on the automated dispensing machines.

We noticed a small room that contained three doors leading to the Big Laboratory, the Small Laboratory, and the rest of the facility. Because all three doors opened inward into this small room, the area could quickly become congested with employees, some of whom were carrying chemotherapy drugs or chemotherapy drug treated wells.

We observed that some employees changed their shoes when leaving the medical laboratory. While this was not a standard operating procedure at the laboratory, numerous employees reported wearing a dedicated pair of shoes within the laboratory and then changing into another pair of shoes before leaving the premises.

Employee training on handling chemotherapy drugs and their potential health effects was very comprehensive. The training video was detailed and discussed safe handling practices; the receipt, storage, labeling, and transport of drugs; the use of BSCs and PPE; and waste disposal and spill control procedures. However, individual training topics were not available for the specific job titles and job tasks at the medical laboratory, resulting in some employees receiving training in areas that were not pertinent to their work.

Exposure Assessment

The 40 surface wipe samples (Table 1) were analyzed for cyclophosphamide; all results were below the LOD of 2 ng per sample. These samples were collected in areas of high chemotherapy drug usage as well as office areas that would not be expected to have chemotherapy drug residue.

Table 1. Cyclophosphamide surface wipe sample results, March 2011

Location	Description	Result (ng/100 cm^2)
Small Laboratory	Liquid handler grill*	ND†
	Grill liquid handler BioProtect II on right*	ND
	Floor directly in front of BSC 2	ND
	Floor seam*	ND
	Floor by liquid handler BioProtect II on right	ND
	BSC 2 airfoil*	ND
	BSC 14 airfoil*	ND
	Chemotherapy waste container lid	ND
	Incubator door	ND
	Floor directly in front of BSC 14	ND
	Floor adjacent to waste container near BSC 4	ND
	BSC 18 work surface	ND
	BSC 18 airfoil*	ND
	Liquid handler BioProtect II waste drop*	ND
	Liquid handler BioProtect II between trays 22-28*	ND
	Liquid handler tray 30*	ND
	Floor next to waste container near liquid handler	ND
Big Laboratory	Floor directly in front of incubator	ND
	BSC 3 work surface	ND
	BSC 3 airfoil*	ND
	Liquid handler BioProtect II waste drop*	ND
	Liquid handler BioProtect II tray 30*	ND
	Liquid handler grill*	ND
	Floor directly in front of liquid handler	ND
	Liquid handler grill*	ND
ICC Room	Countertop near microscope	ND
	Floor near balance	ND
	Balance table	ND
	Floor near freezer	ND
Scanning Room	Countertop	ND
	Floor near center bench	ND
	Counter	ND
Research/ Development	Liquid handler airfoil*	ND
	Floor directly in front of liquid handler	ND
	Liquid handler BioProtect II waste drop*	ND
Shipping/ Receiving	Table	ND
	Floor near refrigerator	ND
Office Area	Desk on second floor	ND
	Desk on first floor	ND
	Desk on first floor	ND

*Estimated 100 cm^2 surface area
†ND = Not detected; below the LOD of 2 ng/sample.

Medical Assessment

The median age of the 51 clinical laboratory technicians and supervisors interviewed was 25 years with a range of 22 to 49 years. Thirty-four (67%) were female. Twenty-five employees worked first shift, and 26 employees worked second shift. The median number of years worked at the laboratory was 1.5 with a range of 7 months to 4 years.

Most (96%) employees reported handling chemotherapy drugs during the course of their work. Their work activities included preparing chemotherapy drugs for treatment, treating tissue samples with chemotherapy drugs, disposing chemotherapy drug waste in the trash, and cleaning surfaces contaminated with chemotherapy drug waste. None reported handling chemotherapy drugs prior to their job at this laboratory.

Most employees denied health symptoms while handling chemotherapy drugs or while working near others handling chemotherapy drugs. Two employees reported experiencing headache, and one employee reported eye irritation either while handling chemotherapy drugs or while working near others who were working with chemotherapy drugs.

None of the employees reported a history of cancer, leukemia, lymphoma, kidney disease, urinary tract disorder, liver disease, skin disorder, or multiple sclerosis. One employee reported a history of a blood disorder that, in most cases, is caused by an autoimmune response. This employee had worked at this laboratory for more than 2 years before receiving this diagnosis. However, the employee had evidence of this disorder before beginning work at this laboratory, making an occupational etiology less likely. This employee's personal physician concurred with this assessment, and none of the other employees reported being diagnosed with any other autoimmune disorder or blood disorder during their employment at the laboratory.

All females interviewed reported having regular menstrual cycles, and none of the male or female employees reported any fertility issues. One employee reported having a miscarriage during the time of her employment. However, her conception occurred prior to the commencement of her employment, and the miscarriage occurred during her training period shortly after being hired. One employee reported having two successful pregnancies during her employment at the laboratory.

Results (continued)

All employees reported being provided with written policies regarding PPE use and receiving training on PPE use in the past 12 months. Most (98%) employees reported receiving training on possible health effects related to exposure to chemotherapy drugs.

All employees involved in preparing chemotherapy drugs reported always using a BSC. All employees reported always wearing double gloves and disposable gowns when handling chemotherapy drugs; these practices were confirmed by our observations. Most reported changing their outer gloves at least every 30 minutes (82%), their inner gloves at least every 60 minutes (78%), and their disposable gown every 3–6 hours (86%). None of the employees reported consuming food and drink in the work area.

Discussion

Cyclophosphamide was not detected in the samples we collected during our visit. Because the facility uses a number of different chemotherapy drugs, it is possible that other drugs may have been present. We believe it is prudent and necessary to control potential exposures to all chemotherapy drugs to levels as low as reasonably achievable. It should be noted that we focused our evaluation on the clinical laboratory employees, so our findings may not be generalizable to other employees at the facility such as those working in the research laboratories or administration areas.

While most clinical laboratory employees at the facility reported handling chemotherapy drugs during the course of their work, none reported chronic health effects associated with their work, and only three reported acute symptoms they associated with their work. We are unable to definitively determine the etiology of the headache and eye irritation reported by these three employees. However, our environmental sampling revealed low exposures, and employees adhered to strict handling of the chemotherapy drugs during our visit, so it is unlikely that these symptoms were related to chemotherapy drug exposure.

Conclusions

Cyclophosphamide was not detected on any work surfaces. Employees were observed performing safe work practices and wearing appropriate PPE. No adverse health effects related to exposure to chemotherapy drugs were identified in employees at the medical laboratory.

Although no cyclophosphamide was detected on any work surfaces, we nonetheless recommend the actions listed below to create a more healthful workplace. We encourage the laboratory to use a labor-management health and safety committee or working group to discuss the recommendations in this report and develop an action plan. Those involved in the work can best set priorities and assess the feasibility of our recommendations for the specific situation at the laboratory. Our recommendations are based on the hierarchy of controls approach. This approach groups actions by their likely effectiveness in reducing or removing hazards. In most cases, the preferred approach is to eliminate hazardous materials or processes and install engineering controls to reduce exposure or shield employees. Until such controls are in place, or if they are not effective or feasible, administrative measures and/or personal protective equipment may be needed. Comprehensive exposure control strategies for chemotherapy drugs can be found in the OSHA Technical Manual, Section VI, Chapter 2: Controlling Occupational Exposure to Hazardous Drugs [OSHA 1999] and the NIOSH Alert: Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings [NIOSH 2004].

Engineering Controls

Engineering controls reduce exposures to employees by removing the hazard from the process or placing a barrier between the hazard and the employee. Engineering controls are very effective at protecting employees without placing primary responsibility of implementation on the employee.

1. Install safeguards (i.e., interlocking system) on the liquid handlers to prevent entry into the robotic head work envelope during use.
2. Use a dedicated chemotherapy drug tray that is at least 2 inches deep to contain any spilled drugs within the tray in case of an accident when transporting chemotherapy drugs or specimen plates containing treated cells. This may be of greatest concern in the congested small room connecting the Small Laboratory and the Big Laboratory.

Administrative Controls

Administrative controls are management-dictated work practices and policies to reduce or prevent exposures to workplace hazards. The effectiveness of administrative changes in work practices for controlling workplace hazards is dependent on management commitment and employee acceptance. Regular monitoring and reinforcement are necessary to ensure that control policies and procedures are not circumvented in the name of convenience or production.

1. Review and revise training materials to make the information more relevant to specific job titles and job requirements at the medical laboratory. For example, consider creating individual training modules addressing safe handling practices; potential health effects from working with chemotherapy drugs; the receipt, storage, labeling, and transport of drugs; the use of BSCs and PPE; and waste disposal and spill control procedures.
2. Ensure that employees know to whom they should report any possible work-related health problems. Encourage employees to notify appropriate management representatives in a timely manner.
3. Inform all employees of the risks, including reproductive risks, associated with exposure to chemotherapy drugs upon hire and annually. More information on the potential effects from occupational exposure to chemotherapy drugs can be found at http://www.cdc.gov/niosh/topics/antineoplastic/effects.html#b.
4. Continue the medical surveillance program for employees and refer to the OSHA Technical Manual: Controlling Occupational Exposure to Hazardous Drugs, Section VI Chapter 2 [OSHA 1999]. The program should include a medical and exposure history, physical examination, a complete blood count with differential and reticulocyte count, and a urine dipstick or urinalysis on hire and annually.

RECOMMENDATIONS (CONTINUED)

Personal Protective Equipment

PPE is the least effective means for controlling employee exposures. Proper use of PPE requires a comprehensive program, and calls for a high level of employee involvement and commitment to be effective. The use of PPE requires the choice of the appropriate equipment to reduce the hazard and the development of supporting programs such as training, change-out schedules, and medical assessment if needed. PPE should not be relied upon as the sole method for limiting employee exposures. Rather, PPE should be used until engineering and administrative controls can be demonstrated to be effective in limiting exposures to acceptable levels.

1. Instruct employees to wear dedicated work shoes at the medical laboratory and change shoes when they leave to prevent contamination of their personal vehicles and homes.

REFERENCES

IARC [1998]. Some antineoplastic and immunosuppressive agents. Lyon: IARC monographs on the evaluation of carcinogenic risks to humans; Vol 26. International Agency for Research on Cancer.

NIOSH [2004]. NIOSH Alert: Preventing occupational exposure to antineoplastic and other hazardous drugs in health care settings. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2004-165.

NIOSH [2010]. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2010. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2010-167.

OSHA [1999]. OSHA technical manual, TED 1–0.15A, Sec VI, Chapter II: Categorization of drugs as hazardous. [http://www.osha.gov/dts/osta/otm/otm_toc.html]. Date accessed: August 2011.

Appendix: Occupational Exposure Limits and Health Effects

In evaluating the hazards posed by workplace exposures, NIOSH investigators use both mandatory (legally enforceable) and recommended OELs for chemical, physical, and biological agents as a guide for making recommendations. OELs have been developed by federal agencies and safety and health organizations to prevent the occurrence of adverse health effects from workplace exposures. Generally, OELs suggest levels of exposure that most employees may be exposed to for up to 10 hours per day, 40 hours per week, for a working lifetime, without experiencing adverse health effects. However, not all employees will be protected from adverse health effects even if their exposures are maintained below these levels. A small percentage may experience adverse health effects because of individual susceptibility, a preexisting medical condition, and/or a hypersensitivity (allergy). In addition, some hazardous substances may act in combination with other workplace exposures, the general environment, or with medications or personal habits of the employee to produce adverse health effects even if the occupational exposures are controlled at the level set by the exposure limit. Also, some substances can be absorbed by direct contact with the skin and mucous membranes in addition to being inhaled, which contributes to the individual's overall exposure.

Most OELs are expressed as a TWA exposure. A TWA refers to the average exposure during a normal 8- to 10-hour workday. Some chemical substances and physical agents have recommended STEL or ceiling values where adverse health effects are caused by exposures over a short period. Unless otherwise noted, the STEL is a 15-minute TWA exposure that should not be exceeded at any time during a workday, and the ceiling limit is an exposure that should not be exceeded at any time.

In the United States, OELs have been established by federal agencies, professional organizations, state and local governments, and other entities. Some OELs are legally enforceable limits, while others are recommendations. The U.S. Department of Labor OSHA PELs (29 CFR 1910 [general industry]; 29 CFR 1926 [construction industry]; and 29 CFR 1917 [maritime industry]) are legal limits enforceable in workplaces covered under the Occupational Safety and Health Act of 1970. NIOSH RELs are recommendations based on a critical review of the scientific and technical information available on a given hazard and the adequacy of methods to identify and control the hazard. NIOSH RELs can be found in the *NIOSH Pocket Guide to Chemical Hazards* [NIOSH 2010]. NIOSH also recommends different types of risk management practices (e.g., engineering controls, safe work practices, employee education/training, personal protective equipment, and exposure and medical monitoring) to minimize the risk of exposure and adverse health effects from these hazards. Other OELs that are commonly used and cited in the United States include the TLVs recommended by ACGIH, a professional organization, and the WEELs recommended by the American Industrial Hygiene Association, another professional organization. The TLVs and WEELs are developed by committee members of these associations from a review of the published, peer-reviewed literature. They are not consensus standards. ACGIH TLVs are considered voluntary exposure guidelines for use by industrial hygienists and others trained in this discipline "to assist in the control of health hazards" [ACGIH 2011]. WEELs have been established for some chemicals "when no other legal or authoritative limits exist" [AIHA 2011].

Outside the United States, OELs have been established by various agencies and organizations and include both legal and recommended limits. The Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA, Institute for Occupational Safety and Health of the German Social Accident

Insurance) maintains a database of international OELs from European Union member states, Canada (Québec), Japan, Switzerland, and the United States. The database, available at http://www.dguv.de/ifa/en/gestis/limit_values/index.jsp, contains international limits for over 1,500 hazardous substances and is updated periodically.

Employers should understand that not all hazardous chemicals have specific OSHA PELs, and for some agents the legally enforceable and recommended limits may not reflect current health-based information. However, an employer is still required by OSHA to protect its employees from hazards even in the absence of a specific OSHA PEL. OSHA requires an employer to furnish employees a place of employment free from recognized hazards that cause or are likely to cause death or serious physical harm [Occupational Safety and Health Act of 1970 (Public Law 91–596, sec. 5(a)(1))]. Thus, NIOSH investigators encourage employers to make use of other OELs when making risk assessments and risk management decisions to best protect the health of their employees. NIOSH investigators also encourage the use of the traditional hierarchy of controls approach to eliminate or minimize identified workplace hazards. This includes, in order of preference, the use of (1) substitution or elimination of the hazardous agent, (2) engineering controls (e.g., local exhaust ventilation, process enclosure, dilution ventilation), (3) administrative controls (e.g., limiting time of exposure, employee training, work practice changes, medical surveillance), and (4) personal protective equipment (e.g., respiratory protection, gloves, eye protection, hearing protection). Control banding, a qualitative risk assessment and risk management tool, is a complementary approach to protecting employee health that focuses resources on exposure controls by describing how a risk needs to be managed. Information on control banding is available at http://www.cdc.gov/niosh/topics/ctrlbanding/. This approach can be applied in situations where OELs have not been established or can be used to supplement the OELs, when available.

Below we provide the OELs and surface contamination limits for the compounds we measured, as well as a discussion of the potential health effects from exposure to these compounds.

Cyclophosphamide

Cyclophosphamide has been categorized as a Group 1 Carcinogen (carcinogenic to humans) [IARC 1998]. This designation means that there is sufficient evidence that cyclophosphamide can cause cancer in humans. Cyclophosphamide metabolizes in the body to acrolein, which can cause adverse health effects in the bladder.

Cyclophosphamide is a cytotoxic drug that is used for a wide range of neoplastic diseases including breast and lung cancer, pediatric malignancies, leukemia, and lymphomas. It can be prescribed as a single agent or in combination with other chemotherapy drugs and can be administered via oral tablets or intravenously.

Cyclophosphamide is normally found in a white powder form for chemical stability and is normally brought into liquid solution by the addition of water and infused with sodium chloride, glucose, or

glucose/saline solutions. Once in solution, it is recommended that cyclophosphamide be administered to the patient within 8 hours to prevent degradation or be stored at cold temperatures (but never frozen).

There are currently no OELs for cyclophosphamide. However, because of the carcinogenic nature of the drug, exposures to cyclophosphamide should be kept as low as reasonably achievable.

Hazardous Drugs in Healthcare Settings

Employee exposures to hazardous drugs including chemotherapy drugs may occur through inhalation, skin contact, skin absorption, ingestion, or injection. Inhalation and skin contact/absorption are the most likely routes of exposure, but unintentional ingestion from hand to mouth contact and unintentional injection through a needlestick or sharps injury are also possible [Duvall and Baumann 1980; Black and Presson 1997; Schreiber et al. 2003].

Protection from hazardous drug exposures depends on safety programs established by employers and followed by employees. Factors that affect employee exposures include drug handling circumstances (preparation, administration, or disposal), amount of drug prepared, frequency and duration of drug handling, potential for absorption, use of ventilated cabinets, PPE, and work practices. The likelihood that an employee will experience adverse effects from hazardous drugs increases with the amount and frequency of exposure and the lack of proper work practices [NIOSH 2004].

Surveys have associated workplace exposures to antineoplastic drugs with acute health effects, primarily in nurses. These included hair loss, headaches, acute irritation, and/or hypersensitivity [Valanis et al. 1993a; Valanis et al. 1993b].

A recent review of 14 studies described an association between exposure to antineoplastic drugs and adverse reproductive effects, and 9 studies showed some positive association [Harrison 2001]. The major reproductive effects found in these studies were increased fetal loss [Selevan et al. 1985; Stücker et al. 1990], congenital malformations depending on the length of exposure [Hemminki et al. 1985], low birth weight and congenital abnormalities [Peelen et al. 1999], and infertility [Valanis et al. 1999].

Several reports have addressed the relationship of cancer occurrence to healthcare employee exposures to chemotherapy drugs [NIOSH 2004]. A significantly increased risk of leukemia has been reported among oncology nurses identified in the Danish cancer registry for the period 1943–1987 [Skov et al. 1992]. The same group [Skov et al. 1990] found an increased, but not significant, risk of leukemia in physicians employed for at least 6 months in a department where patients were treated with chemotherapy drugs.

Currently, no NIOSH RELs, OSHA PELs, or ACGIH TLVs have been established for hazardous drugs in general.

References

ACGIH [2011]. 2011 TLVs® and BEIs®: threshold limit values for chemical substances and physical agents and biological exposure indices. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.

AIHA [2011]. AIHA 2011 Emergency response planning guidelines (ERPG) & workplace environmental exposure levels (WEEL) handbook. Fairfax, VA: American Industrial Hygiene Association.

Black LA, Presson AC [1997]. Hazardous drugs. Occup Med: State of the Art Rev *12*(4):669–685.

CFR. Code of Federal Regulations. Washington, DC: U.S. Government Printing Office, Office of the Federal Register.

Duvall E, Baumann B [1980]. An unusual accident during the administration of chemotherapy. Cancer Nurs *3*(4):305–306.

Harrison BR [2001]. Risks of handling cytotoxic drugs. In: Perry MC ed. The chemotherapy source book. 3rd ed. Philadelphia, PA: Lippincott, Williams and Wilkins, pp. 566–582.

Hemminki K, Kyyrönen P, Lindbohm M-L [1985]. Spontaneous abortions and malformations in the offspring of nurses exposed to anesthetic gases, cytostatic drugs, and other potential hazards in hospitals, based on registered information of outcome. J Epidemiol Commun Health *39*(2):141–147.

IARC [1998]. Some antineoplastic and immunosuppressive agents. Lyon: IARC monographs on the evaluation of carcinogenic risks to humans, vol 26. International Agency for Research on Cancer.

NIOSH [2004]. NIOSH Alert: Preventing occupational exposure to antineoplastic and other hazardous drugs in health care settings. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2004-165.

NIOSH [2010]. NIOSH pocket guide to chemical hazards. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2010-168c. [http://www.cdc.gov/niosh/npg/]. Date accessed: August 2011.

Peelen S, Roeleveld N, Heederik D, Krombout H, de Kort W [1999]. Toxic effects on reproduction in hospital personnel (in Dutch). Netherlands: Elsevier.

Schreiber C, Radon K, Pethran A, Schierl R, Hauff K, Grimm C-H, Boos K-S, Nowak D [2003]. Uptake of antineoplastic agents in pharmacy personnel. Part 2: study of work-related risk factors. Int Arch Occup Environ Health *76*(1):11–16.

Selevan SG, Lindbohm M-L, Hornung RW, Hemminki K [1985]. A study of occupational exposure to antineoplastic drugs and fetal loss in nurses. N Engl J Med *313*(19):1173–1178.

Skov T, Lynge E, Maarup B, Olsen J, Rørth M, Winthereik H [1990]. Risk for physicians handling antineoplastic drugs [letter to the editor]. The Lancet *336*(8728):1446.

Skov T, Maarup B, Olsen J, Rørth M, Winthereik H, Lynge E [1992]. Leukaemia and reproductive outcome among nurses handling antineoplastic drugs. Br J Ind Med *49*(12):855–861.

Stücker I, Caillard J-F, Collin R, Gout M, Poyen D, Hémon D [1990]. Risk of spontaneous abortion among nurses handling antineoplastic drugs. Scand J Work Environ Health *16*(2):102–107.

Valanis BG, Vollmer WM, Labuhn KT, Glass AG [1993a]. Acute symptoms associated with antineoplastic drug handling among nurses. Cancer Nurs *16*(4):288–295.

Valanis BG, Vollmer WM, Labuhn KT, Glass AG [1993b]. Association of antineoplastic drug handling with acute adverse effects in pharmacy personnel. Am J Hosp Pharm *50*(3):455–462.

Valanis B, Vollmer WM, Steele P [1999]. Occupational exposure to antineoplastic agents: self-reported miscarriages and stillbirths among nurses and pharmacists. J Occup Environ Med *41*(8):632–638.

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