Safe Handling of Parenteral Cytotoxics: Recommendations for Ontario

By Esther Green, BScN, MSc(T), Mary Johnston, BSc, Maureen Trudeau, BSc, MA, MD, Lisa Schwartz, BA, MA, PhD, Susan Poirier, BScPharm, Gail Macartney, RN(EC), BScH, MSc(A), CON(C), and Deborah Milliken, BScPharm

From the Oncology Nursing, Systemic Treatment, and Evidence-Based Care Programs, Cancer Care Ontario; Occupational Health and Safety Department, Toronto General Hospital, University Health Network, Toronto; Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton; Pharmacy, Parkwood Hospital, St Joseph's Health Care, London; Division of Neurosurgery, Children's Hospital of Eastern Ontario; and Hematology Department, Ottawa Hospital, Ottawa, Ontario, Canada

Abstract

Purpose: To develop a set of recommendations for the safe handling of parenteral cytotoxics in health care facilities in Ontario, Canada.

Methods: Systematic reviews were conducted to assemble evidence on risks to health care staff who prepare or administer cytotoxic drugs for cancer care and on closed systems for handling these drugs. Recent guidelines on safe handling of hazardous drugs were also reviewed. A multidisciplinary expert panel used an ethical framework to interpret this evidence and develop a set of recommendations to guide oncology practice in Ontario. Practitioners were surveyed and asked to provide input for the final set of recommendations.

Results: Available evidence on risks associated with handling cytotoxic drugs is of poor quality, but it suggests that health care workers exposed to cytotoxic agents may be at increased risk for miscarriages. There is general agreement across guideline development groups in North America, Europe, and Australia concerning recommendations related to policies and procedures for handling cytotoxic drugs, use of personal protective equipment, and standards for ventilated cabinets, syringes and intravenous sets, transport and labeling, and education and training of staff. Limited evidence from poor-quality studies suggests that closed systems may reduce surface contamination with hazardous drugs during preparation.

Conclusion: A set of recommendations was formulated by the expert panel and approved by practitioners surveyed across Ontario.

Introduction

Chemotherapy has an important role in cancer treatment; it is potentially curative when used as adjuvant therapy in patients with early-stage tumors and offers effective palliation in patients with metastatic disease. However, some patients who have been cured of cancer develop secondary malignancies believed to be linked to exposure to their initial chemotherapy regimens.[1-5] If patients receiving potentially curative chemotherapy are at increased risk of developing secondary cancers, what is the risk to health care workers who prepare and administer these agents? Nurses, pharmacists, pharmacy technicians, porters who deliver cancer drugs to chemotherapy units, and physicians may be exposed to cytotoxic agents during care of patients with cancer. In addition to being at risk for exposure-related cancers, these individuals might develop acute toxic effects after accidental spills of cytotoxic agents. In female health care workers who become pregnant, there are also the potential hazards of spontaneous abortions, stillbirths, and teratogenic effects on unborn fetuses. Occupational exposure to cytotoxic drugs was recognized as a potential hazard for health care workers in the 1970s, when Falck et al,[6] studying the mutagenicity of urine samples, first demonstrated potential risk for nurses handling these drugs. Subsequent examinations of the workplace documented detectable levels of drugs in airborne samples and on work surfaces,[7,8] confirming that exposure is possible even in the absence of obvious direct contact. No long-term adverse effects of occupational exposure were conclusively demonstrated, but potential risk was deemed serious enough to warrant the issuing of several drug-handling guidelines during the 1980s and 1990s.[9-20] These guidelines promoted control of exposure through implementation of stringent procedures, use of specialized equipment and personal protective equipment, and education of those handling these drugs or at risk for exposure. As a result, many institutions introduced and implemented policies and procedures designed to minimize occupational exposure and consequent risks associated with handling cytotoxic drugs. Nevertheless, health hazards may still exist for hospital staff, as suggested by environmental contamination studies that have demonstrated measurable levels of contamination in the workplace despite the standards of practice in place.[21] Detectable levels of cytotoxic drugs have been reported in the urine of pharmacists, pharmacy technicians, nurses, and workers in drug manufacturing plants.[22]

In 2003, Cancer Care Ontario (Toronto, Canada) formed a task force to examine evidence on adverse effects among health care workers from exposure to cytotoxic agents. Results of the systematic review and meta-analysis conducted by this task force were published in 2005.[23] Subsequently, an expert panel was assembled to review evidence on adverse effects and on closed handling systems for handling cytotoxics, as well as avail-

Copyright © 2009 by American Society of Clinical Oncology

able guidelines on this topic, and to develop recommendations for use in Ontario. A full report on the recommendations and development process can be found at http://www.cancercare.on.ca/pdf/pebccytos.pdf.

Methods

An expert panel comprising pharmacists, nurses, an ethicist, an oncologist, and an occupational health and safety manager interpreted available evidence, reviewed recommendations made by similar groups in other countries, drafted recommendations, and obtained feedback from practitioners across Ontario.

Initial evidence came from a systematic review of evidence on risks to health care workers from handling cytotoxic drugs; methods for this review have been published elsewhere.[23] The expert panel updated the review before drafting recommendations. The updated review included literature published in full reports or meeting abstracts before July 2006 and addressed questions regarding whether health care workers who work with cytotoxic drugs are at increased risk for cancer, teratogenic births, stillbirths, miscarriages, acute toxic effects (skin rash, nausea, and so on), or having children with developmental delays, compared with a control group of unexposed health care workers.

The panel also conducted two additional systematic reviews: one of existing guidelines and one of closed systems. The National Guideline Clearinghouse database (http://www.guideline.gov), CMA Infobase (http://mdm.ca/cpgsnew/cpgs/index.asp), and MEDLINE (Ovid), CINAHL (Ovid), and EMBASE (Ovid) databases were searched in January 2006 for guidelines published in English after January 2003. Google (http://www.google.ca) was also used to search the Web for documents that included the text "safe handling" or "hazardous drugs." For the review of closed systems, MEDLINE (Ovid), CINAHL (Ovid), EMBASE (Ovid), and HealthStar (Ovid) databases and the Cochrane Central Register of Controlled Trials were searched from inception to July 2006. Proceedings of the annual meetings of ASCO from 2001 to 2005, the American Society of Hematology for 2005, the Oncology Nursing Society from 2003 to 2006, and the Canadian Society of Hospital Pharmacists from 2005 to 2006 were searched for studies published in abstract form but not yet available as full reports. Reference lists of eligible studies and published reviews were scanned to identify additional articles. All study designs were eligible for inclusion in the review.

Methods developed and refined by the Program in Evidence-Based Care (PEBC) of Cancer Care Ontario were used to review evidence and develop recommendations.[24,25] After the review, the expert panel addressed the question, "What precautions should be taken in the workplace to minimize risk of adverse effects among hospital and clinic staff who may be exposed to cytotoxic drugs?" In addition to published evidence and guidelines, the expert panel used an ethical framework invoking the principles listed in Table 1 to reach consensus on a set of recommendations. This framework was developed on the basis of existing proposals for other areas of health care delivery,[26] professional values of panel members, and values inherent in studies and guidelines found in the systematic review.

Table 1. Ethical Framework

Principle
Recognition that there is a duty to provide care, even if providing care is associated with risk, and that trained professionals are the best people to provide this care
Appropriate recognition and support of those who take risks for others
As far as reasonably possible, mitigation of risks for those who take risks to help others
Alertness to the need for extra caution and safety measures, and responsiveness to the reported needs and concerns of staff and experts
Access to and appropriate use of safety measures and equipment
Timely implementation of safety improvements, and encouragement of research that will improve safety measures
Equal opportunity for avoiding risks in reasonable situations (eg, pregnancy)
Availability of ongoing education and updates
Duty to provide care and treatment in the event of harm caused by cytotoxic agents

A detailed report that included a full description of the systematic review, detailed recommendations, and the rationale for the recommendations was reviewed and approved by the PEBC Report Approval Panel, which has expertise in clinical and methodologic issues. The report was sent to 111 oncology pharmacists and nurses in Ontario for review and feedback. The questionnaire included items evaluating the methods, results, and interpretive summary used to inform the draft recommendations and asked whether the draft recommendations should be approved. The expert panel reviewed results of the survey and modified some of its recommendations.

Results

Evidence on Risks to Health Care Workers

Our systematic review of 15 retrospective studies (one cohort study, four case-control studies, and 10 surveys) that compared health care workers exposed to cytotoxic agents with those who were not exposed found that health care workers exposed to cytotoxic agents may be at increased risk for miscarriages, but the quality of available evidence is poor.[23,27] Meta-analysis of data from five retrospective studies detected an excess of spontaneous abortions among those exposed to cytotoxic drugs (pooled odds ratio [OR], 1.46; 95% CI, 1.11 to 1.92). The association between workplace exposure to cytotoxics and congenital malformations, ectopic pregnancies, and stillbirths was unclear. Meta-analysis of data from four studies failed to detect a statistically significant association for congenital malformations (pooled OR, 1.64; 95% CI, 0.91 to

Copyright © 2009 by American Society of Clinical Oncology

2.94). Two studies failed to detect associations with ectopic pregnancies and stillbirths, respectively. There was insufficient evidence in published studies to determine if health care workers exposed to cytotoxic drugs are at increased risk for acute toxic effects or cancer or if their children are at increased risk for learning disabilities.

Existing Guidelines

Eight guidelines on safe handling of hazardous drugs have been published since 2003[28-35] in the United States, Australia, the United Kingdom, and Germany. The most recent guidelines, published in June 2006, were developed by the American Society of Health System Pharmacists (ASHP; Bethesda, MD).[28] None of the guidelines were evidence based (ie, based on a systematic review of evidence), but the ASHP guidelines provided narrative summaries of evidence related to each recommendation. Guidelines by the ASHP and Australian guidelines by WorkSafe Victoria (Melbourne, Australia) covered all areas of interest to the expert panel, and other guidelines included recommendations related to most of these issues. There was general agreement across guideline development groups that appropriate precautions related to policies and procedures, personal protective equipment, ventilated cabinets, syringes and intravenous sets, transport and labeling, and education and training should be employed.

Evidence on Closed Systems

Although seven studies of closed systems for handling hazardous drugs were identified, they provided little evidence to inform decisions about effectiveness of this technology to reduce exposure among health care workers preparing or administering cytotoxic drugs.[36-42] All studies measured surface contamination, and two also measured cytotoxics in urine of pharmacy staff and nurses. The studies were descriptive in nature. Although five studies compared open and closed systems, they were not designed to evaluate differences between groups. None of the studies were randomized, and none included statistical analyses of results. Nevertheless, the observed results suggest potential for contamination to be reduced with closed systems and point to a need to test this hypothesis in well-designed studies.

Recommendations

The final recommendations, which incorporate feedback from the PEBC Report Approval Panel and practitioner survey, are listed in Table 2. The target population for the recommendations includes any employee of a health care facility in Ontario who may be involved in handling cytotoxic drugs or related waste or bodily fluids from patients undergoing treatment with cytotoxic drugs. This generally includes staff in the following departments: medicine, nursing, pharmacy, housekeeping, environmental services, transportation and portering, materials management, clinical laboratory, research, and clinical trials. The recommendations are intended to apply to all health care institutions in Ontario that administer parenteral cytotoxic drugs.

Discussion

The expert panel accepted that the link between exposure of health care workers to cytotoxic drugs and adverse outcomes is biologically plausible. Although the quality of evidence is weak, it does indicate that health care workers exposed to cytotoxic agents may be at increased risk for miscarriages. Evidence related to other risks associated with workplace exposure to cytotoxic drugs is insufficient to reach any firm conclusions. The expert panel concluded that available evidence raises concerns about potential for harm to health care staff working with cytotoxic drugs. The panel agreed that recommendations to address these risks were needed for Ontario and that emphasis should be placed on minimizing exposure to cytotoxic drugs for all staff at all times. The recommendations for Ontario were designed to provide guidance to institutions and individuals without being overly prescriptive about details of implementation and to inform institutions as they assess the adequacy of their facilities, policies, and procedures.

The recommendations draw on the work of guideline developers in North America, Europe, and Australia related to policies and procedures, personal protective equipment, ventilated cabinets, syringes and intravenous sets, transport and labeling, and education and training. To our knowledge, no studies have examined effectiveness of these precautions in reducing rates of cancer, adverse reproductive outcomes, or acute adverse effects associated with exposure to cytotoxic drugs among health care workers, but there is evidence that some types of gloves and gowns offer protection against penetration and permeation by hazardous drugs. Although there is wide acceptance of ideal standards for these practices, implementation is variable and often less than ideal.

There is less agreement across guidelines with respect to closed systems, pregnancy, and medical surveillance of health care workers. Closed systems are a new, expensive, and unproven technology. Their use was not standard practice in Ontario when these recommendations were developed. Although most guideline developers acknowledged that there is evidence of adverse reproductive outcomes among health care workers handling cytotoxics, there is variation among guidelines in the strength of recommendations for protecting pregnant workers from exposure. After considerable discussion, the Ontario panel recommended that employees be informed of the risks and offered alternative duties. Routine medical surveillance for all workers was not recommended, because biologic monitoring for occupational diseases requires an identified hazard and accepted and detectable clinical outcome that can be reliably identified by clinical tests. These elements are lacking in the current research on health effects of cytotoxic drugs among exposed health care workers. There are no exposure limits set for cytotoxic drugs and no standards for interpretation of test results of exposed health care workers to enable meaningful interpretation or action on the basis of biologic monitoring results.

Copyright © 2009 by American Society of Clinical Oncology

Table 2. Key Recommendations

Topic	Recommendation
Policies and procedures	Written policies and procedures for handling cytotoxic drugs, related waste, and body fluid disposal are needed in each setting; development must be collaborative and consultative, involving departments such as medicine, nursing, pharmacy, housekeeping, environmental services, transportation and portering, materials management, clinical laboratory, research, and clinical trials as well as employee health, risk management, industrial hygiene, and safety officers and joint health and safety committees
	Policies and procedures must be readily accessible and focus on training for all relevant employees
	Policies and procedures must be reviewed and updated annually, in consultation with appropriate stakeholders
Personal protective equipment	Personal protective equipment is provided by health care facility for all staff handling cytotoxic drugs
	Staff are required to wear personal protective equipment in accordance with written policies
	Personal protective equipment must be used when preparing or administering cytotoxic drugs, handling waste, or cleaning up spills and must include at least:
	Gloves meeting ASTM D6978-05 standards
	Disposable gown (made of appropriate materials designated protective against cytotoxic drugs) or reusable gown designed to be nonpermeable
	Fluid-resistant mask when there is risk of aerosolization
	Eye and face protection (except when using Class II, Type A2, B1, or B2 biologic safety cabinet for drug preparation)
	Certain circumstances also warrant use of respirator appropriate to hazard; National Institute for Occupational Safety and Health–certified (eg, N100 or P100) respirator or self-contained breathing apparatus is appropriate when there is risk of aerosol generation in space without engineering controls (eg, when cleaning out biologic safety cabinet, cleaning up spills, or other emergency situations)
Ventilated cabinets	Class II or III biologic safety cabinet or aseptic containment isolator is required for preparing cytotoxic drugs
	Biologic safety cabinet must be equipped with continuous monitoring device to allow confirmation of adequate airflow and cabinet performance
Closed systems	Issue of closed systems should be addressed in institutional policies and procedures for handling cytotoxic drugs; closed systems may provide additional layer of protection for staff involved in preparation, administration, or disposal of cytotoxic drugs
	Closed systems are not acceptable substitute for appropriate ventilation or engineering controls (eg, Class II or III biologic safety cabinets or isolators) used along with personal protective equipment
	Closed systems may be used for selected cytotoxic drugs; drug packaging may be incompatible with closed system sets in some instances
Syringes and intravenous sets	Needleless vascular access system with Luer lock connections should be used for administration of cytotoxic drugs
Transport and labeling	Cytotoxic drugs must be transported in containers designed to contain leakage and spills and be clearly labeled as containing hazardous drugs
Education and training	All staff who work with or may be exposed to cytotoxic drugs must have appropriate hands-on and educational training during orientation and at least annually thereafter
	Training should cover potential health risks of cytotoxics, safe practices, containment systems, sources of information, appropriate personal protective equipment, and procedures for handling spills
	Employer is responsible for orientation and ongoing training and will cover associated costs
Pregnancy	Alternative duties should be offered to individuals who are pregnant or breastfeeding, because possible reproductive risks are associated with exposure to cytotoxic drugs
	All staff should be fully informed of reproductive hazards
Surveillance	Medical surveillance is not recommended, because adequate tests are not available for monitoring exposure to cytotoxics or assessing level of risk associated with exposure
	Panel strongly urges additional research to determine if adverse health effects result from exposure of health care workers to cytotoxic drugs and to develop sensitive, specific surveillance tests to detect any adverse health effects
Ethics	Health care facilities have moral and ethical obligations to people who handle cytotoxic drugs to minimize exposure

NOTE. The full set of recommendations can be found at http://www.cancercare.on.ca/pdf/pebccytos.pdf.

Copyright © 2009 by American Society of Clinical Oncology

Accepted for publication on October 9, 2008.

Acknowledgment

Supported by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care. We thank pharmacist Paola Reynolds for her work in the development of the guidelines for safe handling of parenteral cytotoxics.

Authors' Disclosures of Potential Conflicts of Interest

The author(s) indicated no potential conflicts of interest.

Corresponding author: Esther Green, Cancer Care Ontario, 620 University Ave, Toronto, Ontario M5G 2L7 Canada; e-mail: Esther.Green @cancercare.on.ca.

DOI: 10.1200/JOP.091014; posted online ahead of print at http://jop.ascopubs.org on August 20, 2009.

References

1. Matesich SM, Shapiro CL: Second cancers after breast cancer treatment. Semin Oncol 30:740-748, 2003

2. André M, Mounier N, Leleu X, et al: Second cancers and late toxicities after treatment of aggressive non-Hodgkin lymphoma with the ACVBP regimen: A GELA cohort study on 2837 patients. Blood 103:1222-1228, 2004

3. Travis LB, Gospodarowicz M, Curtis RE, et al: Lung cancer following chemotherapy and radiotherapy for Hodgkin's disease. J Natl Cancer Inst 94:182-192, 2002

4. Crump M, Tu D, Shepherd L, et al: Risk of acute leukemia following epirubicin-based adjuvant chemotherapy: A report from the National Cancer Institute of Canada Clinical Trials Group. J Clin Oncol 21:3066-3071, 2003

5. Chronowski GM, Wilder RB, Levy LB, et al: Second malignancies after chemotherapy and radiotherapy for Hodgkin disease. Am J Clin Oncol 27:73-80, 2004

6. Falck K, Gröhn P, Sorsa M, et al: Mutagenicity in urine of nurses handling cytotoxic drugs. Lancet 1:1250-1251, 1979

7. Kleinberg ML, Quinn MJ: Airborne drug levels in a laminar-flow hood. Am J Hosp Pharm 38:1301-1303, 1981

8. deWerk Neal A, Wadden RA, Chiou WL: Exposure of hospital workers to airborne antineoplastic agents. Am J Hosp Pharm 40:597-601, 1983

9. US Department of Labor: Guidelines for Cytotoxic (Antineoplastic) Drugs. Washington, DC, Occupational Safety and Health Administration, Office of Occupational Medicine, publication 8-1.1, 1986

10. Occupational Safety and Health Administration: Directorate of Technical Support: Controlling Occupational Exposure to Hazardous Drugs. Washington, DC, Occupational Health and Safety Administration, OSHA Instruction TED 1.15, 1995

11. American Society of Health System Pharmacists: ASHP technical assistance bulletin on handling cytotoxic drugs in hospitals. Am J Hosp Pharm 42:131-137, 1985

12. American Society of Health System Pharmacists: ASHP technical assistance bulletin on handling cytotoxic and hazardous drugs. Am J Hosp Pharm 47:1033-1049, 1990

13. Oncology Nursing Society: Standards for Cancer Nursing Practice. Pittsburgh, PA, Oncology Nursing, 1982

14. Powell L (ed): Cancer Chemotherapy Guidelines and Recommendations for Practice. Pittsburgh, PA, Oncology Nursing, 1996

15. Clinical Oncology Society of Australia: Guidelines for safe handling of antineoplastic agents. Med J Aust 1:426-428, 1983

16. Guidelines for handling parenteral antineoplastics: Council on Scientific Affairs. JAMA 253:1590-1592, 1985

17. Recommendations for Handling Cytotoxic Agents. Providence, RI, National Study Commission on Cytotoxic Exposure, 1987

18. Guidelines for the Handling and Disposal of Hazardous Pharmaceuticals (Including Cytotoxic Drugs). Ottawa, Canada, Canadian Society of Hospital Pharmacists, 1993

19. Davis J, Jackson J, Kirsa S, et al: SHPA Standards of Practice for the Safe Handling of Cytotoxic Drugs in Pharmacy Departments. Melbourne, Australia, Society of Hospital Pharmacists of Australia, 1997

20. Council directive of 28 June 1990 on the protection of workers from the risks related to exposure to carcinogens at work (90/394/EEC). Off J Eur Commun L196:1-7, 1990

21. Connor TH, Anderson RW, Sessink PJ, et al: Surface contamination with antineoplastic agents in six cancer treatment centers in Canada and the United States. Am J Health Syst Pharm 56:1427-1432, 1999

22. Sessink PJ, Boer KA, Scheefhals AP, et al: Occupational exposure to antineoplastic agents at several departments in a hospital: Environmental contamination and excretion of cyclophosphamide and ifosfamide in urine of exposed workers. Int Arch Occup Environ Health 64:105-112, 1992

23. Dranitsaris G, Johnston 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 Pract 11:69-78, 2005

24. Browman GP, Levine MN, Mohide EA, et al: The practice guidelines development cycle: A conceptual tool for practice guidelines development and implementation. J Clin Oncol 13:502-512, 1995

25. Browman GP, Newman TE, Mohide EA, et al: Progress of clinical oncology guidelines development using the practice guidelines development cycle: The role of practitioner feedback. J Clin Oncol 16:1226-1231, 1998

26. University of Toronto Joint Centre for Bioethics: Stand on guard for thee: Ethical considerations in preparedness planning for pandemic influenza. http://www.jointcentreforbioethics.ca/people/documents/upshur_stand_guard.pdf

27. Martin S: Chemotherapy handling and effects among nurses and their offspring [dissertation]. Columbia University, New York, NY, 2003

28. American Society of Health System Pharmacists: ASHP guidelines on handling hazardous drugs. Am J Health Syst Pharm 63:1172-1193, 2006

29. Society of Hospital Pharmacists of Australia Committee of Specialty Practice in Oncology: SHPA standards for the safe handling of cytotoxic drugs in pharmacy departments. J. Pharm Pract Res 35:44-52, 2005

30. National Institute for Occupational Safety and Health: NIOSH alert: Preventing occupational exposure to antineoplastic and other hazardous drugs in health care settings. http://www.cdc.gov/niosh/docs/2004-165/

31. Blecher CS, Glynn-Tucker EM, McDiarmid M, et al: Safe Handling of Hazardous Drugs. Pittsburgh, PA, Oncology Nursing Society, 2003

32. Health and Safety Executive: HSE information sheet MISC615: Safe handling of cytotoxic drugs. http://www.hse.gov.uk/pubns/misc615.pdf

33. Management and Awareness of the Risks of Cytotoxic Handling Panel: UK guidelines 2003-2005. http://www.marchguidelines.com/index.aspx

34. Victorian WorkCover Authority: WorkSafe Victoria: Handling cytotoxic drugs in the workplace. http://www.worksafe.vic.gov.au/wps/wcm/resources/file/ebd87143a010b85/handling_cytotoxic.pdf

35. German Society of Oncology Pharmacy: QuapoS 3: Quality standard for the oncology pharmacy service with commentary. http://www.esop.li/downloads/library/Quapos-en-with-commentary.pdf

36. Sessink PJM, Rolf ME, Ryden NS: Evaluation of the PhaSeal Hazardous Drug Containment System. Hosp Pharm 34:1311-1317, 1999

37. Vandenbrouke J, Robays H: How to protect environment and employees against cytotoxic agents, the UZ Ghent experience. J Oncol Pharm Pract 6:146-152, 2001

38. Connor TH, Anderson RW, Sessink PJ, et al: Effectiveness of a closed-system device in containing surface contamination with cyclophosphamide and ifosfamide in an i.v. admixture area. Am J Health Syst Pharm 59:68-72, 2002

39. Nygren O, Gustavsson B, Ström L, et al: Exposure to anti-cancer drugs during preparation and administration: Investigations of an open and a closed system. J Environ Monit 4:739-742, 2002

40. Wick C, Slawson MH, Jorgenson JA, et al: Using a closed-system protective device to reduce personnel exposure to antineoplastic agents. Am J Health Syst Pharm 60:2314-2320, 2003

41. Spivey S, Connor TH: Determining sources of workplace contamination with antineoplastic drugs and comparing conventional IV drug preparation with a closed system. Hosp Pharm 38:135-139, 2003

42. Tans B, Willems L: Comparative contamination study with cyclophosphamide, fluorouracil and ifosfamide: Standard technique versus a proprietary closed-handling system. J Oncol Pharm Pract 10:217-223, 2004

Copyright © 2009 by American Society of Clinical Oncology