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## Evidence-based Series Special Report

### Safe Handling of Parenteral Cytotoxics

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S. Poirier, P. Reynolds, T. Savage, L. Schwartz, M. Trudeau*

A Quality Initiative of the  
Program in Evidence-based Care (PEBC), Cancer Care Ontario (CCO)

**Report Date: April 13, 2007**

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- Methods and Results

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## Evidence-based Series Special Report: Section 1

# Safe Handling of Parenteral Cytotoxics: Recommendations

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### **Purpose**

The purpose of this report is to provide recommendations regarding the safe handling of parenteral cytotoxics by health care workers. To accomplish this mandate, the Expert Panel:

- a) Examined evidence regarding the risk of cytotoxic exposure to health care workers. The questions of interest were:
  1. Are health care workers who work with cytotoxic drugs at an increased risk of developing cancer compared to a control group of unexposed health care workers?
  2. Are health care workers who work with cytotoxic drugs at an increased risk of teratogenic births/stillbirths/miscarriage compared to a control group of unexposed health care workers?
  3. Are health care workers who work with cytotoxic drugs at an increased risk of developing an acute toxic effect (skin rash, nausea, etc.) compared to a control group of unexposed health care workers?
  4. Are the children of health care workers who work with cytotoxic drugs at an increased risk of developmental delays compared to children of a control group of unexposed health care workers?
- b) Examined the evidence regarding closed systems for handling cytotoxic drugs and their effectiveness for protecting health care workers from these risks.
- c) Reviewed guidelines that have addressed the safe handling of cytotoxics by health care workers.
- d) Created an ethical foundation on which to frame recommendations on handling cytotoxics.

- e) Developed recommendations for precautions that should be taken in the workplace to minimize the risk of adverse effects among staff who work in health care facilities and may be exposed to cytotoxic drugs.

### **Target Population**

Any employee of a health care facility in Ontario who may be involved in handling cytotoxic drugs, related waste, or bodily fluids from patients undergoing treatment with cytotoxic drugs. This will generally include staff in the following departments: medicine, nursing, pharmacy, housekeeping, environmental services, transportation and portering, materials management, clinical laboratory, research, and clinical trials.

### **Recommendations**

When interpreting and applying the specific recommendations listed below, emphasis should be placed on minimizing exposure to cytotoxic drugs for all staff at all times.

### ***Policies & Procedures***

- Each institution where cytotoxic drugs are used needs to have written policies and procedures for handling cytotoxic drugs, related waste, and bodily fluids from patients undergoing treatment with these agents.
- The development of policies and procedures needs to be collaborative and consultative. Policies and procedures should be developed with input from all departments where there may be exposure to cytotoxic drugs (e.g., 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, where applicable.
- These policies and procedures must be readily accessible and must be the focus of training for all relevant employees. Anyone who may be required to handle cytotoxic drugs, related waste, or bodily fluids from patients undergoing treatment with cytotoxic drugs (such as staff associated with nursing, pharmacy, housekeeping, environmental services, transportation and portering, materials management, medical care, research or clinical trials) should be aware of the policies and procedures.
- Policies and procedures must be reviewed and updated annually, in consultation with the appropriate stakeholders as defined above.

### ***Personal Protective Equipment (PPE)***

- Personal protective equipment is provided by the health care facility for all staff identified above.
- Staff are required to wear PPE in accordance with the written policies.
- PPE must be used when preparing or administering cytotoxic drugs, handling waste, or cleaning up spills, and needs to include at least:
  - double gloves (use powder-free, high-quality gloves made of latex, nitrile, polyurethane, neoprene, or other materials that meet the ASTM\* standard for chemotherapy gloves) or gloves that are 7-9 mil thick (Note: 7–9 mil = 0.18–0.23 mm). All gloves must meet ASTM D6978-05 standards.
  - a disposable gown (made of appropriate materials designated to be protective against cytotoxic drugs) or a reusable gown that is designed to be non-permeable (where there is a mechanism for isolating the used gowns and procedures for cleaning),

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\* American Society for Testing and Materials

- a fluid-resistant mask when there is a risk of aerosolization (not required when using a Class II, Type A2, B1 or B2 biological safety cabinet),
- eye and face protection (except when using a Class II, Type A2, B1 or B2 biologic safety cabinet for drug preparation).
- Staff who change linen, empty bedpans, or clean urine spills in settings where cytotoxic drugs are administered should wear gloves.
- Certain circumstances also warrant the use of a respirator appropriate to the hazard. A National Institute for Occupational Safety and Health (NIOSH)-certified (e.g., N100 or P100) respirator or Self Contained Breathing Apparatus (SCBA) is appropriate when there is a risk of aerosol generation in a space without engineering controls, such as cleaning out the biologic safety cabinet, cleaning up a spill, or other emergency situations (e.g., fire or major system failure).

### ***Ventilated Cabinets***

- A Class II (Type B2 is preferred but Types A2 and B1 are acceptable under certain conditions), Class III biologic safety cabinet (BSC) or an aseptic containment isolator is required for preparing cytotoxic drugs.
- The BSC must be equipped with a continuous monitoring device to allow confirmation of adequate airflow and cabinet performance.

### ***Closed Systems***

- Each health care facility will need to assess the need for closed systems in their environment.
- The issue of closed systems should be addressed in the institutional policies and procedures for handling cytotoxic drugs.
- A closed system (e.g., PhaSeal) is not an acceptable substitute for appropriate ventilation or engineering controls (e.g., Class II or III biological safety cabinets or isolators) used along with PPE.
- Closed systems may provide an additional layer of protection for staff involved in the preparation, administration, or disposal of cytotoxic drugs.
- Closed systems may be used for selected cytotoxic drugs. Drug packaging may be incompatible with closed system sets in some instances.

### ***Syringes and Intravenous (IV) Sets***

- A needleless vascular access system with Luer lock connections should be used for administration of cytotoxic drugs. When starting an IV, a Safety Engineered Medical Sharps (SEMS) (or needleless) catheter is preferred.

### ***Transport and Labelling***

- Cytotoxic drugs must be transported in containers designed to contain leakage and spills.
- Containers must be clearly labelled as containing hazardous drugs.

### ***Education and Training***

- Everyone who works 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 the potential health risks of cytotoxics, safe practice, containment systems and sources of information, appropriate personal protective equipment, and procedures to handle spills.

- Orientation and ongoing training is the responsibility of the employer, who will cover the associated costs.

### ***Pregnancy***

- Alternative duty should be offered to individuals who are pregnant or breast-feeding, because possible reproductive risks have been associated with exposure to cytotoxic drugs.
- All staff should be fully informed of the reproductive hazards.

### ***Surveillance***

- Medical surveillance is not recommended because adequate tests are not available for monitoring exposure to cytotoxics or assessing the level of risk associated with exposure.
- The panel strongly urges further research to determine if there are adverse health effects that result from health care workers' exposure to cytotoxic drugs and to develop sensitive specific surveillance tests to detect any adverse health effects. Health care facilities in Ontario that provide cytotoxic therapy should participate in this research.

### ***Ethics***

- Health care facilities have a moral and ethical obligation to people who handle cytotoxic drugs to minimize exposure.

### **Foundation for Recommendations**

The recommendations above are based on:

- systematic reviews of the evidence on adverse effects and closed systems,
- evidence and recommendations in eight recent guidelines from the United States, Australia, the United Kingdom and Germany, and
- the expert opinion of the multidisciplinary panel.

### ***Adverse Effects***

- The link between exposure of health care workers to cytotoxic drugs and adverse outcomes is biologically plausible. Some cytotoxic drugs in clinical use (e.g., some anthracyclines, epipodophyllotoxins, and alkylating agents) are associated with an increased risk of secondary malignancies among cancer patients receiving cytotoxic therapy. Several studies have shown detectable levels of cytotoxic drugs in the urine of pharmacists, pharmacy technicians, and nurses who prepare and administer cytotoxic drugs, which may have resulted from surface contamination in the workplace. Neither the dose-response relation between chemotherapy nor the long term effects of this exposure are known.
- A systematic review found evidence from 15 retrospective studies (one cohort study, four case-control studies, and ten surveys) that compared health care workers exposed to cytotoxic agents with those who were not exposed. This review found that:
  - Health care workers exposed to cytotoxic agents may be at increased risk for miscarriage, but the quality of the evidence available is poor. Meta-analysis of data from five retrospective studies detected an excess of spontaneous abortions among subjects exposed to cytotoxic drugs (pooled odds ratio [OR], 1.46; 95% confidence interval [CI], 1.11 to 1.92).
  - The association between workplace exposure to cytotoxics and congenital malformation, ectopic pregnancy and stillbirth is 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 2.94). Two studies, in each case, failed to detect an association with ectopic pregnancy or stillbirth.

- There is insufficient evidence from published studies at present to determine if health care workers who work with cytotoxic drugs are at an increased risk of acute toxic effects or cancer, or if their children are at increased risk for learning disabilities.

***Effectiveness of Precautions to Reduce Risk of Adverse Effects***

- There is general agreement across guideline development groups in North America, Europe, and Australia that many of the precautions recommended in this report (related to policies and procedures, personal protective equipment, ventilated cabinets, syringes and IV sets, transport and labelling, and education and training) are appropriate.
- No studies have examined the effectiveness of these precautions to reduce rates of cancer, adverse reproductive outcomes or acute adverse effects associated with exposure to cytotoxic drugs among health care workers.
- There is evidence that some types of gloves and gowns offer protection against penetration and permeation by hazardous drugs.
- There is limited evidence from poor quality studies to suggest that closed systems may reduce surface contamination with hazardous drugs during preparation.
- Available tests for measuring occupational exposure to cytotoxic drugs have inadequate sensitivity and specificity. They would expose workers to unnecessary anxiety without providing useful information on the level of risk for adverse effects.

***Medical Surveillance***

- Biologic monitoring for occupational diseases requires an identified hazard and an accepted and detectable clinical outcome that can be reliably identified by clinical tests. All of these elements are lacking in the current research on health effects of cytotoxic drugs on exposed health care workers.
- There are no identified medical conditions known to result from exposure of health care workers to cytotoxic drugs, 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 based on biological monitoring results.

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