Health Science Campus

**FINAL APPROVAL OF THESIS**
Master of Science in Occupational Health (Industrial Hygiene)

Health Issues Related to the Management of Antineoplastic Drugs

Submitted by:
Ryan Rillo

In partial fulfillment of the requirements for the degree of
Master of Science in Occupational Health

<table>
<thead>
<tr>
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<tr>
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Ryan Rillo

University of Toledo Health Science Campus
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Acknowledgement

I would like to acknowledge and express my gratitude to Dr. Farhang Akbar, my Major Advisor, for his advisement and support throughout the completion of this project and encouragements in my professional development. I also acknowledge my other Advisory Committee members, Dr. Sheryl Milz and Dr. Brian Fink, for their guidance.

I would like to express appreciation to fellow student and colleague, Melissa Braskie, for her assistance in sample collection.

I would also like to recognize Bureau Veritas, Analytical Laboratories, for supplying sample media and their assistance in sample analysis.
Introduction

Overview

Antineoplastic drugs are chemical agents used in the treatment of malignant neoplasms (cancers). There are also cases where these drugs are used as treatments for non-neoplastic forms of disease. Antineoplastic drugs are synonymously called cytotoxic (i.e., toxic to cells) drugs as the mechanism of action for these drugs are to interfere with the DNA and/or protein synthesis of malignant neoplasm cells. These drugs unfortunately cannot differentiate between normal healthy cells and the cells of a malignant neoplasm. This lack of differentiation can cause undesired damage to the body and occasionally create secondary malignancies (including cases of leukemia), mutagenic and teratogenic effects (Sieber, 1975; Weisburger et al., 1975; Rosner, 1976; Kyle, 1984; Sessink and Bos 1999; Turci et al., 2002).

Table 1 lists the antineoplastic drugs that according to the International Agency for Research on Cancer (IARC) have or may have a carcinogenic potential as reported by Turi et al. (2003). There are also acute effects from antineoplastic drugs, such as irritation to the skin, eyes and mucous membranes, nausea, vomiting and diarrhea (Sessink and Bos, 1999).

Table 1. Antineoplastic drugs categorized by carcinogenicity according to IARC as reported by Turi et al. (2003)

| Group 1 - Carcinogenic to Humans | Azathioprine, N,N-Bis(2-chloroethyl)-2-naphthylamine, Cyclophosphamide, 1,4-Butanediol dimethanesulphonate, Chlorambucil, Methyl-CCNU, Etoposide, Melphalan, MOPP when combined with other antineoplastic drugs, Treosulphan, Thiotepa |
| Group 2A - Probably Carcinogenic to Humans | Adriamycin, BCNU, CCNU, Cisplatin, N-Methyl-N-nitrosourea, N-Ethyl-N-nitrosourea, Nitrogen Mustard, Procabazine hydrochloride, Azacitidine, Chlorozotocin, Teniposide |
| Group 2B - Possibly Carcinogenic to Humans | Amsacrine, Aziridine, Bleomycins, Dacarbazine, Daunomycin, Merphalan, Mitoxantrone, Mitomycin C, Nitrogen mustard N-oxide, Streptozotocin |
| Group 3 - Not Classifiable as to its Carcinogenicity to Humans | Ifosfamide, 5-Fluorouracil, 6-Mercaptopurine, Methotrexate, Prednisone, Vinblastine sulfate, Vincristine sulfate |
Antineoplastic drugs come in five main categories. These categories are based upon the drug’s mechanism of action. These categories are alkylating agents, antibiotics, antimetabolites, free radical generators, and mitotic inhibitors (see Table 2).

**Table 2. Antineoplastic drug categories according to mode of action (Turi et al., 2003; NIOSH, 2004-102)**

<table>
<thead>
<tr>
<th>Drug Category</th>
<th>Mode of Action</th>
<th>Drug Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkylating Agents</td>
<td>Alkylating damages the DNA of tumor cells and interferes with the normal mitosis and division of cells</td>
<td>Cyclophosphamide, Chlorambucil, Carmustine</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>Transcription interference in cell DNA by causing single- and double-strand DNA breaks</td>
<td>Doxorubicin, Actinomycin, Bleomycin</td>
</tr>
<tr>
<td>Antimetabolites</td>
<td>Antimetabolites block the synthesis of DNA and RNA by interfering with folic acid, purine and pyrimidine synthesis</td>
<td>Fluorouracil, Mercaptopurine, Methotrexate</td>
</tr>
<tr>
<td>Free Radical Generators</td>
<td>Reduce free radicals around tumor cell DNA</td>
<td>Doxorubicin</td>
</tr>
<tr>
<td>Mitotic Inhibitors</td>
<td>Stop the mitotic mechanism essential to karyokinesis</td>
<td>Vinblastine, Vincristine, Paclitaxel</td>
</tr>
</tbody>
</table>

Concerns over worker exposure to antineoplastic drugs began in the 1970s, after research had demonstrated the carcinogenicity for many of these drugs to animals (Shimkin et al., 1966; Weisberger et al., 1975; Schmahl and Habs, 1978). In 1979, the first hospital based study reported exposure issues demonstrating signs of mutagenicity in the urine among oncology nurses (Falck et al., 1979). Studies have suggested that antineoplastic drugs might be the cause for increases in spontaneous abortions and malformations among children of oncology nurses (Hemminki et al., 1985; Selevan et al., 1985). An association was found between the handling of antineoplastic drugs and abnormal menstrual function (Shortridge et al., 1995).

In 1986, the Occupational Safety and Health Administration (OSHA) published its Guidelines for Cytotoxic (Antineoplastic) Drugs. In 2000, OSHA updated its recommendations on antineoplastic drug exposures in the OSHA Technical Manual [Section VI: Chapter 2 – Controlling Occupational Exposure to Hazardous Drugs]. Likewise, the National Institute for
Occupational Safety and Health (NIOSH) published in 2007 an alert on preventing occupational exposures to antineoplastic and other hazardous drugs.

The occupational exposure routes for antineoplastic drugs are most commonly skin absorption and inhalation. Additional exposure routes are ingestion and injection but are less common (NIOSH, 2004-165). A variety of studies have been conducted looking at the different aspects of occupational exposures in the hospital and pharmacy environment included with various analytical methods for the biological monitoring on exposed workers and environmental sampling of air concentrations and surface contamination levels (Sessink et al., 1996; Sora and Anderson, 1996; Kromhout et al., 2000; Pethran et al., 2002; Turi et al., 2002; Turi et al., 2003; Fransman et al., 2005; Hedmer et al., 2005; Mason et al., 2005; Rekhadevi et al., 2007).

Currently, there are no occupational exposure levels (OELs) established for many antineoplastic drugs. OSHA, NIOSH, and the American Conference for Governmental Industrial Hygienist (ACGIH) have established OELs that would apply to arsenic trioxide under inorganic arsenic compounds (OSHA 29 CFR 1910.1018; NIOSH 2007; ACGIH 2008). Exposure to antineoplastic drugs should be avoided, as it is unknown if there is any level of exposure that will not produce some adverse effect. Therefore, exposure levels need to be kept to the lowest levels possible. In order to ensure that occupational exposures are minimized both NIOSH and OSHA have established protocols and guides for handling and administering antineoplastic drugs (OSHA 2000; NIOSH 2004-165).

NIOSH published the statement “workers may be exposed to a drug (antineoplastic) throughout its life cycle – from manufacture to transport and distribution, to use in healthcare or home care settings, to waste disposal” (NIOSH, 2004-165). There are numerous tasks during which an oncology nurse or pharmacist could expose themselves to antineoplastic drugs (e.g.,
drug preparation, IV priming, and expelling air from filled syringes). When assessing the risk of worker exposure, areas beyond oncology nursing and the pharmacy need to also be explored. Workers in supply chain (i.e., shipping/receiving), environmental/cleaning services (i.e., janitorial), laundry and hazardous waste handling could also have a risk of occupational exposures.

A study found a strong correlation between dermal exposures to cyclophosphamide and the removal of bed linens. The same study also found workers with cyclophosphamide contamination on their foreheads (contaminated gloves touching the head) and forearms (unprotected skin touching surfaces) from cleaning patient toilets (Fransman, 2005). It has also been published that the exterior surfaces of drug packaging has the presence of detectable levels of antineoplastic drugs (Mason et al., 2003; Hedmer et al., 2005). Studies like this indicate that workers in the supply chain and environment of care for oncology departments should be assessed for antineoplastic drug exposure.

The U.S. Environmental Protection Agency (EPA), through the Resource, Conservation and Recovery Act (RCRA), regulates hazardous waste. The EPA currently regulates 9 antineoplastic drugs as RCRA hazardous waste (EPA 40 CFR 260-279). These drugs are listed in Table 3. Waste handlers of antineoplastic drugs also have the potential for the exposure (NIOSH, 2004-165).

**Table 3. Antineoplastic Drugs listed as RCRA Hazardous Waste (40 CFR 261 – Subpart D; Pines and Smith 2006)**

<table>
<thead>
<tr>
<th>Antineoplastic Drug</th>
<th>EPA RCRA Waste Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorambucil</td>
<td>U035</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>U058</td>
</tr>
<tr>
<td>Daunomycin</td>
<td>U059</td>
</tr>
<tr>
<td>Diethylstilbestrol</td>
<td>U089</td>
</tr>
<tr>
<td>Melphalan</td>
<td>U150</td>
</tr>
<tr>
<td>Mitomycin C</td>
<td>U010</td>
</tr>
<tr>
<td>Streptozotocin</td>
<td>U206</td>
</tr>
<tr>
<td>Uracil Mustard</td>
<td>U237</td>
</tr>
<tr>
<td>Arsenic Trioxide</td>
<td>P012</td>
</tr>
</tbody>
</table>
Problem Statement

The occupational exposure routes for antineoplastic drugs are inhalation, dermal absorption, ingestion and injection. Studies have demonstrated that occupational exposures are taking place in spite of control measures being taken (Pethran et al., 2002; Turci et al., 2002; Turci et al., 2003; Fransman et al., 2005; Hedmer et al., 2005). Trace levels of hazardous chemicals are left on the surface of many areas in pharmacies and oncology treatment rooms. Studies have shown significant levels of drugs on surfaces such as working trays, door handles, refrigerators, and vials coming from manufacturers (Mason et al., 2003; Turci et al., 2003). Exposures even take place when all engineering, administrative, and personal protective tools are used.

Hypothesis

I. Surface contamination for cyclophosphamide is not detectable within the institution.

II. Surface contamination for taxol is not detectable within the institution.

III. Surface contamination of 5-fluorouracil is not detectable within the institution.

IV. The institution (hospital) has a functional antineoplastic exposure prevention program (based on the compliance assessment questionnaires).

Approach

It is believed that occupational exposure or potential exposure can take place throughout the entire supply chain of antineoplastic drugs, specifically cyclophosphamide, 5-fluorouracil and taxol. This chain consists of shipping/receiving personnel that unload materials from transportation vehicles, delivery of the drugs to storage areas and drug preparation sites (e.g., pharmacies), patient areas where drug infusion takes place, and the waste collection and disposal
sites. This study conducted a compliance assessment on potential points of exposure of the entire process based upon the recommendations set forth by OSHA and NIOSH. Additionally, surface (wipe) sampling was conducted for the presence or absence of selected antineoplastic drugs along the supply chain of a large metropolitan academic medical center.

**Time Table**

- Complete proposal by December 2008.
- Present proposal to thesis advisory panel on February 18 at 9:00 am.
- Complete data collection completed by mid-March 2009.
- Have thesis final draft completed and all applicable forms submitted by April 7, 2009.
- Thesis defense on April 29, 2009 from 1-3 pm.
Literature Review

Keywords
chemotherapeutic drugs, antineoplastic drugs, cytotoxic drugs, hazardous drugs, occupational exposure, hospital, oncology, nurses

Terminology
Antineoplastic – inhibiting or preventing the growth and spread of neoplasms or malignant cells
Chemotherapy – the use of chemical agents in the treatment or control of disease or mental disorder
Cytotoxin – a substance (as a toxin or antibody) that has a toxic effect on cells
Malignant neoplasm (cancer) – an abnormal proliferation of cells that are exhibiting either uncontrolled growth, invasiveness and/or are metastizing

In 2005, a study was published involving the investigation of cyclophosphamide and ifosfamide contamination on drug packaging and surfaces within a hospital pharmacy in Sweden. This study was the first of its kind to look at the primary packaging of tablets (i.e., blister packages) and the outer packaging of drug vials. Surface (wipe) samples were collected from undamaged containers and surfaces believed to not contain any spill residue. Samples were analyzed using liquid chromatography. The results showed that cyclophosphamide was present in amount of 0.2 – 5.1 ng per sample on all outer packages of drug vials. Only on 5 outer packages of drug vials was ifosfamide found in small amounts. Cyclophosphamide was found on all samples taken from the inside surfaces of outer packaging. The median amount of cyclophosphamide was 3.2 ng. An amount of 25 ng of ifosfamide was also found on the inside
surface of an outer package. All the drug vials and vial cap covers sampled tested positive for
cyclophosphamide. Surface samples also came back positive for cyclophosphamide from the
floor of drug preparation areas, floors of dressing rooms, office floors, working surfaces of the
biological safety cabinet, and various surfaces throughout the drug preparation area (Hedmer et
al., 2005).

In 2002, a study conducted by Turi et al. at a large hospital in Italy researched the
biological monitoring of hospital personnel exposed to chemotherapeutic (antineoplastic) drugs.
The study discusses how there are various methods for detecting chemotherapeutic drug
exposure (e.g., looking at biomarkers or air monitoring) but is a proponent for urine analysis that
screens for specific chemicals. The study looked at cyclophosphamide, ifosfamide, methotrexate
and platinum. Urine samples were collected for two days from workers preparing and
administering drugs. Urine samples were collected at the beginning, during (when available) and
after the shift. Pre-shift samples were taken before workers were in uniform and post-shift
samples were collected once workers were out of uniform. All workers prepared drugs in
vertical laminar flow safety hoods and wore protective clothing (e.g., surgical masks and latex
gloves). All drugs were prepared and administered during the same shift. Up to five
chemotherapy treatments were prepared during the shift. Lab analysis was conducted using high
performance liquid chromatography/tandem mass spectrometry. Day one urine samples produced
results ranging from 50 – 4637 ng/l of cyclophosphamide in six of the eleven workers sampled.
Day two urine samples produced results ranging from 73 – 10,031 ng/l in six of the fourteen
workers sampled. For ifosfamide, only one sample was detectable (153 ng/l). No methotrexate
was detected. Three platinum samples came back positive with a concentration ranging from
920 – 1300 ng/l. The researchers observed that workers did not follow proper guidelines while
working with chemotherapeutic (antineoplastic) drugs. Staff working directly with patients did not typically wear personal protective equipment so as “not to alarm their patients.” Glove change was not frequent and samples collected from the internal side of the gloves tested positive for chemotherapeutic drugs. The report of this study recommended that closed loop biological safety cabinets be used as they hypothesized that high efficiency particulate air (HEPA) filter may not have pore sizes small enough to contain and collect drugs such as cyclophosphamide (Turi et al., 2002).

A study published in 2006 by Meijster et al. investigated occupational exposures to chemotherapeutic agents (antineoplastic drugs) outside of the clinical setting of a hospital. The study identified eight job sectors that have the potential for exposure: pharmaceutical industry, pharmacies, universities, veterinary medicine, nursing homes, home care, laundry facilities, and waste treatment. The study identified veterinary medicine, home care, nursing homes, and laundry facilities as the jobs that had the greatest likelihood of exposure. Air samples collected from the laundry facility produced detectible levels of cyclophosphamide when workers were directly handling the soiled linens. The median concentration was 4.5 ng/m$^3$. This exposure level of laundry workers was greater than oncology nurses. Home care workers likely have an occupational exposure level similar to that of an oncology nurse. Home care workers do not have the same frequency of exposure but due to education issues, e.g., lack of hazard awareness, little to no use of personal protective equipment, the infrequent exposures tend to be higher than that of an oncology nurse. Veterinary clinics had very high levels of carboplatin in surface (wipe) sample results. Samples were detected on the gloves and preparation areas. The concentration of carboplatin on gloves ranged from non-detect levels to 534 ng. The concentration of carboplatin on preparation area were high with the median amount detected in
the laminar air flow cabinet was 652 ng. Researchers observed visible levels of drug splashing during preparing and administrating the drug. Veterinary clinics often lack IV safety devices such as the Luer-Lock, which would help minimize exposure during the drug administering process. Nursing home workers were believed to have a much lower exposure than hospital outpatient or inpatient oncology nurses as quite often the drugs are taken to outpatient oncology patients for treatment. Nursing home staff administering chemotherapy often will lack the education and task frequency needed to safely administer the treatment (Meijster et al., 2006).

In 2003, a study by Mason et al. reported levels of contamination on the exterior of drug vials. There were no signs of damage to the exterior of drug packaging. The study looked at carboplatin, cisplatin, cyclophosphamide, ifosfamide and methotrexate drug vials (30 vials of each drug). All drug vials were shipped in by three different manufacturers. All vials showed contamination levels above the detection limit. One hundred percent of vials used for carboplatin were found contaminated. Additionally, a 0.5 m² floor area in front of drug storage was surface (wipe) sampled with results showing drug contamination (Mason et al., 2003).

A 2005 study by Fransman et al. examined potential and actual dermal exposures to cyclophosphamide for various jobs involved in and around an oncology department. These tasks included drug preparation, the handling of patient’s urine, patient bathing, handling of patient bed linens and the cleaning of patient’s toilets. Gloves worn during job activities were collected to determine potential hand exposures. Cotton pads were attached to workers forearms for sample collection. Forehead wipe samples were collected from workers. Concentrations of cyclophosphamide were examined in the patient’s urine, water used for bathing patients, and cleaning water used on patient’s toilets. Included in the sampling were safety cabinets, outside of infusion bags and syringes, outside of urinals and bedpans before cleaning, inside of bedpans
after cleaning, toilet seats after cleaning and mop handles. It was found that the outside surfaces of gloves worn during the preparation of cyclophosphamide in the pharmacy were contaminated. Only in one case was cyclophosphamide found on the hands underneath the gloves. In multiple cases the glove and/or hand contamination was found on nurses involved in the handling of patient’s urine, patient bathing and the changing of bed linens. Cleaning staff showed signs of cyclophosphamide exposure; multiple times the gloves worn during cleaning, mop handles, cleaning clothes, and cleaning water (when cleaning cloth was put in water) showed contamination. Occasionally, forehead and arm wipe samples showed contamination. Cyclophosphamide levels were some of the highest when collected during changing the bed linens and bathing the patients. This study demonstrates the importance of wearing gloves (Fransman et al., 2005).

A study published by Pethran et al. (2003) monitored urinary concentration of antineoplastic drugs (cyclophosphamide, ifosfamide, doxorubicin, epirubicin and platinum) in pharmacy and hospital employees. The study involved 14 German hospitals and included data collection over a course of 3 years. The study found that 40% of pharmacist and oncology workers had one of the tested drugs in their urine. Twenty-four of those monitored had no positive results. Twelve workers had a positive test during every sampling cycle. All monitored staff was involved in the preparation of drugs. The detected contamination is evidence that even though protective measures were taken (e.g., vertical laminar flow safety cabinets and personal protective equipment) exposure was still possible. Urine samples were collected on a fourth day of work after three continuous work days. Urine samples were collected for the period of 24-hour in polyethylene bottles and held at -20°C until analysis. Urine samples were compared to
controlled internal standards for urine developed by the institution. Lab analysis was performed using GC-MS (Pethran et al., 2003).

An article printed in 2000 by Kromhout et al. looked at the dermal exposure of antineoplastic drugs among hospital workers using three workplace surveys. The study was conducted in both outpatient and inpatient oncology treatment departments. The study focused on the exposures due to leaks from IV infusions, spilled urine and airborne contamination. Dermal exposure seems to be the most dominant mode of occupational uptake of antineoplastic drugs but inhalation is also another common exposure mode. A fluorescent tracer (UV blacklight) was used to “visualize” the contamination. The researchers developed and validated a technique of visually scoring the contamination (i.e., “quantifying” the amount of drug present) on IV’s and urine. The airborne samples were collected using medium flow inhalable dust samplers (PAS-6 and GSP) and analysis was conducted using GS-MSMS. Results indicated contamination during 4 different IV infusion systems, in patient toilets, in utility rooms, in soils of nurse’s shoes, and on the skin of patients and nurses; guest restrooms were a control and showed no contamination. Air samples indicated concentrations ranging from 0.46 – 1.66 ng/m³. As an additional note this study cites another study (Opiolka et al., 2000) that found air concentrations up to 130 ng/m³ exhausting from biological safety cabinets. This demonstrated that air contaminates can be potential pathway of considerable exposure (Kromhout et al., 2000).
Materials

The major materials used in this study are as follows:

- Compliance assessment questionnaires designed by the researcher (See Appendices)
- Alpha Text wipe swabs supplied by Bureau Veritas, Detroit Lab
- Amber glass vials (used for holding wipe sample during storage and transportation)
- Methanol (100%)
- Sampling template (10 cm x 10 cm; 100 cm²) supplied by Bureau Veritas, Detroit Lab
- Nitrile gloves – specifically Esteem with Neu Thera from Cardinal Health (these are a powder-free nitrile exam glove, lab tested for possible drug contamination)
Methods

Overview

The compliance assessment (determining areas of likely exposure or incorrect practice) was conducted throughout the supply chain of the antineoplastic drugs. The compliance assessment was conducted using recommended best practices by the NIOSH Alert – Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings (2004) and OSHA’s Technical Manual – Section VI: Chapter 2 – Controlling Occupational Exposure to Hazardous Drugs (2000). A compliance assessment was created based on the guidelines of these documents for determining areas with potential for exposure. The compliance assessment forms, designed by the researcher, were completed for each step in the antineoplastic drug supply chain life cycle in the hospital. The compliance assessment forms were completed by the researcher based upon visual inspection and questions posed to hospital staff. The assessment was completed during times of normal (day-time) business operations. The compliance assessments forms are in the pilot state to be validated through this study.

Surface (wipe) sampling was conducted on surfaces perceived by the researcher to have potential for contamination from antineoplastic drugs. The drugs included in the study were cyclophosphamide, 5-fluorouracil and taxol. These drugs were selected based on how commonly they are administered in the outpatient oncology areas of the hospital studied. Surface (wipe) samples were collected using Alpha Text swabs. Each swab was prefixed with 100% methanol. After sampling, swabs were transferred into amber glass vials for storage and transport. Samples were shipped to the lab frozen using dry ice. Sampled surfaces were collected within the area confined by the 100 cm² template supplied by analytical lab. Each
surface (wipe) sample could only be analyzed for one drug. Lab analysis was completed using liquid chromatography. Lab results were reported in total mass.

Recommended locations for sampling were:

- Arm rails and table on patient infusion chair
- Arm rails and table on patient infusion bed
- Floors in multiple patient infusion rooms
- Surfaces of (yellow) chemotherapy waste bucket
- Floor surrounding (yellow) chemotherapy waste bucket
- Front of oncology pharmacy drug preparation hood
- Floor immediately in front of oncology pharmacy drug preparation hood
- Counter and IV bins (bins contain prepped chemotherapy IV bags) in oncology pharmacy window

The Bureau Veritas, Detroit Lab performed the lab analysis for all surface (wipe) samples.

Sampling Plan

The monitoring plan involved two phases of field sample collection. During the first phase, surface (wipe) samples were collected in six locations (i.e., surface locations) within the infusion areas of outpatient oncology. At each location six samples were collected (two for each drug – a regular sample and a duplicate sample). In the second phase, the surface area sampled by each swab was increased from 100 cm$^2$ to 300 cm$^2$ in an attempt to increase have samples achieving contamination levels that would be detectable by the lab. As a result of each swabs increased area of surface collection, not all sampling locations were large enough to allow for the collection of six samples. When locations did not provide enough surface area for six samples to be collected synonymous locations throughout the department were sampled (e.g., three different
yellow chemotherapy waste containers were sampled – each for a different drug). During phase two both regular and duplicate samples were collected. The samples were analyzed for either cyclophosphamide, 5-fluorouracil or taxol. Blank samples were also submitted to the lab (10% of sample number).
Results

I. Compliance Assessment Forms

All compliance forms can be seen in the Appendix.

Compliance Assessment A: Shipping and Receiving (Package Handling)

<table>
<thead>
<tr>
<th>Questions</th>
<th>Score</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are antineoplastic and other hazardous drugs labeled on the exterior packaging?</td>
<td>X</td>
<td>Full compliance: contents of drug shipping container clearly marked contents (e.g., Hercepton 440 mg)</td>
</tr>
<tr>
<td>Is shipping/receiving prepared to respond to an antineoplastic drug spill?</td>
<td>X</td>
<td>Full compliance: antineoplastic drug spill kits are located in the pharmacy-receiving department. However, it is unclear whether any extensive spill response training has been taken place (e.g., HAZWOPER).</td>
</tr>
<tr>
<td>Is any personal protective equipment worn while opening packaging? If so, what kind</td>
<td>X</td>
<td>Full compliance: workers unpacking pharmaceuticals were wearing chemotherapeutic drug resistant nitrile gloves</td>
</tr>
<tr>
<td>Are hazardous drugs stored separately from other drugs?</td>
<td>X</td>
<td>Full compliance: antineoplastic drugs are stored separately from other drugs in the pharmacy-receiving department for inpatient oncology. There are areas for both room temperature and refrigerated drug storage. Both locations are marked accordingly. Antineoplastic drugs for outpatient oncology are brought directly to the outpatient pharmacy for storage.</td>
</tr>
<tr>
<td>Do storage containers minimize the risk of container breakage?</td>
<td>X</td>
<td>Full compliance: drugs are stored in either the manufacturer original box packaging or in plastic bins on shelving (both at the room temperature and refrigerated storage).</td>
</tr>
<tr>
<td>Do storage locations have general exhaust to dilute airborne concentrations?</td>
<td>X</td>
<td>No compliance: there is no ventilation other than the general HVAC system for both the pharmacy-receiving department and oncology outpatient pharmacy.</td>
</tr>
<tr>
<td>Is there an emergency exhaust fan to purge airborne concentrations from a large spill?</td>
<td>X</td>
<td>No compliance: there is no ventilation other than the general HVAC system for both the pharmacy-receiving department and oncology outpatient pharmacy.</td>
</tr>
</tbody>
</table>

Scoring key: 0 = no compliance 1 = 25% compliance 2 = 50% compliance 3 = 75% compliance 4 = full compliance

Interpretation on Shipping and Receiving (Package Handling): The workers receiving the antineoplastic drugs are aware of the hazards associated with the chemicals and wear appropriate gloves. The ventilation issues need to be further investigated.
## Compliance Assessment B: Drug Preparation

<table>
<thead>
<tr>
<th>Questions</th>
<th>Score</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has the pharmacy identified points where drugs can be released, e.g., the outside of containers?</td>
<td>X</td>
<td><strong>Full compliance</strong>: pharmacy director monitors current literature on exposure studies. Pharmacy director has requested that additional sampling be conducted to the outside of unopened drug vials (per results shown in current literature of contamination). However, it is not clear whether the department has an established list of exposure points.</td>
</tr>
<tr>
<td>Do drug preparation areas have limited access?</td>
<td>X</td>
<td><strong>Full compliance</strong>: pharmacy doors are always locked to none-authorized individuals.</td>
</tr>
<tr>
<td>Are ventilated cabinets used during drug preparation, e.g., biological safety cabinet (BSC)?</td>
<td>X</td>
<td><strong>Full compliance</strong>: all antineoplastic drugs are prepared in a biological safety cabinet.</td>
</tr>
<tr>
<td>Is personal protective equipment (PPE) being worn, e.g., gloves (double), gowns (polyethylene-coated polypropylene)? If so, when (at all times or only during certain tasks)?</td>
<td>X</td>
<td><strong>Partial compliance</strong>: the pharmacy technician (individual doing the majority of drug preparations) wore scrubs and drug resistant nitrile gloves (single gloves) while preparing drugs in the biological safety cabinet. There were two pharmacists in the pharmacy; both wore street clothes and only one of them had a lab coat on over the street closes. A pharmacist removed prepared drug IV bags from the biological safety cabinet without wearing hand protection. It is assumed by the pharmacy that the exterior of the drug containers are not contaminated by drugs.</td>
</tr>
<tr>
<td>Are gloves compatible with antineoplastic drugs? How often are they changed (recommended every 30 minutes)?</td>
<td>X</td>
<td><strong>Full compliance</strong>: gloves worn were made of drug resistant nitrile. Gloves were changed between each drug preparation.</td>
</tr>
<tr>
<td>Are “sleeve covers” worn?</td>
<td>X</td>
<td><strong>No compliance</strong>: no sleeve covers were worn. Only scrubs with long sleeve t-shirt worn underneath.</td>
</tr>
<tr>
<td>Are proper techniques taught or evaluated?</td>
<td>X</td>
<td><strong>No compliance</strong>: there is no periodic review on drug preparation techniques. The only training is offered during academic training and job orientation training.</td>
</tr>
<tr>
<td>Are drug containers closed before being removed from BSC?</td>
<td>X</td>
<td><strong>Full compliance</strong>: all containers observed were closed before being removed from the biological safety cabinet.</td>
</tr>
</tbody>
</table>

**Scoring key:**  
0 = no compliance  
1 = 25% compliance  
2 = 50% compliance  
3 = 75% compliance  
4 = full compliance

**Interpretation on drug preparation:** The use of single pair drug resistant gloves should be sufficient as long as the gloves are regularly changed, i.e., every 30 minutes. The use of additional personal protective equipment appears to be relaxed in the oncology pharmacy. The issue of periodic review should be further investigated.
### Compliance Assessment C: Drug Administration

<table>
<thead>
<tr>
<th>Questions</th>
<th>Score</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does the pharmacy prime the IV tubing and syringes in the biological safety cabinet or with non-drug solutions? It is recommended that this is not done in the patient area.</td>
<td>X</td>
<td>Full compliance: all IV bags coming from the pharmacy have their IV lines primed before leaving the pharmacy.</td>
</tr>
<tr>
<td>Are closed systems being used?</td>
<td>X</td>
<td>Full compliance: all observed instances involved the use of closed systems. The oncology department utilizes PhaSeal® devices to decrease the opportunity for drug release when connecting lines. A staff nurse mentioned that it is possible that not all nurses are using the PhaSeal® devices. The PhaSeal® devices are a closed system drug transfer device that mechanically eliminates the transfer of environmental contaminants into the system and the escape of hazardous drug aerosols or vapors.</td>
</tr>
<tr>
<td>Is personal protective equipment (PPE) being worn? Double gloves, eye protection, gowns?</td>
<td>X</td>
<td>Partial compliance: oncology nurses are not required to wear gloves while starting antineoplastic IV’s as it is assumed that the external surfaces of the drug containers are uncontaminated by drugs. Gloves were still worn two out of three observations on starting drug IV’s. Gloves were worn 100% of the time while removing antineoplastic drug IV’s. No eye protection or gowns worn. Only scrubs.</td>
</tr>
<tr>
<td>Is tubing removed from IV bags that contain antineoplastic drugs?</td>
<td>X</td>
<td>Full compliance: tubing is not removed from IV bag containing antineoplastic drugs.</td>
</tr>
<tr>
<td>Is tubing disconnected from the system before being flushed?</td>
<td>X</td>
<td>Full compliance: all tubing was flushed in saline before being disconnected from the tubing system.</td>
</tr>
<tr>
<td>Are yellow containers (antineoplastic waste) kept closed?</td>
<td>X</td>
<td>No compliance: all yellow (trace antineoplastic waste) containers were observed open while not being filled/emptied.</td>
</tr>
<tr>
<td>Are hands washed after PPE removal?</td>
<td>X</td>
<td>Full compliance: hands were always washed after glove removal.</td>
</tr>
</tbody>
</table>

**Scoring key:**
- 0 = no compliance
- 1 = 25% compliance
- 2 = 50% compliance
- 3 = 75% compliance
- 4 = full compliance

**Interpretations on drug administration:** The use of single pair drug resistant gloves should be sufficiently protective as long as the gloves are regularly changed, i.e., every 30 minutes. The use of personal protective equipment appears to be relaxed among oncology nursing staff.

Yellow containers need to be kept closed while not being filled/emptied.
Compliance Assessment D: Environmental Services (Housekeeping)

<table>
<thead>
<tr>
<th>Questions</th>
<th>Score</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are double gloves worn while handling linens, feces, urine, etc?</td>
<td></td>
<td>X Partial compliance: the use of single pair drug resistant gloves should be sufficiently protective as long as the gloves are regularly changed, i.e., every 30 minutes. Environmental Services workers do not handle linens, feces, or urine. The only contact with urine or feces would be in and around the toilet in the patient bathrooms. After patient room was wiped down with bleach based cleaner (gloves worn), gloves were not worn while mopping the room.</td>
</tr>
<tr>
<td>Are gowns worn and discarded or washed after each use?</td>
<td>X</td>
<td>No compliance: no gowns were worn. Only clothing worn was the typical Environmental Services work uniform throughout the hospital.</td>
</tr>
<tr>
<td>Are hands washed after cleaning and glove removal?</td>
<td>X</td>
<td>No compliance: no hand washing observed.</td>
</tr>
</tbody>
</table>

Scoring key: 0 = no compliance 1 = 25% compliance 2 = 50% compliance 3 = 75% compliance 4 = full compliance

Interpretations on environmental services (housekeeping): Environmental Services is relaxed with the use of personal protective equipment and hand washing.

Compliance Assessment E: Waste Disposal

<table>
<thead>
<tr>
<th>Questions</th>
<th>Score</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are “trace” and “bulk” wastes separated?</td>
<td></td>
<td>X Full compliance: all observed containers had waste properly segregated.</td>
</tr>
<tr>
<td>Are antineoplastic sharps going into yellow (antineoplastic waste) or red (biohazardous waste) containers?</td>
<td>X</td>
<td>Full compliance: all antineoplastic sharps go into the rigid yellow containers for incineration.</td>
</tr>
<tr>
<td>How are expired antineoplastic drugs handled?</td>
<td>X</td>
<td>Full compliance: it is very rare for the outpatient oncology pharmacy to have expired drugs. When drugs do expire they are handled through reverse distribution.</td>
</tr>
</tbody>
</table>

Scoring key: 0 = no compliance 1 = 25% compliance 2 = 50% compliance 3 = 75% compliance 4 = full compliance

Interpretations on waste disposal: Observations indicate that antineoplastic waste is being handled properly.

II. Surface Sampling Results – Phase 1

The phase 1 surface (wipe) sampling results for cyclophosphamide, taxol, and 5-fluorouracil are presented in Table 4. One cyclophosphamide sample received a lab value of 12
ng. Taxol samples had lab values ranging from 0.27 µg to 0.93 µg. No 5-fluorouracil samples received lab values.

Table 4. Surface Sampling Results – Phase 1

<table>
<thead>
<tr>
<th>Sample Location</th>
<th>Cyclophosphamide</th>
<th>Taxol</th>
<th>5-Fluorouracil</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lab Value (ng)</td>
<td>Lab Value (µg)</td>
<td>Lab Value (µg)</td>
</tr>
<tr>
<td>Room 1 - Bed Table</td>
<td>&lt;10</td>
<td>&lt; 0.2</td>
<td>&lt; 0.2</td>
</tr>
<tr>
<td>Room 4 - Infusion Chair Rail</td>
<td>&lt;10</td>
<td>0.44</td>
<td>&lt; 0.2</td>
</tr>
<tr>
<td>Room 4 - Bathroom - Yellow Bucket</td>
<td>&lt;10</td>
<td>0.33</td>
<td>&lt; 0.2</td>
</tr>
<tr>
<td>Room 4 - Bathroom - Floor Toilet</td>
<td>&lt;10</td>
<td>&lt; 0.2</td>
<td>&lt; 0.2</td>
</tr>
<tr>
<td>Pharmacy Floor</td>
<td>12</td>
<td>&lt; 0.2</td>
<td>&lt; 0.2</td>
</tr>
<tr>
<td>Pharmacy Hood</td>
<td>&lt;10</td>
<td>&lt; 0.2</td>
<td>&lt; 0.2</td>
</tr>
</tbody>
</table>

Note: Each wipe sample was collected within a 100 cm² area.

III. Surface Sampling Results – Phase 2

The phase 2 sampling differed from phase 1 in that each swab’s sampling area increased from 100 cm² to 300 cm² and the addition and subtraction of some sampling locations.

The phase 2 surface (wipe) sampling results for cyclophosphamide, taxol, and 5-fluorouracil are presented in Table 5. Two taxol samples received a lab value of 0.22 µg and 0.37 µg. No cyclophosphamide or 5-fluorouracil samples received lab values.
Table 5. Surface Sampling Results – Phase 2

<table>
<thead>
<tr>
<th>Sample Location</th>
<th>Cyclophosphamide</th>
<th>Taxol</th>
<th>5-Fluorouracil</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lab Value (ng)</td>
<td>Lab Value (µg)</td>
<td>Lab Value (µg)</td>
</tr>
<tr>
<td>Room 6 - Bed rail and call button*</td>
<td>-</td>
<td>-</td>
<td>&lt; 0.2</td>
</tr>
<tr>
<td>Room 6 - Floor by patient bed</td>
<td>-</td>
<td>-</td>
<td>&lt; 0.2</td>
</tr>
<tr>
<td>Room 6 - Top of Med Cart</td>
<td>&lt;10</td>
<td>&lt; 0.2</td>
<td>-</td>
</tr>
<tr>
<td>Room 4 - Bathroom - Yellow Bucket</td>
<td>&lt;10</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Room 4 - Bathroom - Floor Toilet</td>
<td>-</td>
<td>0.22</td>
<td>-</td>
</tr>
<tr>
<td>Room 4 - Bathroom - Floor Toilet</td>
<td>-</td>
<td>&lt; 0.2</td>
<td>-</td>
</tr>
<tr>
<td>Nursing Station Counter</td>
<td>&lt;10</td>
<td>&lt; 0.2</td>
<td>&lt; 0.2</td>
</tr>
<tr>
<td>Room 2 - Bathroom - Yellow Bucket</td>
<td>-</td>
<td>&lt; 0.2</td>
<td>-</td>
</tr>
<tr>
<td>Room 2 - Bathroom - Floor Toilet</td>
<td>&lt;10</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Room 11 - Patient Infusion Chair</td>
<td>&lt;10</td>
<td>&lt; 0.2</td>
<td>&lt; 0.2</td>
</tr>
<tr>
<td>Room 11 - Bathroom - Yellow Bucket</td>
<td>-</td>
<td>0.37</td>
<td>&lt; 0.2</td>
</tr>
<tr>
<td>Room 11 - Bathroom - Floor Toilet</td>
<td>-</td>
<td>-</td>
<td>&lt; 0.2</td>
</tr>
<tr>
<td>Oncology Pharmacy</td>
<td>&lt;10</td>
<td>&lt; 0.2</td>
<td>&lt; 0.2</td>
</tr>
<tr>
<td>Window/Counter</td>
<td>&lt;10</td>
<td>&lt; 0.2</td>
<td>&lt; 0.2</td>
</tr>
</tbody>
</table>

*Bed rail and call button sample was not collected from 300 cm² area. The sample was collected from this location because patient in bed was receiving treatment with 5-fluorouracil.

Note: Each wipe sample was collected within a 300 cm² area.

Calculation of Average Levels

The calculated average concentration of cyclophosphamide was 5.29 ng (N = 24 (1 lab value/23 estimated values)). This calculation was generated using the reported lab values and estimated values from samples not receiving a detectable value from the lab. For each cyclophosphamide sample receiving a lab value of < 10 ng was assigned an estimated value of 5 ng. The estimated value was calculated based upon Hornung and Reed’s (1990) method for estimating average concentrations in the presence of non-detectable values when the majority of reported values are non-detect. These estimated values can be used since there is an uncertainty as to whether or not there is drug contamination between the values of 0 – 10 ng.

The calculated average concentration of taxol was 0.18 µg (N = 24 (7 lab values/17 estimated values)). This calculation was generated using the reported lab values and estimated...
values from samples not receiving a detectable value from the lab. For each taxol sample receiving a lab value of < 0.2 µg was assigned an estimated value of 0.1 µg. The estimated value was calculated based upon the same Hornung and Reed’s (1990) method used for calculating the estimated value for cyclophosphamide.

The calculated average concentration of 5-fluorouracil was 0.1 µg (N = 24 (0 lab values/24 estimated values)). This calculation was generated using the reported lab values and estimated values from samples not receiving a detectable value from the lab. For each 5-fluorouracil sample receiving a lab value of < 0.2 µg was assigned an estimated value of 0.1 µg. The estimated value was calculated based upon the same Hornung and Reed’s (1990) method used for calculating the estimated value for cyclophosphamide.
Discussion

Results suggest that the institution has to improve its antineoplastic drug handling practices in order to have a functional exposure prevention program. The pharmacy-receiving department and storage locations have to be evaluated for and improve the general and spill response ventilation. It is suggested that the use of personal protective equipment (PPE) to be enhanced; the use of PPE appears to be relaxed in multiple phases of the antineoplastic drug life cycle. In the pharmacy, protective sleeves are to be worn while mixing drugs in the biological safety cabinet. The pharmacists are to wear gloves when handling drug containers assuming that the exterior packaging is contaminated. During patient infusion, oncology nurses are to always wear gloves while handling drug containers from the pharmacy assuming that the exterior packaging is contaminated. Environmental Services are to wear gloves; it was observed that workers in this section were not wearing gloves during some steps of the room cleaning process. The pharmacy should have regular evaluations to ensure that all staff conducts their drug preparations in a manner that will minimize the possibility for exposure. The yellow waste buckets for trace level antineoplastic waste need to be kept closed. Environmental services needs to make sure that with each change of glove and after each task to always wash their hands.

Results show that cyclophosphamide contamination was detectable by one surface (wipe) sample. Cyclophosphamide was detected on the floor of the pharmacy at an amount of 12 ng in 100 cm\(^2\) of surface area. The floor sample was collected on the floor directly in front of the biological safety cabinet. See Appendix H for picture of sample location. Cyclophosphamide contamination could potentially be present on more locations below the level detectable by the lab. The calculated average concentration of cyclophosphamide was 5.29 ng. Higher
concentrations of cyclophosphamide were detected by another study (Hedmer et al., 2005) on a
drug preparation area floors ranging from 46 – 260 ng in 400 cm$^2$ of surface area. Additional
studies have various areas of the hospital sampled for cyclophosphamide but the Hedmer et al.,
(2005) were the only researchers sampling and reporting floor contamination to
cyclophosphamide in drug preparation areas.

Results show that taxol contamination was detectable. Taxol was detected on the arm
rests of a patient infusion chair at the amount of 0.44 µg and 0.27 µg in 100 cm$^2$ surface areas.
Taxol was detected on the backrest of infusion chair at the amount of 0.37 µg in 300 cm$^2$ surface
area. An additional note is that the surface samples from the arm rests of the patient infusion
chair were collected after the chair had already been considered cleaned (i.e., the chair surfaces
had been wiped with a surface cleaner) from the prior patient’s treatment. See Appendix I for a
picture of a patient infusion chair. Taxol was detected on the outer walls of the yellow waste
buckets (trace level antineoplastic waste – i.e., RCRA empty containers) at the amount of 0.33
µg and 0.27 µg in 100 cm$^2$ surface areas. See Appendix J for a picture of a yellow waste bucket.
Taxol was detected on the floor surfaces of the patient bathrooms directly in front of the toilet at
the amount of 0.93 µg in 100 cm$^2$ surface areas and 0.22 µg in 300 cm$^2$ surface area. See
Appendix K for a picture of a bathroom floor sample location. The calculated average
concentration of taxol was 0.18 µg. This result coincides with the results detected ranging from
0.016 – 11.15 µg/dm$^2$ as studied by Minoia et al., 1999 [reported by Turci et al., 2003].

Results show that 5-fluorouracil was not detectable on the surfaces sampled. The
calculated average concentration of 5-fluorouracil was 0.1 µg.

The implications of these results would suggest that employees might receive exposures
to antineoplastic drugs throughout the antineoplastic drug life cycle thru exposure to
contaminated surfaces. This study did not verify worker exposure or uptake concentrations of antineoplastic drugs.

The limitations of this study are space and time. This study was limited by space as all surfaces within the life cycle of the antineoplastic drug had not been sampled. This study was limited by time as this was the first step taken in this kind of study for the institution. Additional time limitations would be the number of times samples have been collected. This study was limited by finances and was only able to look at limited number of surfaces for contamination detection and screen for a limited number of drugs.
Conclusions

Results show that cyclophosphamide contamination was detectable by one surface (wipe) sample. Therefore, the hypothesis that “surface contamination for cyclophosphamide is not detectable within the institution” is rejected.

The results indicated that there was taxol contamination. Therefore, the hypothesis that “surface contamination for taxol is not detectable within the institution” is rejected.

The results indicated that there was not 5-fluorouracil contamination. Therefore, the hypothesis “surface contamination of 5-fluorouracil is not detectable within the institution” is not rejected.

The results indicated that there were antineoplastic drug handling practices that need improvement. Therefore, the hypothesis that “the institution has a functional antineoplastic exposure prevention program, based on the compliance assessment questionnaires” is rejected.
Summary

Antineoplastic drugs are chemical agents used in the treatment of malignant neoplasms (cancers) and occasionally non-neoplastic forms of disease. These drugs unfortunately cannot differentiate between normal healthy cells and the cells of a malignant neoplasm, which can cause undesired damage to the body and occasionally create secondary malignancies (including cases of leukemia), mutagenic and teratogenic effects.

Concerns over worker exposure to antineoplastic drugs began in the 1970s, after research had demonstrated the carcinogenicity for many of these drugs to animals. In 1979, the first hospital based study reported exposure issues demonstrating signs of mutagenicity in the urinary tract among oncology nurses. Other side effects seen among occupationally exposed oncology staff have increases in spontaneous abortions, malformations among children of oncology nurses abnormal menstrual function. In 2000, OSHA added its recommendations on antineoplastic drug exposures to the OSHA Technical Manual. In 2007, the National Institute for Occupational Safety and Health (NIOSH) published an alert on preventing occupational exposures to antineoplastic and other hazardous drugs.

This study tested these hypotheses: the institution has a functional antineoplastic exposure prevention program (based on the compliance assessment questionnaires); and, surface contamination for cyclophosphamide, taxol and 5-fluorouracil is not detectable within the institution. Data were collected to test these hypotheses through a compliance assessment on potential points of exposure of the entire process based upon the recommendations set forth by OSHA and NIOSH and through surface (wipe) sampling to detect the presence or absence of cyclophosphamide, taxol and 5-fluorouracil along the institution’s chemotherapy (antineoplastic) drug supply chain.
The results of compliance assessment showed that the institution has to improve its antineoplastic drug handling practices in order to have a functional exposure prevention program. Therefore, the hypothesis that “the institution has a functional antineoplastic exposure prevention program, based on the compliance assessment questionnaires” is rejected. Surface sampling results indicated detectable levels of contamination for cyclophosphamide and taxol. Therefore, the hypotheses that “surface contamination for cyclophosphamide and taxol is not detectable within the institution” are rejected. None of the samples analyzed for 5-fluorouracil had detectable levels of contamination. Therefore, the hypothesis “surface contamination of 5-fluorouracil is not detectable within the institution” is not rejected.
References


Appendices

Appendix A – Compliance Assessment Form Shipping and Receiving (Package Handling)

Compliance Assessment - Antineoplastic Drug Exposure

Work Area: Shipping and Receiving (Package Handling)

Scoring key: 0 = no compliance 1 = 25% compliance 2 = 50% compliance 3 = 75% compliance 4 = full compliance

1. Are antineoplastic and other hazardous drugs labeled on the exterior packaging?
   0 1 2 3 4
   Comments:

2. Is shipping/receiving prepared to respond to an antineoplastic drug spill?
   0 1 2 3 4
   Comments:

3. Is any personal protective equipment worn while opening packaging? If so, what kind?
   0 1 2 3 4
   Comments:

4. Are hazardous drugs stored separately from other drugs?
   0 1 2 3 4
   Comments:

5. Do storage containers minimize the risk of container breakage?
   0 1 2 3 4
   Comments:

6. Do storage locations have general exhaust to dilute airborne concentrations?
   0 1 2 3 4
   Comments:

7. Is there an emergency exhaust fan to purge airborne concentrations from a large spill?
   0 1 2 3 4
   Comments:
### Appendix B – Compliance Assessment Form Drug Preparation (Pharmacy)

Compliance Assessment - Antineoplastic Drug Exposure

Work Area: Drug Preparation

Scoring key: 0 = no compliance  1 = 25% compliance  2 = 50% compliance  3 = 75% compliance  4 = full compliance

1. Has the pharmacy identified points where drugs can be released, e.g., the outside of containers?
   - 0 1 2 3 4
   Comments:

2. Do drug preparation areas have limited access?
   - 0 1 2 3 4
   Comments:

3. Are ventilated cabinets used during drug preparation, e.g., biological safety cabinet (BSC)?
   - 0 1 2 3 4
   Comments:

4. Is personal protective equipment (PPE) being worn, e.g., gloves (double), gowns (polyethylene-coated polypropylene)? If so, when, (at all times or during certain tasks)?
   - 0 1 2 3 4
   Comments:

5. Are gloves compatible with antineoplastic drugs? How often are they changed (recommended every 30 minutes)?
   - 0 1 2 3 4
   Comments:

6. Are sleeve covers worn?
   - 0 1 2 3 4
   Comments:

7. Are proper techniques taught or evaluated?
   - 0 1 2 3 4
   Comments:

8. Are drug containers closed before being removed from BSC?
   - 0 1 2 3 4
   Comments:
Appendix C – Compliance Assessment Form Drug Administration (Point of Infusion)

Compliance Assessment - Antineoplastic Drug Exposure

Work Area:  Drug Administration

Scoring key:  0 = no compliance  1 = 25% compliance  2 = 50% compliance
            3 = 75% compliance  4 = full compliance

1. Does the pharmacy prime the IV tubing and syringes in the biological safety cabinet or with non-drug solutions? It is recommended that this is not done the patient area.
   0  1  2  3  4
   Comments:

2. Are closed systems being used?
   0  1  2  3  4
   Comments:

3. Is personal protective equipment (PPE) being worn? Double gloves, eye protection, gowns?
   0  1  2  3  4
   Comments:

4. Is tubing removed from IV bags that contain antineoplastic drugs?
   0  1  2  3  4
   Comments:

5. Is tubing disconnected from the system before being flushed?
   0  1  2  3  4
   Comments:

6. Are yellow containers (antineoplastic waste) kept closed?
   0  1  2  3  4
   Comments:

7. Are hands washed after PPE removal?
   0  1  2  3  4
   Comments:
Appendix D – Compliance Assessment Form Drug Environmental Services (Housekeeping)

Compliance Assessment - Antineoplastic Drug Exposure

Work Area: Environmental Services (Housekeeping)

Scoring key: 0 = no compliance  1 = 25% compliance  2 = 50% compliance
              3 = 75% compliance  4 = full compliance

1. Are double gloves worn while handling linens, feces, urine, etc?
   0  1  2  3  4
   Comments:

2. Are gowns worn and discarded or washed after each use?
   0  1  2  3  4
   Comments:

3. Are hands washed after cleaning and glove removal?
   0  1  2  3  4
   Comments:
Appendix E – Compliance Assessment Form Drug Waste Disposal

Compliance Assessment - Antineoplastic Drug Exposure

Work Area: Waste Disposal

Scoring key: 0 = no compliance  1 = 25% compliance  2 = 50% compliance  3 = 75% compliance  4 = full compliance

1. Are “trace” and “bulk” wastes separated?
   0 1 2 3 4
   Comments:

2. Are antineoplastic sharps going into yellow (antineoplastic waste) or red (biohazardous waste) containers?
   0 1 2 3 4
   Comments:

3. How are expired antineoplastic drugs handled?
   0 1 2 3 4
   Comments:
Appendix F – Sampling Protocol

Pre-Sample
- Collect sampling supplies and paper work
  - Nitrile Gloves
  - Cooler containing ice or dry ice to hold samples
  - Alpha Text Wipe Swabs
  - Glass Amber Vials
  - 100% methanol
  - 100 cm² Sampling Template (10 cm x 10 cm)
  - Sample key
  - Camera
  - Sample labels
  - Fine tip permanent marker
  - Pen

Sample Collect
- Select sample location
- Don new pair of nitrile gloves
- Remove alpha text wipe swab from container and moisten with 100% alcohol
- Place sampling template on sample location
- Run swab on interior sample location
- Put swab into plastic storage vial
- Mark vial with sample number and complete information on sample key
- Store sample in cooler

Post Sample
- Discard all sampling materials
  - Templates and gloves should go into trace level antineoplastic waste containers
  - Other trash can go into general waste receptacles

Keep all samples refrigerated (i.e., below 40°F) at all times, including during shipment.
### Appendix G – Sample Key

<table>
<thead>
<tr>
<th>Sample Number</th>
<th>Sample Location</th>
<th>Date</th>
<th>Cyclophosphamide</th>
<th>Taxol</th>
<th>5-Fluorouracil</th>
<th>Blank</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix H – Pharmacy Floor

Photograph taken by researcher
Appendix I – Patient Infusion Chair

Photograph taken by researcher
Appendix J – Yellow Waste Bucket

*Photograph taken by researcher*
Appendix K – Patient Bathroom Floor

*Photograph taken by researcher*
Abstract

Occupational exposures to antineoplastic drugs in clinical settings can take place through inhalation, dermal absorption, ingestion and injection. The objective of this study was to explore surface (wipe) sampling as a method to determine if surfaces are contaminated by antineoplastic drugs. Additionally, a compliance assessment, based on professional guidelines, was conducted on all areas of the antineoplastic drug life cycle within a hospital to determine areas where policy and practices are to be enhanced. Surface (wipe) sample results indicated surface contamination to drugs in pharmacy floors, infusion chairs, bathroom floors and the exterior surfaces of antineoplastic waste containers. The compliance assessment indicated lack of sound practices during drug preparation and administration. The results of this study indicated that some surfaces throughout the outpatient oncology department are being contaminated by antineoplastic drugs, which might lead to unacceptable exposures.