In-Depth Survey Report

Engineering Control Evaluation at Veterinary Hospital G

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Division of Field Studies and Engineering
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EPHB Report No. DART 18-181
Animal Specialty & Emergency Center

Revised June 2021

Site Surveyed: Veterinary Hospital G

NAICS Code: 541940 Animal hospitals

Survey Dates: August 2018

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Abstract

NIOSH researchers conducted a field survey at Veterinary Hospital G in August 2018. The purpose of the site visit was to identify and evaluate hazardous drug engineering controls as well as to sample for potential surface contamination at the hospital. NIOSH researchers also observed and interacted with the hospital's veterinarians and staff to obtain information about the hazardous drug work practices, daily activities, and oncology treatment processes.

A TSI® VelociCalc™ Plus Model 9565-P thermal anemometer was used to measure air velocities at the face of the biological safety cabinet (BSC), while a Wizard Stick handheld smoke generator was used to visualize air movement inside and around the periphery of the hood. Both the qualitative and quantitative tests showed that the BSC was operating appropriately. The BSC's average face velocity measured (0.51 m/s [100 fpm]) which is right at the minimum recommended face velocity of 0.51 m/s (100 fpm) for a Class II Type A2 BSC.

The manometer function of the anemometer measured the oncology department's static room pressure to be negative. The pressure difference from the small kennel to the oncology room was negative with a pressure reading of -0.021 and -0.020 inches of water gauge (in. w.g.) with the oncology room's BSC blower on and off, respectively. The pressure difference from large kennel to the oncology room was negative with a pressure reading of -0.011 and -0.008 in. w.g. with BSC blower on and off, respectively. The pressure difference from the oncology office area to the oncology room was negative with a pressure reading of -0.027 and -0.024 in. w.g. with BSC blower on and off, respectively. These pressure measurements (excluding the -0.008 in. w.g. reading) meet United States Pharmacopeia (USP) <800>'s negative pressure requirements (-0.01 to -0.03 in. w.g.).

A TSI Accubalance® Plus Air Capture Hood Model 8373 was used to measure mechanically generated supply and exhaust airflows in the oncology room. The oncology room is designed to be under negative pressure and thus has more mechanical exhaust air (0.26 m^3/s or 550 cfm) than supply air (0.22 m^3/s or 472 cfm). The oncology room's volume (56.58 m^3 [1998 ft^3]) and mechanical exhaust airflow were used to calculate the room's ventilation rate as 16.5 air changes per hour (ACH) (with BSC exhaust blower deactivated). When the oncology room's BSC exhaust was activated, the overall room's exhaust rate increased by the amount of the BSC's exhaust, resulting a calculated ventilation rate of 26 ACH. Both of these ventilation rates exceed the minimum 12 ACH specified for unclassified containment secondary engineering controls.

The presence of potential surface contamination was evaluated with wipe samples. These were collected in areas where the staff handled chemotherapy drugs within the oncology department. Wipe samples were also collected in less obvious places (i.e., telephone, door handles, floor of nearby restroom) to determine if current workplace safety practices at the hospital were adequate to prevent inadvertent contamination of these surfaces. In some cases, a single sample could be evaluated

for more than one analyte simultaneously. The drugs administered during the NIOSH visit were vinblastine, vincristine, mitoxantrone, zoledronic acid injection, doxorubicin, Tanovea, asparaginase, and carboplatin. Sample results revealed that 4 of 6 wipe samples were positive for carboplatin (1.0 to 6.1 ng/sample). All of the 9 wipe samples were non-detectable (ND) for vinblastine. The ND determination means that contamination was either not present, or was present at levels below the detectable limit of the analytical method. Three of 14 wipe samples were positive for cyclophosphamide (1.6-3.9 ng/sample) while simultaneously being ND for doxorubicin, vincristine, methotrexate, and epirubicin. Two of the carboplatin and two of the cyclophosphamide wipe samples were between the LOD and LOQ. Nine out of 9 wipe samples submitted for N-methyldiethanolamine (MDEA) were positive (6.8 to 106 ng). Three out of 9 wipe samples submitted for toceranib, chlorambucil, and lomustine were positive for toceranib (2.2 to 1250 ng). MDEA was monitored as a potential stable marker for the highly unstable antineoplastic drug mustargen as explained in the text.

Although many of the wipe sample analytical results were ND, there is no safe level of exposure when handling hazardous drugs. The presence of the carboplatin contamination is a reminder that the patients themselves can be a source of exposure, even when the drugs are not being directly handled. The cyclophosphamide (on surfaces), MDEA, toceranib, and methotrexate presence serves as two reminders: (1) that hazardous drug contamination can sometimes linger despite cleaning efforts and (2) the detected contamination on bathroom floor one might ordinarily think of as “safe,” emphasizes the importance of proper work practices regarding the use of gloves and shoe covers, hand washing, and food/drink prohibitions within the hazardous drug handling environments. The detected contamination on the outside of the chemo transport bag serves as a reminder of the meticulous work practices required to avoid cross-contamination of surfaces expected to be “clean” as well as a reminder to treat all surfaces as potentially contaminated within the oncology treatment areas. Therefore, it is important to continue to use engineering controls (e.g., biological safety cabinets), supplementary controls (e.g., closed system drug-transfer devices), protective work practices (e.g., surface cleaning after every oncology patient, regardless of whether I.V. chemotherapy was administered), and personal protective equipment (e.g., gloves and gowns rated for chemotherapy protection, respirators, shoe covers, eye protection) to reduce unintentional exposures to the staff or pet owners.

Introduction

Background for Control Technology Studies

The National Institute for Occupational Safety and Health (NIOSH) is the primary Federal agency engaged in occupational Safety and health research. Located in the Department of Health and Human Services, it was established by the Occupational Safety and Health Act of 1970. This legislation mandated NIOSH to conduct a number of research and education programs separate from the standard setting and enforcement functions carried out by the Occupational Safety and Health Administration (OSHA) in the Department of Labor. An important area of NIOSH research deals with methods for controlling occupational exposure to potential chemical and physical hazards. The Engineering and Physical Hazards Branch (EPHB) of the Division of Field Studies and Engineering has been given the lead within NIOSH to study the engineering aspects of health hazard prevention and control.

Since 1976, EPHB has conducted a number of assessments of health hazard control technology on the basis of industry, common industrial process, or specific control techniques. Examples of these completed studies include the foundry industry; various chemical manufacturing or processing operations; spray painting; and the recirculation of exhaust air. The objective of each of these studies has been to document and evaluate effective control techniques for potential health hazards in the industry or process of interest, and to create a more general awareness of the need for or availability of an effective system of hazard control measures.

These studies involve a number of steps or phases. Initially, a series of walk-through surveys is conducted to select plants or processes with effective and potentially transferable control concept techniques. Next, in-depth surveys are conducted to determine both the control parameters and the effectiveness of these controls. The reports from these in-depth surveys are then used as a basis for preparing technical reports and journal articles on effective hazard control measures. Ultimately, the information from these research activities builds the data base of publicly available information on hazard control techniques for use by health professionals who are responsible for preventing occupational illness and injury.

Background for this Study

The 2004 *NIOSH Alert: Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings* introduced a standard of universal precautions for handling hazardous drugs safely [NIOSH 2004]. The health effects due to occupational exposure to these drugs are extensive and can include chromosomal and other types of genetic damage, reproductive damage [NIOSH 2004], and exposure can cause adverse pregnancy outcomes [Albin 2010]. The NIOSH Alert states that its guidance applies to any worker who handles hazardous drugs, including veterinary medicine and animal care (VM/AC) workers [NIOSH

2004]. Cancer is a leading cause of death among cats and dogs and attributes to 50 percent of pet deaths each year [Crump 2013]. In addition, chemotherapy is widely used to treat animals with cancer and other ailments as owners wish to prolong the lives of their beloved pets [Fielding and Lacroix 2009]. As chemotherapy drug (most are identified as hazardous drugs) use increases and lower-cost generic drugs become available, many veterinarians are administering chemotherapy drugs on their own or through a veterinary oncologist [MacDonald 2009].

In the U.S., there are an estimated 500,000 VM/AC workers, not including young adults who work part-time or during school breaks [Mobo et. al 2010]. This project specifically benefits special population/priority population groups as 95% of veterinary technicians are women of reproductive age with a mean age of 38 [Technicians 2008]. Veterinary medicine is similar to human healthcare in that the professional objective is to provide medical, surgical, and preventive healthcare to a patient. Both veterinary medicine and human healthcare personnel are vulnerable to needlestick injuries, radiation exposure, and hazardous drugs [Hall et. al 2013]. However, VM/AC workers are more likely to have accidents and occupational diseases, as they are susceptible to animal bites, zoonoses, animal-related respiratory hazards, physical injury, and veterinary-related reproductive hazards [Epp and Waldner 2012; Hall et. al 2013]. Although both professions handle hazardous drugs, there are differences in how veterinary clinics obtain, prepare, and administer the drugs, house the dosed patient, and handle a dosed patient's excreta or vomitus [Seibert 2013]. A recent study showed that VM/AC workers were exposed to hazardous drug concentrations 15 times higher than human healthcare personnel, partly due to how chemotherapy is administered in animals versus humans [Klahn 2014]. Cost, time, inconvenience, and discomfort are just some of the reported barriers for VM/AC workers not using safety measures in their practices [Klahn 2014]. Also, unlike human health care, veterinary medicine's job duties are not compartmentalized. It is common for administrative personnel to conduct day-to-day animal-care activities, especially in small clinics [Seibert 2013]. Administrative personnel may restrain animals for hazardous drug administration, clean cages, feed the animals, and assist the veterinarian. When they occur, tasks involving unsafe work practices not only affect the primary task worker, they put other VM/AC workers, such as veterinary assistants, kennel attendants, or animal care workers, at risk for occupational exposure to chemotherapy drugs. This work-task diversity emphasizes the need for a thorough evaluation (and cross-training) of safety practices in the handling of hazardous drugs (and the patients the drugs are administered to) in veterinary medicine. VM/AC workers need to be educated in: 1) the risk of the drugs they are handling; 2) how to handle the drugs safely through proper use of engineering controls and personal protective equipment (PPE); and 3) how to avoid exposure to hazardous drugs and their metabolites through carefully delineated safe work procedures.

Conversations with veterinary stakeholders revealed that the warnings and guidance in the NIOSH Alert are not effectively reaching VM/AC workers. Animal oncology clinics are staffed with general practitioners and clinic staff without awareness of chemotherapy safety [Klahn 2014]. In one reported case study, a

veterinarian admitted pouring hazardous drugs down the sink at his clinic. He then developed thyroid cancer at the age of 35, reportedly as a result of handling hazardous drugs. It was further estimated that over 4,000 veterinary practices administer chemotherapy without any safety measures [Smith 2010]. While the NIOSH Alert has had a significant impact upon hazard awareness and exposure prevention within human healthcare, there are significant differences (real and perceived) between the practices of human and veterinary medicine. These differences have reportedly been a roadblock in the NIOSH Alert's positive impact upon veterinary medicine. Controlling exposures to occupational hazards is the fundamental method of protecting workers. Traditionally, a hierarchy of controls establishes preferences in determining how to implement feasible and effective controls. The most preferred control, the elimination or substitution away from the use of hazardous drugs, is not realistic for this industry. The use of personal protective equipment is considered to be the least effective exposure control on a consistent basis [Mobo et. al 2010]. Therefore, engineering controls and work practice guidelines together form the first lines of defense for VM/AC worker protection against hazardous drug exposure.

Hospital Description

The Veterinary Hospital G provides primary, specialty, and emergency care to small animal patients. The hospital offers various services including oncology. The oncology department administers chemotherapy to patients five days a week with an average administration of 2 to 10 infusions a day. Chemotherapy drugs are prepared and administered in one room of the hospital. A Nuaire Labgard biological safety cabinet (BSC) (Class II, Type A2, Model NU-425-400, Nuaire, Plymouth, MN) is located in the room (Figure 1). The BSC was certified on May 2, 2018. The chemotherapy preparation and administration room is adjacent to a small kennel area for cats, a large kennel run, and an oncology office area.

Chemotherapy Preparation and Administration

Closed System Drug-Transfer Devices (CSTDs)

Veterinary Hospital G uses the Equashield CSTD (Equashield LLC, Port Washington, NY) to prepare and administer liquid forms of chemotherapy (Figure 2). By definition, a CSTD mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor concentrations outside the system [NIOSH 2004]. CSTDs limit the potential for aerosolizing drug contamination and can reduce worker exposure to sharps, thus reducing the likelihood of occupational exposure to hazardous drugs [NIOSH 2004]. Each CSTD system traditionally consists of a syringe adapter (i.e., CSTD syringe connector) plus three component adapters: vial adapter, intravenous (I.V.) port adapter or Y-site adapter, and a bag adapter or infusion adapter. Each of these adapters mates with the syringe adapter.

Oral Chemotherapy

For oral chemotherapy, the patient is given the pill in either in a flavored pill pocket or a pill gun (or piller). After the technician verifies the patient swallowed the pills, the patient is placed in a holding kennel until discharged to go home.

Chemotherapy Injection

For chemotherapy injection, the liquid drug is administered to the patient by subcutaneous or intramuscular route. No CSTD is used; only a drug-filled syringe and needle.

I.V. Chemotherapy

Sometimes a patient needs to receive chemotherapy through I.V. via a catheter (Figure 3). Although technique varies among technicians administering the dose, the overall process is similar. First the area is prepped by shaving the injection site and cleaning the area with alcohol. After the area is prepped, the indwelling intravenous catheter and then the T-port are inserted. Then the catheter and T-port are wrapped with bandage to keep the catheter in place. The CSTD Y-site adapter is connected to the catheter and the catheter is flushed with saline. Then the syringe with CSTD adapter is connected to the Y-site adapter, which is attached to the catheter. The chemotherapy is given until the syringe is empty. Once the drug-filled syringe is empty, it is disconnected and a syringe filled with saline is connected to the Y-site. Saline from the syringe is pushed into the catheter to flush the line. The T-port's line is closed and the catheter is removed from the patient's vein. The patient is bandaged and held in a kennel or discharged to go home.

Occupational Exposure Limits and Health Effects

As a guide to the evaluation of the hazards posed by workplace exposures, NIOSH investigators use mandatory and recommended occupational exposure limits (OELs) when evaluating chemical, physical, and biological agents in the workplace. Generally, OELs suggest levels of exposure to which most workers may be exposed up to 10 hours per day, 40 hours per week for a working lifetime without experiencing adverse health effects. It is, however, important to note that not all workers will be protected from adverse health effects even though their exposures are maintained below these levels. A small percentage may experience adverse health effects because of individual susceptibility, a pre-existing medical condition, and/or hypersensitivity (allergy). In addition, some hazardous substances may act in combination with other workplace exposures, the general environment, or with medications or personal habits of the worker to produce health effects even if the occupational exposures are controlled at the level set by the exposure limit. Combined effects are often not considered in the OEL. Also, some substances are absorbed by direct contact with the skin and mucous membranes, and thus can increase the overall exposure. Finally, OELs may change over the years as new information on the toxic effects of an agent become available.

Most OELs are expressed as a time weighted average (TWA) exposure. A TWA exposure refers to the average airborne concentration of a substance during a

normal 8- to 10-hour workday. Some substances have recommended short-term exposure limit (STEL) or ceiling values which are intended to supplement the TWA where there are recognized toxic effects from higher exposures over the short-term.

In the U.S., OELs have been established by Federal agencies, professional organizations, state and local governments, and other entities. The U.S. Department of Labor OSHA permissible exposure limits (PELs) [CFR 2003] are occupational exposure limits that are legally enforceable in covered workplaces under the Occupational Safety and Health Act. NIOSH recommendations are based on a critical review of the scientific and technical information available on the prevalence of health effects, the existence of safety and health risks, and the adequacy of methods to identify and control hazards [NIOSH 1992]. They have been developed using a weight of evidence approach and formal peer review process. Other OELs that are commonly used and cited in the U.S. include the threshold limit values (TLVs) recommended by ACGIH®, a professional organization [ACGIH 2010]. ACGIH TLVs are considered voluntary guidelines for use by industrial hygienists and others trained in this discipline "to assist in the control of health hazards." Workplace environmental exposure levels (WEELs) are recommended OELs developed by AIHA, another professional organization. WEELs have been established for some chemicals "when no other legal or authoritative limits exist" [AIHA 2007].

OSHA requires an employer to furnish employees a place of employment that is free from recognized hazards that are causing or are likely to cause death or serious physical harm [Occupational Safety and Health Act of 1970, Public Law 91–596, sec. 5(a)(1)]. Thus, employers are required to comply with OSHA PELs. Some hazardous agents do not have PELs, however, and for others, the PELs do not reflect the most current health-based information. Thus, NIOSH investigators encourage employers to consider the other OELs in making risk assessment and risk management decisions to best protect the health of their employees. NIOSH investigators also encourage the use of the traditional hierarchy of controls approach to eliminating or minimizing identified workplace hazards. This includes, in preferential order, the use of: (1) substitution or elimination of the hazardous agent, (2) engineering controls (e.g., local exhaust ventilation, process enclosure, dilution ventilation), (3) administrative controls (e.g., limiting time of exposure, employee training, work practice changes, medical surveillance), and (4) PPE (e.g., respiratory protection, gloves, eye protection, hearing protection).

Occupational Exposure Limits and Hazardous Drugs

Currently there are no PELs, RELS, or TLVs® for hazardous drugs [NIOSH 2004]. However, a PEL, REL, and TLV® have been established for inorganic arsenic compounds, such as arsenic trioxide, an antineoplastic drug [NIOSH 2004]. A WEEL has been established for some antibiotics. Some pharmaceutical manufacturers

develop risk-based OELs and that information may be listed on the safety data sheets (SDSs) [NIOSH 2004].

Methodology

BSC and Oncology Department Performance Evaluations

Equipment: BSC Face Velocity Measurements

A TSI® VelociCalc™ Plus Model 9565-P thermal anemometer (TSI Incorporated, St. Paul, MN) was used to measure air velocities at the face of the BSC located in the oncology room (Figure 4).

Procedure

To determine the BSC's average face velocity, the open face of the hood was divided into an equal-area grid of squares measuring approximately 0.09 square meters (m^2) (1 square foot [ft^2]) each. A 5-second average velocity measurement was taken at the center of each square, while holding the anemometer perpendicular to the inward airflow direction. The average face velocity across the entire hood face was then determined by calculating the average of the equal-area square velocity measurements.

Equipment: BSC Qualitative Smoke Test

A Wizard Stick (Zero Toys, Inc., Concord, MA) handheld "smoke" generator was used to visualize air movement inside and around the periphery of the BSC in the buffer room (Figure 5). The wizard stick produces a stream of safe, condensed vapor droplets and contains no actual solid 'smoke' particles, however the vapor droplets float in the air, appearing similar to smoke, and their flow path is indicative of the flowpath of the air in which they are suspended.

Procedure

The "smoke" was released around the periphery of the BSC's open face and in the interior of the hood to qualitatively evaluate the capture efficiency and evaluate potential areas of concern. If the smoke was captured quickly and directly by the hood at the point where compounding operations are performed, it indicated acceptable control design and performance. If the smoke was slow to be captured or took a circuitous route to the hood exhaust intake, this indicated a potential problem. In addition, the adverse effect of cross drafts upon hood capture was evaluated by releasing smoke near the periphery of the hood face. Lack of direct capture or evidence of reverse-flow turbulence would be indicative of poor hood performance.

Equipment: Compounding Lab Static Pressure Measurements

The manometer function of the TSI® VelociCalc™ Plus Model 9565-P thermal anemometer was used to measure room static pressure in the oncology room, relative to that in the adjacent corridor. This served as an indication of whether the room was under positive or negative pressure.

Procedure

Initially, the manometer was zeroed by attaching opposite ends of the same manometer sampling tube to the high-pressure and low-pressure manometer sampling ports. Next, with the manometer positioned outside of the oncology room, one end of a manometer sampling tube was attached to the low-pressure port on the anemometer while the free end of the tube was routed through the air gap under the lab entry door and several inches into the compounding lab. The high-pressure port was left open to the corridor and the differential pressure across the entry door threshold was recorded in inches of water gauge (in. w.g.) pressure.

Equipment: Measurement of Supply and Exhaust Airflow Rates in the Oncology Department

A TSI Accubalance® Plus Air Capture Hood Model 8373 (TSI Incorporated, St. Paul, MN) was used to measure airflow for the supply and return ventilation in the oncology room (Figure 6).

Procedure

The instrument was setup according to the manual using the 0. 6m x 0.6 m (2 ft x 2 ft) flow hood to match the supply and exhaust louvers. The instrument was turned on and the hood was placed over the supply or exhaust vent. The measured airflow was displayed in cubic feet per minute (cfm) on the instrument's screen during measurement.

Wipe Sampling Method

Surface wipe samples were collected throughout Veterinary Hospital G using different sampling methods. Samples were collected in areas where drugs were handled by the workers in the oncology room, and in places similar to those where traces of drugs have been found in human studies, such as door and cabinet handles [Connor et. al 2010; Hon et. al 2013]. Wipe samples were also taken in less obvious places to determine if the hospital's current workplace safety practices were successful in preventing secondary contamination. NIOSH researchers were careful not to collect two samples from the same surface area. It should be noted that each of these wipe sampling methods are internal methods created specifically for this research study. There is limited data on recovery studies from various surfaces.

Wipe Sampling Method 1: Bureau Veritas North America Analytical Method

The Bureau Veritas North America wipe sample collection method uses Texwipe™ Alpha™ Polyester Series Swabs (TX715, ITW Texwipe, Kernersville, NC) and a 50:50 mixture of methanol and water (both high-performance liquid chromatography grade) solvent to collect surface wipe samples. Although the subsequent analytical methods may vary by analyte, this wipe sample collection method is applicable for analysis of carboplatin, vincristine, methotrexate, cyclophosphamide, epirubicin, doxorubicin, and vinblastine (sulfate). Carboplatin is analyzed using Bureau Veritas North America's internal method, BV-2017-30843 (Bureau Veritas North America, Novi, MI), which uses high performance liquid chromatography/mass spectrometry (HPLC/MS) to find platinum. Vinblastine (sulfate) is analyzed using MAXAAM's internal method NAT 2006-14763, which uses HPLC. Vincristine, methotrexate, cyclophosphamide, epirubicin, and doxorubicin are analyzed using MAXAAM's internal method BV-2016-29599, which also uses HPLC/MS. Table I shows the analytical limit of detection (LOD), limit of quantification (LOQ), and analytical range for each of the analytes.

Prior to the visit to Veterinary Hospital G, several 16 mL amber vials with screw caps were filled with 1 mL of a 50:50 mixture of methanol and water. During the site visits, once a sampling location was identified, a surface wipe sample was collected using the Texwipe™ Alpha™ Polyester Series Swabs and solvent. First, the cap of the amber vial was removed and one of the swabs was inserted. After the swab was wetted with the solvent, the swab was pressed against the sample location and moved back and forth, progressing over an approximate 10 centimeter (cm) x 10 cm surface. The swab was then turned over and the same back and forth movement was repeated in a perpendicular direction to that first taken over the same 10 cm x 10 cm surface area. The excess solvent in the vial was poured onto an absorbent pad in a closable plastic bag for later disposal. The swab was placed head first partially into the vial opening and lateral pressure was applied to the swab stick to snap the head off and deposit it in the vial without touching. The cap and a label were placed on the vial. This surface wipe sampling collection method was repeated throughout the hospital. The samples were placed on ice packs until they were delivered to the NIOSH contract laboratory and stored frozen until analysis. Results are reported in nanogram of drug per sample (ng/sample). Vinblastine results are reported in microgram of drug per sample (µg/sample).

Wipe Sampling Method 2: NIOSH Internal Analytical Method

NIOSH developed a solvent system for surface wipe sampling and analysis using one of two wipe sampling media: Texwipe™ Alpha™ Polyester Series Swabs and Whatman™ filter papers (number 1442-055, 55-mm ashless circles, GE Healthcare, Chicago, IL).This sampling method applies to chemical analyses for lomustine (or CCNU), toceranib, N-methyldiethanolamine (MDEA), and chlorambucil. MDEA was the actual analyte tested for in the sample analysis, as an indicator for mustargen. Table II shows the analytical LD), LOQ, and analytical range for each of the analytes.

The solvent used to moisten sampling media for collection of this set of analytes was 83% acetonitrile/17% dimethylsulfoxide/0.20% hydrochloric acid. This blend resulted from extensive experiments conducted in the lead-in to the first site survey performed in this study (March 2017) and subsequent modifications. The blend provided stability in solution and adequate recoveries from quality control samples for all four of the antineoplastic drug analytes in this group via control of pH, solubility and other factors. The same solvent was used for preparation of calibration standards and in-house quality control samples to ensure compatibility with field samples during analysis.

After the swab/filter paper was wetted with the solvent, the wipe sample procedure was the same as that described in Wipe Sampling Method 1. Upon collection, the sampling media was placed over the 125 mL translucent polypropylene jar (Nalgene™ Wide-Mouth Straight-Sided Polypropylene copolymer [2118-0004], Thermo Scientific™, Rochester, NY) opening. If the swab was used for wipe sampling, then the swab (head first) was placed over the jar's opening and a lateral pressure applied to the swab stick to snap the head off and into the jar without touching. A second swab was wetted and the surface wipe sample collection was repeated for the same area using the same technique. The two wetted swabs made up one sample.

If the filter paper was used for wipe sampling, then a petri dish, separated into its top and bottom halves, was used for preparing the sample. First one Whatman™ filter paper was placed into each half of the petri dish. A pipettor and pipette were used to measure 250 microliters (µL) of the solvent onto each filter paper. An area of approximately 10 cm x 10 cm was sampled with one wetted filter paper and placed into a polypropylene jar. The same 10 cm x 10 cm area was then re-sampled, in a wiping progression perpendicular to the first filter using the second wetted filter paper. The second wetted filter paper was placed into the same jar. The two wetted filter papers made up one sample.

Upon sample collection, the lid and a sample label were placed on the jar. The samples were placed on ice packs and transported to a NIOSH laboratory freezer for cold storage until analysis. For processing, the samples were brought to room temperature and extracted by 1 hour of agitation on an orbital shaker (180 rpm) after the addition of 9.5 mL of the aforementioned solvent, for a total of 10 mL sample volume. Extracts were filtered (0.22 µm polyvinylfluoridene syringe filters) and transferred to 2 mL capped glass autosampler vials. Analysis was performed using liquid chromatography–mass spectrometry (LC-MS). Results are reported in mass of drug (ng).

The analysis utilized controlled parent ion fragmentation (MS/MS) to yield multiple product ions for each compound. Two ions were monitored for each analyte and the more intense response was used for quantification. Positive responses for an analyte were indicated by peak responses in the chromatograph above calculated limits of detection (q.v.) and by the presence of both expected fragment ions as previously exhibited by the calibration standards. Additionally, the intensity ratio of

fragment ion responses for samples was compared to the average ratio observed for pure analyte standards, as an additional parameter for identifying reliable positive responses in the field samples. No isotopically labeled analyte standards were available for use in the HPLC/MS analysis, but all samples and calibration standards were fortified with a low concentration of hexamethylphosphoramide, a compound strongly responsive in HPLC/MS. The response of this compound was monitored throughout the analysis to indicate any significant changes in instrument response or chromatographic performance

Results

BSC and Oncology Room Performance Evaluations

BSC Face Velocity Measurements

Hood velocity measurements were collected on the BSC in the oncology room. The average centerline face velocity of the hood (n=4 measurements) was 0.51 meters per second (m/s) (101 feet per minute [fpm]) as measured by the anemometer. The maximum centerline face velocity was 0.59 m/s (116 fpm) with a minimum centerline face velocity of 0.45 m/s (89 fpm).

BSC Qualitative Smoke Test

The Wizard Stick smoke generator was used to qualitatively test the capture efficiency of the BSC. Smoke was released inside the hood at the center compounding position, inside the hood along the perimeter of the open hood face, outside of the hood along the perimeter of the open hood face, and outside of the BSC directly in front of the hood face opening. In each case, the smoke was captured quickly, pulled further into the hood, and removed via the exhaust system. This showed the BSC had acceptable performance.

Oncology Room Static Pressure Measurements

The manometer function of the anemometer was used to measure the oncology department's room static pressure. The instrument's pressure specification has an accuracy of ±0.005 inches of water gauge (in. w.g.) of the reading [TSI 2016]. The room pressure was negative. The small kennel to oncology room was negative with a reading of -0.021 and -0.020 in. w.g. with BSC blower on and off, respectively. The large kennel run to oncology room was negative with a reading of -0.011 and -0.008 in. w.g. with BSC blower on and off, respectively. The oncology office area to oncology room was negative with a reading of -0.027 and -0.024 in. w.g. with BSC blower on and off, respectively.

Measurement of Supply and Exhaust Airflow Rates in the Oncology Department

The TSI Accubalance® Plus Air Capture Hood was used to measure mechanically generated supply and exhaust airflows in/out of the oncology room. The oncology room is designed to be under negative pressure and thus has more mechanical exhaust air (0.26 m^3/s or 550 cfm) than supply air (0.22 m^3/s or 472 cfm). The oncology room's volume (56.58 m^3 [1998 ft^3]) and exhaust airflow were used to

calculate the ventilation rate in air changes per hour (ACH) to be 16.5 with the BSC exhaust blower deactivated (Equation 1). When the oncology room's BSC exhaust was activated, the overall room's exhaust rate increased by the amount of the BSC's exhaust, resulting in a calculated ventilation rate of 26 ACH.

Equation 1:

$$ACH = \frac{Airflow\ (^{m^3}/_{s}) \times 3600\ sec}{Room\ Volume\ (m^3)}$$

$$ACH = \frac{Airflow\ (^{ft^3}/_{min}) \times 60\ min}{Room\ Volume\ (ft^3)}$$

Wipe Sampling

Surface wipe samples were collected throughout Veterinary Hospital G's oncology room. Tables III and V report the analytical chemistry results from these samples. Sample results revealed that 4 of 6 wipe samples were positive for carboplatin (1.0 to 6.1 ng/sample). All of the 9 wipe samples were non-detectable (ND) for vinblastine. The ND determination means that contamination was either not present, or was present at levels below the detectable limit of the analytical method. Three of 14 wipe samples were positive for cyclophosphamide (1.6-3.9 ng/sample) while simultaneously being ND for doxorubicin, vincristine, methotrexate, and epirubicin. Two of the carboplatin and two of the cyclophosphamide wipe samples were between the LOD and LOQ. Nine out of 9 wipe samples submitted for MDEA were positive (6.8 to 106 ng). Three out of 9 wipe samples submitted for toceranib, chlorambucil, and lomustine were positive for toceranib (2.2 to 1250 ng).

General Observations

NIOSH researchers observed and interacted with hospital's pharmacist, veterinarians, and staff to obtain information about the day-to-day activities along with oncology treatment processes. General observations are listed below:

- Staff wear PPE when preparing and administering chemotherapy. This includes disposable gown and chemotherapy gloves.

- Disposable chemotherapy gowns are worn for up to one week unless mustargen is prepared or administered, in which case they are used once and discarded.
- No signage on cabinet where chemotherapy drugs are stored.
- Chemotherapy bins are used to dispose of waste potentially contaminated with drugs.
- For each patient, chemotherapy administration sets are transported via a plastic plate lined with disposable adsorbent pads.
- Disposable adsorbent pads are used to line the direct compounding area of the BSC in case of a spill.
- Mustargen is double bagged and stored in the BSC.

Discussion

The BSC was recently certified and operating effectively. The hood's average centerline velocity was 0.51 m/s (101 fpm), which is right at the recommended face velocity of 0.51 m/s (100 fpm) for a Type A2 BSC [CDC 2009; USP 2019]. The room also met the minimum ventilation rate (12 ACH) and negative pressure for an unclassified containment segregated compounding area [USP 2019]. The pressure measurements (excluding the -0.008 in. w.g. reading) meet USP <800>'s negative pressure requirements (-0.01 to 0.03 in. w.g.) [USP 2019]. The -0.008 in. w.g. reading, while low, was within the instrument's error range (0.005 in. w.g.) of the pressure requirement.

The NIOSH researchers' strategy was to collect surface wipe samples after each chemotherapy treatment and randomly throughout the oncology room. During the site visit, chemotherapy was administered to 11 patients. The drugs administered were vinblastine, vincristine, mitoxantrone, zoledronic acid injection, doxorubicin, Tanovea, asparaginase, and carboplatin. Surface wipe samples were analyzed by NIOSH's lab and a contract lab, Bureau Veritas North America. The analytical results from all of the Bureau Veritas North America's field samples were ND except for seven, which were positive for carboplatin and cyclophosphamide. These positive wipe samples were collected from the plastic mat when a patient was given carboplatin, the BSC airfoil and downstream of the high efficiency particulate air (HEPA) filter, and the refrigerator, storage cabinet, and bin handles. Two of the carboplatin and two of the cyclophosphamide results were between the LOD and LOQ. Studies have shown the vaporization potential of certain antineoplastic drugs [Connor et. al 2000; Kiffmeyer et. al 2002]. This vaporization potential appears to be validated by the contamination found downstream of the HEPA filter. NIOSH's lab analyses of the wipe samples found MDEA on the floor mat where chemotherapy is administered to large breed dogs, counter, examination table, telephone, chemotherapy waste bins, downstream of the HEPA filter in the BSC, and the highest concentration of MDEA was found on the BSC's airfoils. Toceranib was found on the chemotherapy waste bins and on top/underneath the BSC's airfoil.

Field blanks were collected during the surface wipe sampling. Field blanks are used to evaluate the amount of contamination that may have occurred during sample preparation, packaging, shipping, and/or storage before laboratory analysis [NIOSH 2016]. Field blanks are prepared in the same manner as a typical wipe sample except the media does not touch any surface. Field blank results are expected to result in NDs, however, sometimes field blanks yield positive results. Of ten field blanks generated during this survey, one field blank was positive for MDEA. The field blank was 6.8 ng. The exact cause of the contaminated field blank is difficult to determine. While meticulous procedures are in place to minimize such occurrences, contamination does sometimes occur and in this case, the contamination could have occurred anytime within the sample preparation to the sample analysis processes.

It is common to have a wipe sample analyses for hazardous drug contamination result in a ND finding, even in the presence of a hazardous drug manipulations [NIOSH 2012]. Some of the hazardous drugs, such as doxorubicin, are not stable and can decay rapidly [NIOSH 2012]. Instability due to several factors has been anecdotally observed for lomustine and chlorambucil in the course of development of the NIOSH analytical method for these drugs, and degradation is expected to be especially rapid in open workplace environments without controlled parameters. Thus, a number of the drugs under study are less likely to be detected from surface wipe samples.

Particular note should be made regarding the compound MDEA, which was the indicator analyte for mustargen contamination. Mustargen is especially reactive in uncontrolled environments (e.g., when local pH does not promote stability) which contributes to its particularly hazardous nature. Typically, mustargen rapidly decays to degradation products of which MDEA is the most important in environments with typical humidity levels. Since it was very unlikely that intact mustargen would be detected at a workplace site if sampling and/or analysis occurred outside of a spill event, and since safety issues prevented the development of a direct mustargen detection method in the NIOSH laboratory, the decision was made to focus instead on MDEA, as a potential marker for the original compound. However, positive sample results for MDEA may not be indicative of actual mustargen contamination, since ethanolamine compounds (of which MDEA is one) are often used in modern manufacturing techniques and cleaning media. For purposes of this investigation, MDEA presence in workplace samples should only serve as a potential warning of and cannot be conclusively linked to a particular source. Thus, it may not indicate actual mustargen contamination.

In earlier surveys conducted under this umbrella project, an effort was made to qualify the link between MDEA detected in samples with mustargen at the work sites by using an alternate HPLC/MS method to screen for the presence of other ethanolamine compounds such as diethanolamine (DEA) and triethanolamine (TEA). If these other widely used compounds were present in field samples along with MDEA, it might indicate general ethanolamine contamination rather than the prior presence of mustargen as a specific source for the observed MDEA. In these

screening tests DEA and TEA were always observed along with MDEA, and indeed were also present in some samples for which MDEA levels were ND, illustrating the ubiquity of ethanolamines in workplace environments. However, no meaningful quantitative correlations were found between levels of MDEA and DEA or TEA, suggesting that when MDEA was present it was not neccessarily just a contaminant or intentional component of whatever sources had contributed the other ethanolamines. In summary, it is not possible to guarantee or dismiss that when MDEA is detected in a workplace sample that it definitely signals the presence of a prior mustargen contamination event. This caveat should be kept in mind when considering the positive MDEA responses in this report.

The hospital also used CSTDs to prepare and administer chemotherapy, which studies have shown can reduce surface contamination [Sessink and Bos 1999; Nygren et al. 2002; NIOSH 2004; Harrison et al. 2006; Nyman et al. 2007; Yoshida et al. 2009; Sessink et al. 2010; Vyas 2013]. Another possible reason most of the samples did not detect any drug is that the level of hazardous drugs on surfaces may vary over time. This variation is influenced by drug amounts handled, patient load, and work practices [NIOSH 2012].

One limitation of the study is there are currently only a handful of analytical methods covering a small fraction of the 218 hazardous drugs on the *NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings* [NIOSH 2016]. The hospital uses several hazardous drugs for which the NIOSH researchers were not able to sample due to the absence of an analytical method. An additional limitation is the time between sample collection and analysis. Although surface wipe samples are shipped on ice within 24-hours of their collection, it may be much longer before the analytical laboratories can analyze the samples. This delay in sample analysis could decrease the chances of detecting a positive wipe sample.

Conclusions and Recommendations

The carboplatin, cyclophosphamide, MDEA, and toceranib presence serves as two reminders: (1) that hazardous drug contamination can sometimes linger despite cleaning efforts and (2) the detected contamination on surfaces one might ordinarily think of as “safe,” emphasizes the importance of proper work practices regarding glove use, hand washing, and food/drink prohibitions within the hazardous drug handling environments. Therefore, it is important to continue to use engineering controls (biological safety cabinets), supplementary controls (CSTDs), protective work practices (surface cleaning after every oncology patient, regardless of whether I.V. chemotherapy was administered) and PPE (gloves and gowns rated for chemotherapy protection, respirators, eye protection) to reduce unintentional exposures to the staff and other patients.

NIOSH researchers observed proper work practices that Hospital G had in place during the visit. The hospital is encouraged to:

- Continue using the hospital's standard operating procedures (SOPs) for administering of drugs, spills, post administration of drug cleaning, and patient management [USP 2019].

- Continue to use the BSC to prepare chemotherapy treatments for patients [NIOSH 2004; USP 2019].
- Continue to clean the BSC each time a hazardous drug is used inside the cabinet even if there is no noticeable spill or leak. United States Pharmacopeia (USP) <797>, Pharmaceutical Compounding: Sterile Preparations, has a section on cleaning and disinfecting compounding areas [USP 2019].

- Continue to use PPE for handling hazardous drugs [NIOSH 2004; NIOSH 2010; USP 2019].

- Continue to use gloves during all tasks involving a chemotherapy patient [USP 2019]. Hospital G staff wear's American Society for Testing and Materials (ASTM)-tested chemotherapy gloves [USP 2019]. Continue to change gloves every 30 minutes unless otherwise recommended by the glove manufacturer or if contaminated, torn, or punctured [USP 2019].

- Continue to use CSTDs during compounding and administering of hazardous drugs [NIOSH 2004; USP 2019]. Although CSTDs may reduce worker exposure to hazardous drugs, they may not entirely eliminate exposure [Sessink and Bos 1999; Nygren et al. 2002; NIOSH 2004; Harrison et al. 2006; Nyman et al. 2007; Yoshida et al. 2009; Sessink et al. 2010; Vyas 2013]. The NIOSH Alert identifies CSTDs as supplemental controls that should only be used in combination with ventilated primary engineering controls (i.e., biological safety cabinets and containment isolators) to further protect against worker exposures to hazardous drugs [NIOSH 2004]. Therefore, it is important to continue to use the BSC and proper PPE to protect the staff, even when CSTDs are used.

- Continue the practice of washing hands after compounding, administering, or handling hazardous drugs [USP 2019].

- Continue to clean area after each chemotherapy administration [USP 2019].

- Continue to prevent other staff from entering the room unprotected during chemotherapy administration [NIOSH 2010; USP 2019].

Below are a few recommendations for consideration within the hospital's work practices as well as towards the facility design that could reduce unintentional exposures to hazardous drugs:

- Ensure that all employees expected to wear respiratory protection are trained and fit-tested on the specific respirator in use. The respirator must be used as part of a comprehensive respiratory protection program and the user must be enrolled into a Respiratory Protection Program in accordance with the requirements of OSHA 1910.134 [OSHA 2011].

  Respirators should be used in a proper respirator program under the supervision of a properly trained respirator program administrator. Respirators used without such a program, with all its essential elements, cannot be relied upon to protect workers.

  Each worker required to wear a respirator must be medically evaluated and cleared by a physician to wear the specific respirator before performing assigned tasks. For respirators to be effective and protect workers from harmful exposures, they must be selected, inspected, and maintained properly. Respirators should be inspected by the worker prior to each use for any defects. Reuseable respiratory protective equipment should also be cleaned, disinfected, and re-inspected after each use. Respiratory protective devices should never be worn when a satisfactory face seal cannot be obtained. Many conditions may prevent a good seal between the worker's face and the respirator. Some of these conditions include facial hair, glasses, or an unusually structured face. All workers required to wear a respirator must be properly trained on the selection, use, limitations, and maintenance of the respirator. They also must be fit–tested to assure a proper seal between the workers face and the specific make/model of respirator assigned for their use, prior to performing work tasks in a contaminated area.

  All workers should receive annual fit–testing with a quantitative testing device. When not in use, respirators must be stored in a clean environment located away from any source of contamination.

- Develop an SOP for receiving a hazardous drug shipment [USP 2019].

- Ensure that the BSC is certified on a yearly basis and after it has been repaired or relocated [CDC 2009]. Ensure that the hood certification process includes the most recent edition of the National Sanitation Foundation (NSF) Standard 49, Biosafety Cabinetry Certification [NSF/ANSI 2016].

- Do not reuse disposable gowns. Use gowns once and throw them away in chemotherapy waste [USP 2019].

- Gloves should also be worn when unpacking hazardous drug shipment [USP 2019].

- Clean scissors and other tools, such as razors, after each use with chemotherapy patients [NIOSH 2010; USP 2019].

- Wash clothing and blankets that could be contaminated with drug separately from items with no anticipated drug contamination [USP 2019].

- Ensure dedicated cleaning supplies (mops, rags, buckets, etc.) used within chemotherapy treatment areas are not used in other areas of the hospital [NIOSH 2004].
- Consider replacing the *Danger Do Not Enter* sign with a *Chemotherapy Treatment in Process* sign [NIOSH 2010; USP 2019].

- Place color-coded neckbands on patients recently treated with chemotherapy drugs [NIOSH 2012].

Acknowledgements

NIOSH researchers would like to thank the staff at Veterinary Hospital G. The staff allowed the researchers to observe their work practices, complete an engineering assessment, collect wipe samples, and ask questions. Without the staff's willingness to participate in the research, the project's goals are not possible. The NIOSH researchers would also like to thank Jack Pretty, Ph.D., of NIOSH/HELD/CBMB and the Bureau Veritas North America contract laboratory for their analysis of the field samples.

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Appendixes

Table I. LOD[1]/LOQ[2] and analytical ranges of analyte for BVNA Methods

Analyte	LOD (ng)[3]	LOQ (ng)	Analytical Range (ng)
Carboplatin	0.8	2.7	0.4 to 200
Cyclophosphamide	0.8	2.7	0.4 to 100
Doxorubicin	0.8	2.7	0.4 to 100
Epirubicin	0.8	2.7	0.4 to 100
Methotrexate	0.8	2.7	0.4 to 100
Vincristine	0.5	1.7	0.5 to 75

Table II. LOD[1]/LOQ[2] and analytical ranges of analyte for NIOSH Method

Analyte	LOD (ng)[3]	LOQ (ng)	Analytical Range (ng)
Methyldiethanolamine (MDEA: marker for mustargen)	3.8	12	5.0 – 1000
Lomustine	38	127	25 – 5000
Chlorambucil	0.35	1.1	5.0 – 1000
Toceranib	0.13	0.42	5.0 - 100

*Limits of detection for an analyte in the NIOSH method were determined by running injections of blank sample solvent prior to analysis and collecting peak height values covering the elution period of the analyte in HPLC/MS (typically about 0.40 min). The standard deviation of these peak height values is determined and Sigma is defined as 2(SD). The slope of the peak height calibration plot (m) is also determined. LOD is then calculated as [3(Sigma)]/m and LOQ as [10(Sigma)]/m.

[1] LOD = limit of detection
[2] LOQ = limit of quantification
[3] ng = nanogram of drug

Table III. Chemotherapy Drugs in Surface Wipe Samples, Day 1

Location and Sample Identification	Sample Description	Wipe Sampling Method	Results (ng/sample)[4]
Oncology Department	Saliva from patient given carboplatin (Figure 7)	BV-2017-30843[5] (Carboplatin)	6.1
Oncology Department	Plastic mat where patient was given carboplatin (Figure 7)	BV-2017-30843	(1.0)[6]
Oncology Department	Spill on mat where patient was given carboplatin (Figure 7)	BV-2017-30843	(2.1)
Oncology Department	Telephone	BV-2016-29599 (vincristine, methotrexate, cyclophosphamide, epirubicin, doxorubicin)	ND[7]
Oncology Department	Infusion pole	BV-2016-29599	ND
Oncology Department	Examination table	NAT 2006-14763 (Vinblastine)	ND
Oncology Department	Plastic plate where prepared drugs are placed	NAT 2006-14763	ND
Oncology Department	Chemotherapy waste and cabinet handles	NAT 2006-14763	ND

[4] ng/sample = nanogram of drug per sample
[5] Bureau Veritas North America's Internal Method
[6] ( ) = Result between the limit of detection (LOD) and limit of quantification (LOQ)
[7] ND = results are not detected at the LOD

Table IV. Chemotherapy Drugs in Surface Wipe Samples, Day 2

Location and Sample Identification	Sample Description	Wipe Sampling Method	Results (ng/sample)[8]
Oncology Department	Plastic mat where patient was given carboplatin (Figure 8)	BV-2017-30843[9] (Carboplatin)	3.4
Oncology Department	Plastic mat where patient was on doxorubicin	BV-2016-29599 (vincristine, methotrexate, cyclophosphamide, epirubicin, doxorubicin)	ND[10]
Oncology Department	Plastic plate where prepared drugs are placed	BV-2016-29599	ND
Oncology Department	Examination table	BV-2016-29599	ND
Oncology Department	BSC airfoil and lip (Figure 9)	BV-2016-29599	(1.6)[11] for cyclophosphamide; ND for the other drugs
Oncology Department	Downstream of BSC's HEPA filter (Figure 10)	BV-2016-29599	(1.6) for cyclophosphamide; ND for the other drugs
Oncology Department	Chemotherapy bin's handle (located under sink)	BV-2016-29599	ND
Oncology Department	Refrigerator, storage cabinet, and chemotherapy bin handles (Figures 11, 12, 13)	BV-2016-29599	3.9 for cyclophosphamide; ND for the other drugs
Oncology Department	Plastic mat	BV-2016-29599	ND
Oncology Department	Plastic mat (patient on mitoxantrone)	BV-2016-29599	ND
Oncology Department	Plastic mat where patient was given vinblastine	NAT 2006-14763 (Vinblastine)	ND
Oncology Department	Plastic mat where patient was given vinblastine	NAT 2006-14763	ND
Oncology Department	Razor	NAT 2006-14763	ND
Oncology Department	Examination table where patient was given vinblastine	NAT 2006-14763	ND

[8] ng/sample = nanogram of drug per sample
[9] Bureau Veritas North America's Internal Method
[10] ND = results are not detected at the LOD
[11] ( ) = Result between the limit of detection (LOD) and limit of quantification (LOQ)

Table V. NIOSH Lab Results: Chemotherapy Drugs in Surface Wipe Samples, Day 2[12]

Location and Sample Identification	Sample Description	Wipe Sampling Method	Results (ng)[13]
Oncology Department	Plastic mat on floor[17]	NIOSH Method (paper)	(6.8)[14] (MDEA[15]); ND[16] (toceranib, chlorambucil, and lomustine)
Oncology Department	Counter by door leading to common area[14]	NIOSH Method (paper)	23.2 and 23.3 (MDEA); ND (toceranib, chlorambucil, and lomustine)
Oncology Department	Examination table[17]	NIOSH Method (paper)	(10.0) (MDEA); ND (toceranib, chlorambucil, and lomustine)
Oncology Department	Chemotherapy waste bins [14.17]	NIOSH Method (paper)	(10.0) and (8.5) (MDEA); 2.2 and 2.3 (toceranib); ND (chlorambucil and lomustine)
Oncology Department	Telephone[17]	NIOSH Method (paper)	(11.4) (MDEA); ND (toceranib, chlorambucil, and lomustine)
Oncology Department	BSC's airfoil (top)[14]	NIOSH Method (paper)	17.0 and 16.6 (MDEA); 4.3 and 4.5 (toceranib); ND (chlorambucil and lomustine)
Oncology Department	BSC's airfoil (underneath)[14]	NIOSH Method (swab)	106 (MDEA); 1250 and 1280 (toceranib); ND (chlorambucil and lomustine)
Oncology Department	Downstream of HEPA filter in BSC	NIOSH Method (swab)	29.5 (MDEA); ND (toceranib, chlorambucil, and lomustine)
Oncology Department	Floor in front of BSC[17]	NIOSH Method (swab)	(7.2) (MDEA); ND (toceranib, chlorambucil, and lomustine)

[12] Wipe samples for this method were not collected on Day 1
[13] ng = mass of drug
[14] Presence of two numerical values for a sample indicates that the sample was selected for rerun and the second value was obtained for the second analysis
[15] MDEA = N-methyldiethanolamine
[16] ND = results are not detected at the LOD
[17] ( ) = Result between the limit of detection (LOD) and limit of quantification (LOQ)

Figure 1. BSC, Nuaire Labgard Class II, Type A2 (Photo Credit: NIOSH)

Figure 2. Equashield CSTD (syringe adapters shown) (Photo Credit: NIOSH)

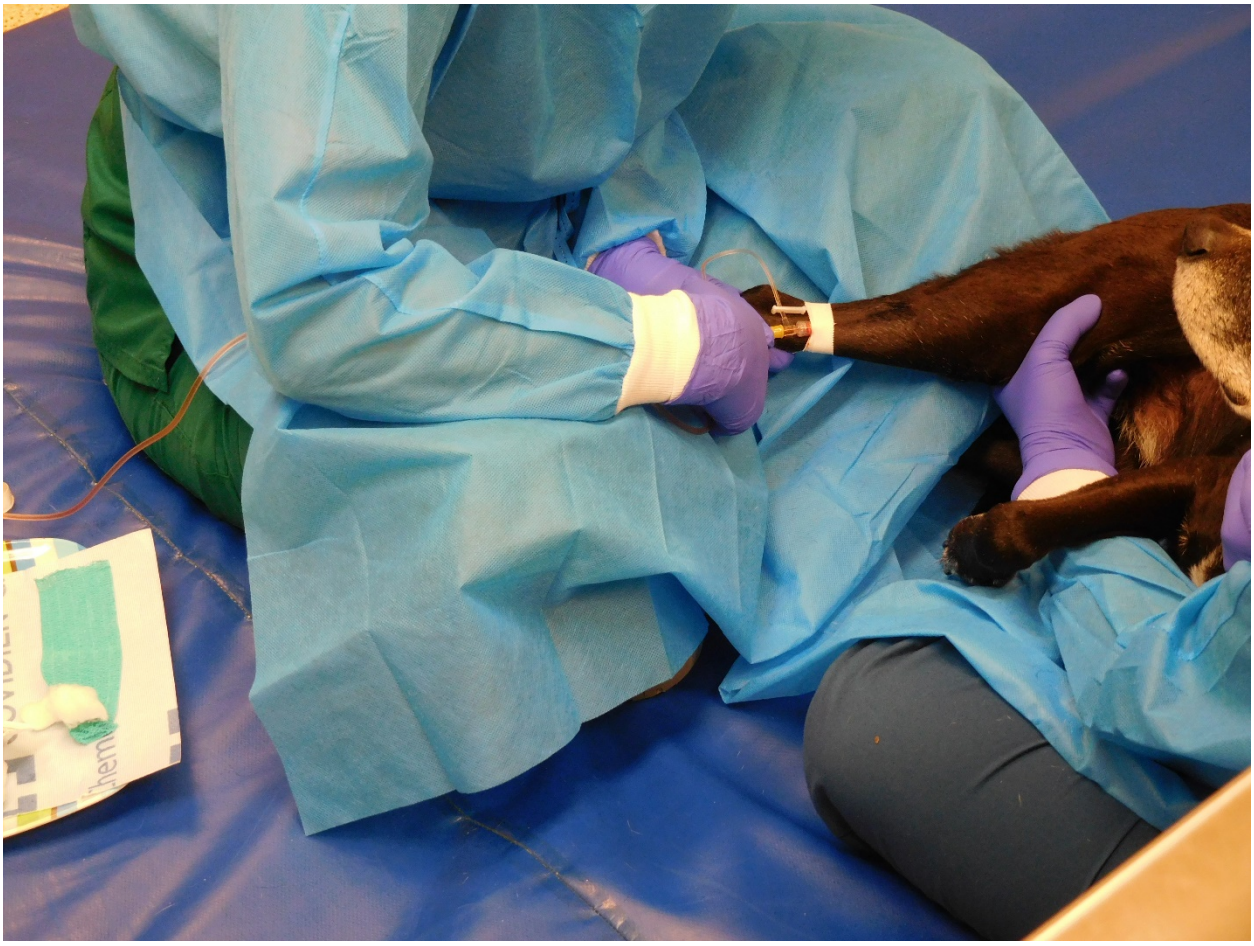

Figure 3. Patient being given doxorubicin via catheter (Photo Credit: NIOSH)

Figure 4. TSI® VelociCalc™ Plus Model 9565-P thermal anemometer (Photo Credit: NIOSH)

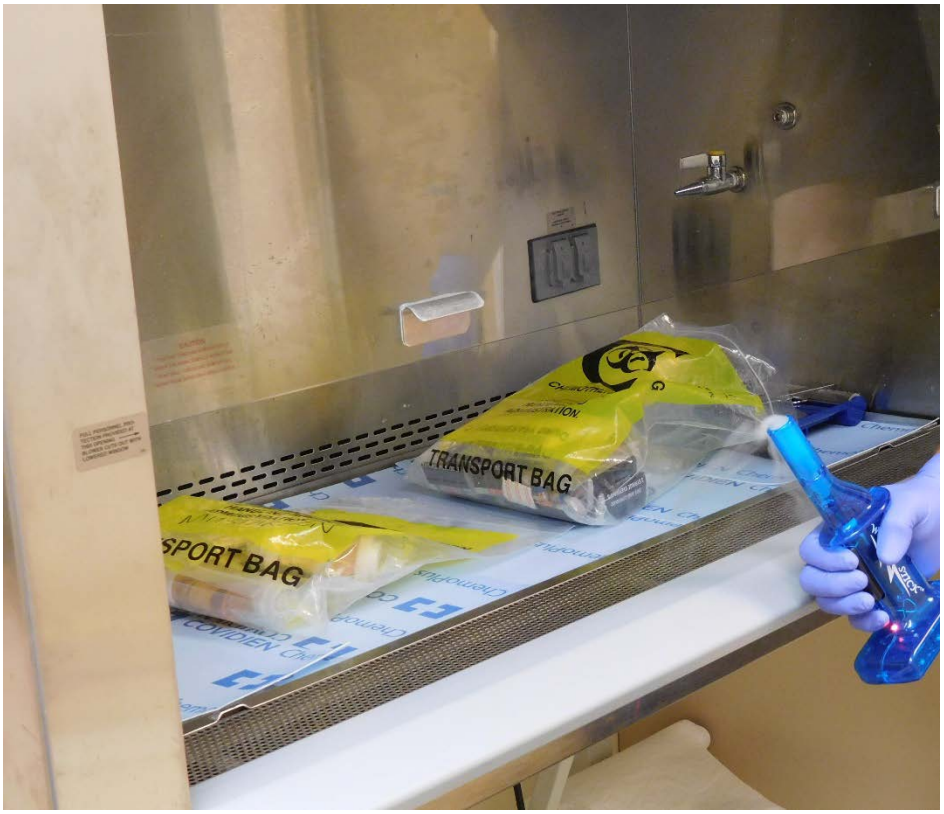

Figure 5. Qualitative smoke test with Wizard Stick Smoke Generator (Photo Credit: NIOSH)

Figure 6. TSI Accubalance® Plus Air Capture Hood (Photo Credit: NIOSH)

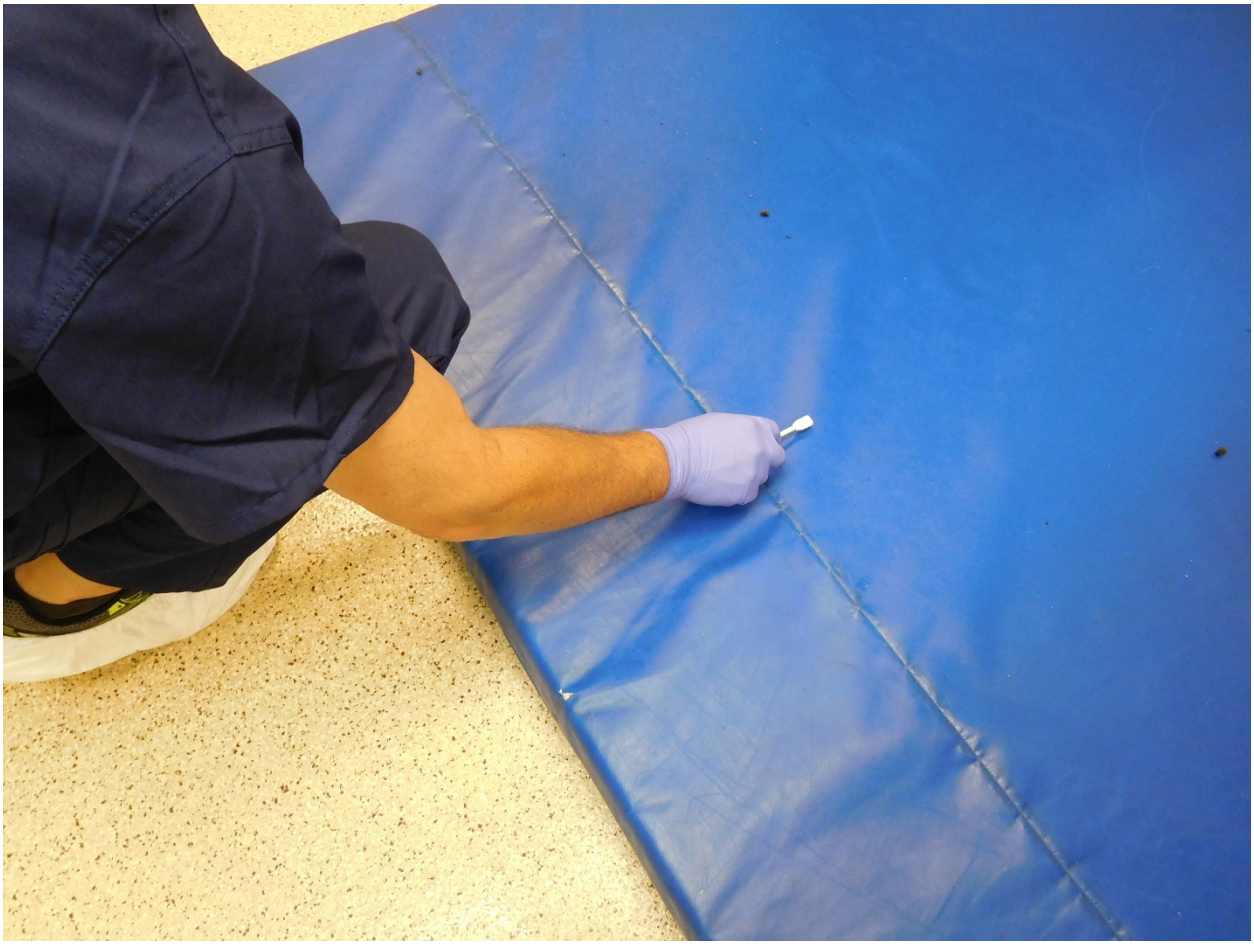

Figure 7. Sample spot where saliva from carboplatin patient. Other samples collected from this plastic mat were where the carboplatin patient was laying and a spill. (Photo Credit: NIOSH)

Figure 8. Sampling on plastic mat after patient was administered carboplatin (Photo Credit: NIOSH)

Figure 9. Surface wipe sample collected on BSC's airfoil and lip (Photo Credit: NIOSH)

Figure 10. Surface wipe sample collected downstream of BSC's HEPA filter (Photo Credit: NIOSH)

Figure 11. Surface wipe sample collected from refrigerator's handle (Photo Credit: NIOSH)

Figure 12. Surface wipe sample collected from storage cabinet handle (Photo Credit: NIOSH)

Figure 13. Surface wipe sample collected from chemotherapy waste bin (Photo Credit: NIOSH)

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