

# In-Depth Survey Report

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## In-depth Engineering Control Evaluation at Veterinary Hospital A

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## Abstract

NIOSH researchers conducted two field surveys at Veterinary Hospital A in March 2017 and one field survey in August 2018. The purpose of the site visits 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 and daily activities along with the oncology treatment processes.

A TSI® VelociCalc™ Plus Model 9555-P thermal anemometer was used to measure air velocities at the face of the Class II Type A Model BBF-2SSCH biological safety cabinet (BSC), while a Wizard Stick handheld smoke generator was used to visualize air movement inside and around the periphery of the BSC. The average face velocity of the hood was 0.32 m/s (63 fpm), which is below the minimum recommended face velocity (i.e., 0.38 m/s [75 fpm]) for a Class II Type A1 BSC. However, the qualitative test on the hood using a Wizard Stick handheld smoke generator indicated good capture efficiency. The BSC recirculated 100% of the filtered exhaust air back into the chemotherapy preparation room and did not exhaust to the outdoors. The room static pressure was measured using the manometer function of the TSI® VelociCalc™ and found to be under negative pressure.

The presence of potential surface contamination was evaluated with wipe samples. These were collected in areas where the workers handled chemotherapy drugs, such as the examination rooms and chemotherapy preparation room. Wipe samples were also collected in less obvious places (i.e., telephones, door handles) to determine if current workplace safety practices at the hospital were adequate to prevent inadvertent contamination of these surfaces. Sampling and analytical procedures varied by the hazardous drug for which they would be evaluated (i.e., the analyte). In some cases, a single sample could be evaluated for more than one analyte simultaneously. Vincristine, doxorubicin, and vinblastine were the only hazardous drugs actually in use during the two NIOSH visits.

Sample analyses results revealed that 4 of 13 wipe samples submitted for toceranib analyses were positive (0.11 to 0.44 ng) while simultaneously being non-detectable (ND) for mitoxantrone, lomustine, and chlorambucil during the two surveys in March 2017. Thirteen out of 13 samples submitted for N-methyldiethanolamine (MDEA) analyses were also positive (4.6 to 1940 ng) during the two surveys in March 2017. For the August 2018 survey, 3 of 3 wipe samples submitted for MDEA were positive (17.6 to 44.1 ng) while simultaneously being ND for lomustine, chlorambucil, and toceranib. During the two surveys in March, six samples submitted for vinblastine, five samples submitted for carboplatin and 21 samples submitted for simultaneous vincristine, methotrexate, cyclophosphamide, epirubicin, and doxorubicin analyses all resulted in a ND except for one, which was positive for vincristine. The ND determination means that contamination was either

not present, or it was present at levels below the limit of detection of the analytical method. 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 vincristine contamination is a reminder that the patients themselves can be a source of exposure, even when the drugs are not handled directly by hospital personnel. The toceranib and MDEA presence serves as two reminders: (1) that hazardous drug contamination can sometimes linger despite cleaning efforts and (2) the detected contamination on cabinet surfaces 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. 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, which is the subject of the report, is referred to as Veterinary Hospital "A" in order to preserve its anonymity. Veterinary Hospital A provides specialty care to small animal patients. Oncology makes up 50% of the hospital's practice. The hospital staff does not compound chemotherapy drugs but the staff does routinely prepare (i.e., withdraw drug from vial) and administer chemotherapy to patients every day. The hospital hosts a chemo clinic once a week, where they administer chemotherapy to a large number of patients in a short amount of time. The hospital typically sees about 18 to 34 chemotherapy patients a day. This number quadruples during the chemo hospital. There are five examination rooms, a chemotherapy preparation room, special procedure room, kennel, radiology room, office, reception and lobby area, break room, and restrooms. The chemotherapy preparation room has a Class II Type A Model BBF-2SSCH biological safety cabinet (BSC) (Germfree Laboratories Incorporated, Ormond Beach, FL, last certification on March 10, 2017) (Figure 1). The BSC filtered and recirculated the exhaust airstream back into the chemotherapy preparation room; it did not exhaust to the outdoors. The special procedure room does not have mechanical ventilation (Figure 2). The kennel houses patients recovering from medical procedures or waking up from anesthesia (Figure 3). The kennel is used for temporary housing with no overnight patients.

## Chemotherapy Preparation and Administration

### *Closed System Drug-Transfer Devices (CSTDs)*

Veterinary Hospital A uses the MILA CHEMO Safety System (Mila International, Inc., Florence, KY). The MILA CHEMO Safety System is a CSTD made specifically for veterinary use (Figure 4). 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. dosing via catheter (Figure 5). Although technique varies among technicians administering the dose, the overall process is similar. First, the patient is prepped by shaving the injection site and cleaning it with a chlorhexidine scrub followed by alcohol. After the area is prepped, the indwelling intravenous catheter and the T-port are inserted. Next, 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. Next, 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 then 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. 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 (PELs) [CFR 2003] are occupational exposure limits that are legally enforceable in covered workplaces under the Occupational Safety and Health Act. NIOSH *recommended exposure limits* (RELs) 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]. Other OELs that are commonly used and cited in the U.S. include the *threshold limit values* (TLVs<sup>®</sup>) recommended by ACGIH<sup>®</sup>, 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 the American Industrial Hygiene Association (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<sup>®</sup> for hazardous drugs [NIOSH 2004]. However, a PEL, REL, and TLV<sup>®</sup> 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 product’s safety data sheets (SDSs) [NIOSH 2004].

## Methodology

### Compounding Hood Performance Evaluations

#### *Equipment: Compounding Hood Face Velocity Measurements*

A TSI® VelociCalc™ Plus Model 9555-P thermal anemometer (TSI Incorporated, St. Paul, MN) was used to measure air velocities at the face of the BSC located in the chemotherapy preparation room (Figure 6).

#### *Procedure*

To determine the Compounding Hood's average face velocity, the open face of the hood was divided into an equal-area grid of six squares measuring approximately 0.09 square meters (m<sup>2</sup>) (1 square foot [ft<sup>2</sup>]) 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 determined by calculating the average of the equal-area square velocity measurements.

#### *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 chemotherapy preparation 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 compounding lab, 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: Hood 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 chemotherapy preparation room (Figure 7). 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 flow path 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 of 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.

## **Wipe Sampling Methods**

Surface wipe samples were collected throughout Veterinary Hospital A using different sampling methods. Samples were collected in areas where drugs were handled by the workers, such as the examination rooms and chemotherapy preparation room, and in places similar to those where traces of drugs have been found in human studies, such as door handles and telephones [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 Methods*

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 Bureau Veritas North America’s internal method NAT 2006-14763, which uses HPLC. Vincristine, methotrexate, cyclophosphamide, epirubicin, and doxorubicin are analyzed using Bureau Veritas North America’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 A, 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, mitoxantrone, N-methyldiethanolamine (MDEA), and chlorambucil. MDEA was the actual analyte tested for in the sample analysis, as an indicator for mustargen. Tables III and IV show the analytical LOD, LOQ, and analytical range for each of the analytes.

The solvent used to moisten sampling media for collection of this set of analytes was 50% acetonitrile/50% 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. Samples were placed on ice packs and transported to a NIOSH laboratory freezer for storage at approximately -10 °C until analysis. Samples were returned to room temperature and were processed by extraction via orbital shaker using a total of 10 mL of the aforementioned solvent blend. The supernatant was filtered and 2 mL was transferred to autosampler vials for analysis via HPLC/MS. Results are reported as mass of drug (ng).

## Results

### BSC and Chemotherapy Preparation Room Performance Evaluations

#### *BSC Face Velocity Measurements*

Hood velocity measurements were collected on a Germfree Laboratories Incorporated Class II Type A Model BBF-2SSCH BSC, located in the chemotherapy preparation room. The average face velocity of the hood was 0.32 meters per second (m/s) (63 feet per minute [fpm]) as measured by the anemometer. The maximum face velocity was 0.56 m/s (111 fpm) with a minimum face velocity of 0.15 m/s (30 fpm).

#### *Chemotherapy Preparation Room Static Pressure Measurements*

The manometer function of the anemometer was used to measure the chemotherapy preparation room's 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, however, the magnitude of the negative pressure was too small to quantify.

#### *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 BSC 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 hood 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.

## Wipe Sampling

Surface wipe samples were collected throughout Veterinary Hospital A's examination rooms, special procedures room, break room, kennel, and the chemotherapy preparation room, which housed the BSC. Tables V through X report the analytical chemistry results from these samples. Sample analyses results revealed that 4 of 13 wipe samples submitted for toceranib analyses were positive (0.11 to 0.44 ng) while simultaneously being non-detectable (ND) for mitoxantrone, lomustine, and chlorambucil during the two surveys in March 2017. Three of the four positive toceranib samples were between the LOD and LOQ. Thirteen out of 13 samples submitted for MDEA analyses were also positive (4.6 to 1940 ng) during the two surveys in March 2017. Seven of the 13 positive MDEA samples were between the LOD and LOQ. For the August 2018 survey, 3 of 3 wipe samples submitted for MDEA were positive (17.6 to 44.1 ng) while simultaneously being ND for lomustine, chlorambucil, and toceranib. Mitoxantrone was not analyzed for during the August 2018 survey. During the two surveys in March, six samples submitted for vinblastine, five samples submitted for carboplatin and 21 samples submitted for simultaneous vincristine, methotrexate, cyclophosphamide, epirubicin, and doxorubicin analyses all resulted in a ND except for one, which was positive for vincristine. The ND determination means that contamination was either not present, or it was present at levels below the limit of detection of the analytical method.

## General Observations

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

- During a chemotherapy treatment with vincristine, the drug syringe was placed on the floor (Figure 8).
- During a separate chemotherapy treatment with doxorubicin, red spots were noted on the floor and gloves (Figure 9). These red spots could be from blood or doxorubicin.
- During surface wipe sampling, NIOSH researchers noted a possible doxorubicin or bloodstain on one of the plastic container lids in the special procedures room (Figure 10).
- For all the observed chemotherapy administrations and preparations, only a single layer of gloves were used. No other PPE, such as a chemotherapy gown, NIOSH-approved respirator, hair net, goggles/eye protection, or second pair of gloves, was used by the staff. Two pairs of safety glasses were on top of the BSC in the chemotherapy preparation room but were not observed to be used when staff was preparing the chemotherapy drug for

administration (Figure 11).

- A staff member prepared doxorubicin in the chemotherapy preparation room and did not remove gloves before leaving the room.
- A staff member touched the refrigerator in the chemotherapy preparation room with the same gloved hands after preparing a chemotherapy drug (Figure 11).
- The BSC was not cleaned after chemotherapy drugs were prepared.
- The BSC is turned off after chemotherapy drug preparation.
- The smoke detector was not intact (Figure 12).

## Discussion

The Class II Type A Model BBF-2SSCH BSC is unique in that it has a negative pressure plenum like a Class II Type A2 BSC, however, the inflow velocity of the model is similar to a Class II Type A1 BSC [Germfree 2017]. A Class II Type A1 BSC should have a minimum inflow velocity of 0.38 meters per second (m/s) (75 feet per minute [fpm]) whereas a Class II Type A2 BSC should have a minimum inflow velocity of 0.51 m/s (100 fpm) [USP 2019]. The engineering assessment showed that the BSC's average face velocity (0.32 m/s [63 fpm]) was below the recommended face velocity for a Class II Type A1 BSC [CDC 2009; USP 2019]. However, the qualitative test on the hood using the handheld smoke generator indicated good capture efficiency. Engineering evaluations also measured the chemotherapy preparation room's static pressure. The room's negative pressure was too low to quantify and did not meet USP <800>'s guidance to be externally exhausted to the outdoors [USP 2019].

The NIOSH researchers' strategy was to collect surface wipe samples after each chemotherapy treatment as well as randomly throughout the hospital. Vincristine, doxorubicin, and vinblastine were the only drugs used during the two NIOSH visits. Sampling for some drugs, such as cyclophosphamide, was conducted even though the drug was not used during the visits. Surface wipe samples were analyzed by either the NIOSH lab or a contract lab, Bureau Veritas North America. It is not uncommon to have a wipe sample for hazardous drug result in a ND in the presence of a hazardous drug [NIOSH 2012]. Some of the hazardous drugs, such as doxorubicin, are not stable and can decay rapidly [NIOSH 2012]. These drugs are less likely to be positive for a surface wipe sample. 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 varies over time. This

variation is influenced by drug amounts handled, patient load, and work practices [NIOSH 2012].

The positive vincristine sample was not surprising since a patient was injected with the drug during the NIOSH visit. All the field samples analyzed for toceranib and MDEA were positive. Although toceranib and mustargen (for the purposes of sampling for mustargen, MDEA was the analyte analyzed) were not used during the NIOSH visit, the drugs were present on the samples. The toceranib and MDEA contamination likely originated from its prior therapeutic use within Veterinary Hospital A. One of the highest wipe sample results (1900/1940 ng) was for MDEA. This surface wipe sample was collected in the special procedures room's door front on a cabinet. Its lingering contamination serves as a warning in regards to the potential exposures to veterinary staff, long after the actual drug administration.

In-house NIOSH HPLC-MS analyses employed controlled fragmentation (MS/MS) of the parent ion of each analyte. Two fragment ions were monitored for each, with the more intense ion used for quantification and the other for confirmation. Positive response for an analyte was indicated by quantification ion response above the calculated LOD (q.v.) and by the presence of both expected fragment ions. Additionally, the ratio of intensities of the two fragment ion responses observed for field samples was compared to the average ratio observed for pure analyte (i.e., the calibration standards) as an additional metric for assessing positive analyte response in samples. If both ions were present but their ratio differed significantly from the expected value, it suggested that the quantitative value determined for the analyte might be affected by an unresolved interference and could thus be suspect. These results are designated appropriately in Tables VIII through X (q.v.).

No isotopically labeled standards for the analytes of interest were available for use in the HPLC/MS analysis. To track stability of instrument performance throughout the analysis, low-level calibration standards were periodically interspersed with field samples and responses were compared to expected levels. Additionally, quality controls were prepared by spiking several levels of analytes onto applicable wiping media, which were processed and run with field samples to demonstrate extraction procedure efficacy and instrument performance. Finally, several field samples were rerun to determine whether reanalysis produced analyte values similar to initial values; in these cases both separate results are listed in Tables VIII through X.

Instability has been anecdotally observed for lomustine and chlorambucil in the course of NIOSH analytical method development, and documented for doxorubicin and other drugs elsewhere [NIOSH 2012]. Degradation of unstable compounds is expected to be especially rapid in open workplace environments absent controlled parameters. Mustargen is also very reactive in uncontrolled environments and rapidly decays to several products, of which the ethanolamine MDEA is the most important in environments with typical humidity levels. Since it was unlikely that intact mustargen would be detected at a workplace site if sampling and/or analysis took place long after a spill event, the decision was made to quantify MDEA, which was readily detectable via HPLC/MS, 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 and cannot be conclusively linked to a particular source. Thus, it may not indicate actual mustargen contamination. After quantification of the antineoplastic drugs was completed, all field samples from this survey were screened for other ethanolamine compounds, which were found to be widely present. However, no meaningful quantitative correlations existed between these compounds and MDEA, suggesting that when MDEA was present it could not be automatically considered as a contaminant or intentional component of whatever sources had contributed the other ethanolamines. It is therefore not possible to guarantee or to dismiss that detection of MDEA in a field sample, as occurred in the present survey, definitely signals the presence of a prior mustargen contamination event.

Another 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 had several hazardous drugs in the chemotherapy preparation room for which 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 due to analyte instability as discussed above.

## Conclusions and Recommendations

The presence of vincristine contamination is a reminder that the patients themselves can be a source of exposure, even when the drugs are not handled directly. The toceranib and MDEA presence serves as two reminders: (1) that hazardous drug contamination can sometimes linger despite cleaning efforts and (2) the detected contamination on cabinet 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 (BSC), supplementary controls (CSTDs), protective work practices (surface cleaning after every oncology patient, regardless of whether I.V. chemotherapy was administered) and personal protective equipment (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 A had in place during the visit. The hospital is encouraged to:

- Continue to get the BSC recertified on a yearly basis and after it has been repaired or relocated [CDC 2009]. Ensure that the BSC certification process includes the most recent edition of the National Sanitation Foundation (NSF) Standard 49, Biosafety Cabinet Certification [NSF/ANSI 2016].
- Continue to use the BSC to prepare chemotherapy treatments for patients [NIOSH 2004; USP 2019].
- Continue to use CSTDs while compounding and administering 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 primary engineering controls (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.

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. Reusable 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.

- Ensure that the BSC used for preparation of chemotherapy drugs is externally vented (preferred) or has redundant-HEPA filters in series and is placed in a negative pressure room [USP 2019].
- Separate the chemotherapy preparation room [NIOSH 2004]. Currently, the chemotherapy is prepared in the same room as the dark room (Figure 11).
- Use disposable absorbent underpads on surfaces where the drug will be compounded and/or administered [NIOSH 2010].
- 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].
- Use two pairs of gloves during all tasks involving a chemotherapy patient [USP 2019]. Staff should wear American Society for Testing and Materials (ASTM)-tested chemotherapy gloves [USP 2019].
- Dispose of PPE after each use or whenever it becomes contaminated [NIOSH 2004].
- Use a designated chemotherapy waste bin and bags. This would isolate the hazardous waste from non-hazardous regular waste [NIOSH 2010].
- Use the *chemotherapy treatment in process* sign. This deters other staff from entering the room unprotected when hazardous drugs are in use [USP 2019].
- Continue washing hands after compounding, administering, or handling hazardous drugs.
- Continue using the hospital oncology department's standard operating procedures (SOPs) for administering of drugs, spills, post administration cleaning, and patient management.

- Do not allow drinks (caps and no caps) to be in areas where chemotherapy is prepared or administered.
- Label all cabinets and refrigerators used to store antineoplastics.
- Ensure that all hazardous drugs, including refrigerated hazardous drugs, are stored in a negative pressure room with at least 12 air changes per hour [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].
- Wash clothing and blankets that could be contaminated with drug separately from items with no anticipated drug contamination [USP 2019].
- Place the prepared drug in a labeled chemotherapy transport bag and then place it in the small white tray [NIOSH 2010; USP 2019]. The clinic currently uses small white trays to store prepared drugs for the patient (Figure 13). By using a transport bag, the chances for hazardous drug contamination are reduced. If the syringe leaks, then the drug is contained in the bag instead of the tray.

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## Appendixes

**Table I. LOD<sup>1</sup>/LOQ<sup>2</sup> and analytical ranges of analyte for Bureau Veritas North America's Internal Methods (March 2017)**

Analyte	LOD (ng) <sup>3</sup>	LOQ (ng)	Analytical Range (ng)
Carboplatin	5	17	5 to 200
Vinblastine <sup>4</sup>	1	3.3	1 to 60
Cyclophosphamide	5	17	5 to 200
Doxorubicin	5	17	5 to 200
Epirubicin	5	17	5 to 200
Methotrexate	5	17	5 to 200
Vincristine	5	17	5 to 200

**Table II. LOD/LOQ and analytical ranges of analyte for Bureau Veritas North America's Internal Methods (August 2018)**

Analyte	LOD (ng)	LOQ (ng)	Analytical Range (ng)
Cyclophosphamide	0.8	2.7	0.4 to 100
Doxorubicin	0.8	2.7	0.4 to 100
Epirubicin	2	5.9	1 to 100
Methotrexate	0.8	2.7	0.4 to 100
Vincristine	0.8	2.7	0.4 to 100

**Table III. LOD/LOQ and analytical ranges of analyte for NIOSH Method (March 2017)**

Analyte	LOD (ng)	LOQ (ng)	Analytical Range (ng)
Methyldiethanolamine (MDEA: marker for mustargen)	3.8	11	10 to 2500
Lomustine	11	35	100 to 20000
Chlorambucil	0.56	1.9	10 to 2500
Toceranib	0.042	0.14	10 to 300
Mitoxantrone	0.68	2.3	25 to 2500

\*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  $[3(\text{Sigma})]/m$  and LOQ as  $[10(\text{Sigma})]/m$ .

<sup>1</sup> LOD = limit of detection

<sup>2</sup> LOQ = limit of quantification

<sup>3</sup> ng = nanogram of drug

<sup>4</sup> Results for this method were reported in micrograms/sample ( $\mu\text{g}/\text{sample}$ )

**Table IV. LOD/LOQ and analytical ranges of analyte for NIOSH Method (August 2018)**

<b>Analyte</b>	<b>LOD (ng)</b>	<b>LOQ (ng)</b>	<b>Analytical Range (ng)</b>
<b>Methyldiethanolamine (MDEA: marker for mustargen)</b>	0.14	0.45	5 to 1000
<b>Toceranib</b>	0.052	0.017	5 to 100
<b>Lomustine</b>	0.48	1.6	25 to 5000
<b>Chlorambucil</b>	0.23	0.77	5 to 1000

**Table V. Bureau Veritas North America Results: Chemotherapy Drugs in Surface Wipe Samples, Day 1 (March 2017)**

Location and Sample Identification	Sample Description	Wipe Sampling Method	Results (ng/sample) <sup>5</sup>
<b>Chemotherapy Preparation Room</b>	Inside BSC's on work surface	BV-2017-30843 <sup>6</sup> (Carboplatin)	ND <sup>7</sup>
<b>Examination Room</b>	Examination table	BV-2017-30843 (Carboplatin)	ND
<b>Chemotherapy Preparation Room</b>	Inside BSC's on work surface	NAT 2006-14763 (Vinblastine)	ND
<b>Examination Room</b>	Examination table	NAT 2006-14763 (Vinblastine)	ND
<b>Chemotherapy Preparation Room</b>	Surface counter in front of BSC	BV-2016-29599 (vincristine, methotrexate, cyclophosphamide, epirubicin, doxorubicin)	ND
<b>Examination Room</b>	Floor where vincristine was administered to a dog (Figure 8)	BV-2016-29599	68 for vincristine; ND for the other drugs
<b>Examination Room</b>	Floor where vincristine was administered to a dog	BV-2016-29599	ND
<b>Examination Room</b>	Examination table	BV-2016-29599	ND
<b>Special Procedures Room</b>	Counter	BV-2016-29599	ND
<b>Special Procedures Room</b>	Anesthesia equipment and knobs	BV-2016-29599	ND
<b>Special Procedures Room</b>	Floor near examination table	BV-2016-29599	ND
<b>Kennel</b>	Bottom of kennel	BV-2016-29599	ND
<b>Kennel</b>	Base of examination table	BV-2016-29599	ND
<b>Break Room</b>	Food table	BV-2016-29599	ND
<b>Break Room</b>	Microwave's key pad and open button	BV-2016-29599	ND
<b>Waiting Room</b>		BV-2016-29599	ND

<sup>5</sup> ng/sample = nanogram of drug per sample

<sup>6</sup> Bureau Veritas North America's Internal Method

<sup>7</sup> ND = results are not detected at the limit of detection (LOD)

**Table VI. Bureau Veritas North America Results: Chemotherapy Drugs in Surface Wipe Samples, Day 2 (March 2017)**

Location and Sample Identification	Sample Description	Wipe Sampling Method	Results (ng/sample)
<b>Chemotherapy Preparation Room</b>	Inside BSC's on work surface	BV-2017-30843 <sup>8</sup> (carboplatin)	ND <sup>9</sup>
<b>Chemotherapy Preparation Room</b>	Inside BSC's on work surface	BV-2017-30843 (carboplatin)	ND
<b>Chemotherapy Preparation Room</b>	Outside of carboplatin vial	BV-2017-30843 (carboplatin)	ND
<b>Examination Room</b>	Floor where vinblastine injection was given	NAT 2006-14763 (Vinblastine)	ND
<b>Examination Room</b>	Floor where vinblastine injection was given	NAT 2006-14763 (Vinblastine)	ND
<b>Examination Room</b>	Examination table (table had just been cleaned)	NAT 2006-14763 (Vinblastine)	ND
<b>Examination Room</b>	Examination table (table had just been cleaned)	NAT 2006-14763 (Vinblastine)	ND
<b>Examination Room</b>	Examination table; vincristine (direct injection) given to patient	BV-2016-29599 (vincristine, methotrexate, cyclophosphamide, epirubicin, doxorubicin)	ND
<b>Examination Room</b>	Chair; vincristine given to patient	BV-2016-29599	ND
<b>Examination Room</b>	Vincristine given to patient	BV-2016-29599	ND
<b>Examination Room</b>	Vincristine given to patient	BV-2016-29599	ND
<b>Examination Room</b>	Floor; vincristine given to patient	BV-2016-29599	ND
<b>Examination Room</b>	Floor; vincristine given to patient	BV-2016-29599	ND
<b>Special Procedures Room</b>	Plastic lid of container (Figure 10); doxorubicin given to patient	BV-2016-29599	ND
<b>Special Procedures Room</b>	Floor where doxorubicin was given to patient	BV-2016-29599	ND
<b>Chemotherapy Preparation Room</b>	Outside of cyclophosphamide vial	BV-2016-29599	ND

<sup>8</sup> Bureau Veritas North America's Internal Method

<sup>9</sup> ND = results are not detected at the limit of detection (LOD)

**Table VII. Bureau Veritas North America Results: Chemotherapy Drugs in Surface Wipe Samples, Day 3 (August 2018)**

Location and Sample Identification	Sample Description	Wipe Sampling Method	Results (ng/sample)
<b>Chemotherapy Preparation Room</b>	Filter Backside	BV-2016-29599 (vincristine, methotrexate, cyclophosphamide, epirubicin, doxorubicin)	ND <sup>10</sup> (two samples collected)
<b>Chemotherapy Preparation Room</b>	Ceiling tile above BSC	BV-2016-29599	ND
<b>Chemotherapy Preparation Room</b>	Switches on the BSC	BV-2016-29599	ND

<sup>10</sup> ND = results are not detected at the limit of detection (LOD)

**Table VIII. NIOSH Lab Results: Chemotherapy Drugs in Surface Wipe Samples, Day 1 (March 2017)**

<b>Location and Sample Identification</b>	<b>Sample Description</b>	<b>Wipe Sampling Method</b>	<b>Results (ng)<sup>11</sup></b>
<b>Chemotherapy Preparation Room</b>	Inside BSC	NIOSH Method (filter paper)	(5.6) <sup>12,13</sup> (MDEA <sup>14</sup> ); ND <sup>15</sup> for toceranib, lomustine, chlorambucil, and mitoxantrone
<b>Special Procedures Room</b>	Floor by examination table (far from door) (Figure 2)	NIOSH Method (filter paper)	8.1 (MDEA); ND for toceranib, lomustine, chlorambucil, and mitoxantrone
<b>Special Procedures Room</b>	Floor by examination table (near door) (Figure 2)	NIOSH Method (filter paper)	9.2 and 14 <sup>16</sup> (MDEA); ND for toceranib, lomustine, chlorambucil, and mitoxantrone
<b>Special Procedures Room</b>	Door front on cabinet (Figure 2)	NIOSH Method (filter paper)	1900 and 1940 (MDEA); ND for toceranib, lomustine, chlorambucil, and mitoxantrone
<b>Kennel</b>	Examination table base (Figure 14)	NIOSH Method (filter paper)	15 and 16 (MDEA); ND for toceranib, lomustine, chlorambucil, and mitoxantrone
<b>Kennel</b>	Floor by water bowl inside of kennel (Figure 15)	NIOSH Method (filter paper)	(8.0) (MDEA); ND for toceranib, lomustine, chlorambucil, and mitoxantrone
<b>Kennel</b>	Outside litter box (Figure 16)	NIOSH Method (filter paper)	(9.8) (MDEA); ND for toceranib, lomustine, chlorambucil, and mitoxantrone

<sup>11</sup> ng = mass of drug

<sup>12</sup> *Italics* = Result between the limit of detection (LOD) and limit of quantification (LOQ)

<sup>13</sup>( ) = Values for which fragment ion ratio suggest inaccuracy

<sup>14</sup> MDEA = N-methyldiethanolamine

<sup>15</sup> ND = results are not detected at the limit of detection (LOD)

<sup>16</sup> 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

**Table IX. NIOSH Lab Results: Chemotherapy Drugs in Surface Wipe Samples, Day 2 (March 2017)**

<b>Location and Sample Identification</b>	<b>Sample Description</b>	<b>Wipe Sampling Method</b>	<b>Results (ng)<sup>17</sup></b>
<b>Kennel</b>	Examination table (Figure 17)	NIOSH Method (swab)	<i>(6.0)</i> <sup>18,19</sup> (MDEA <sup>20</sup> ); ND <sup>21</sup> for toceranib, lomustine, chlorambucil, and mitoxantrone
<b>Kennel</b>	Inside kennel (cage) (Figure 15)	NIOSH Method (swab)	<i>(5.8)</i> (MDEA); ND for toceranib, lomustine, chlorambucil, and mitoxantrone
<b>Special Procedures Room</b>	Under examination table (Figure 2)	NIOSH Method (filter paper)	<i>(6.5)</i> and <i>5.2</i> <sup>22</sup> (MDEA); <i>(0.49)</i> and <i>0.44</i> (toceranib); ND for lomustine, chlorambucil, and mitoxantrone
<b>Special Procedures Room</b>	Near door and base of examination table (Figure 2)	NIOSH Method (filter paper)	<i>4.6</i> (MDEA); <i>(0.23)</i> (toceranib); ND for lomustine, chlorambucil, and mitoxantrone
<b>Kennel</b>	Inside kennel (cage) (Figure 15)	NIOSH Method (filter paper)	<i>(9.1)</i> and <i>7.6</i> (MDEA); <i>(2.0)</i> and <i>(2.2)</i> (toceranib); ND for lomustine, chlorambucil, and mitoxantrone
<b>Examination Room</b>	Examination room floor (Figure 18)	NIOSH Method (filter paper)	<i>10</i> and <i>9.3</i> (MDEA); <i>0.11</i> and <i>0.24</i> (toceranib); ND for lomustine, chlorambucil, and mitoxantrone

<sup>17</sup> Ng = mass of drug

<sup>18</sup> *Italics* = Result between the limit of detection (LOD) and limit of quantification (LOQ)

<sup>19</sup>( ) = Values for which fragment ion ratio suggest inaccuracy

<sup>20</sup> MDEA = N-methyldiethanolamine

<sup>21</sup> ND = results are not detected at the limit of detection (LOD)

<sup>22</sup> 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

**Table X. NIOSH Lab Results: Chemotherapy Drugs in Surface Wipe Samples, Day 3 (August 2018)**

Location and Sample Identification	Sample Description	Wipe Sampling Method	Results (ng) <sup>23</sup>
<b>Chemotherapy Preparation Room</b>	Switches on BSC (Figure 19)	NIOSH Method (swab)	39.5 and 44.1 <sup>24</sup> (MDEA <sup>25</sup> ); ND <sup>26</sup> for toceranib, lomustine, and chlorambucil <sup>27</sup>
<b>Chemotherapy Preparation Room</b>	Horizontal surface near outlet of BSC (Figure 20)	NIOSH Method (swab)	17.6 and 20.3 (MDEA); ND for toceranib, lomustine, and chlorambucil
<b>Chemotherapy Preparation Room</b>	HEPA <sup>28</sup> filter box surface (Figure 21)	NIOSH Method (swab)	25.1 and 25.7 (MDEA); ND for toceranib, lomustine, and chlorambucil

<sup>23</sup> ng = mass of drug

<sup>23</sup> 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

<sup>25</sup> MDEA = N-methyldiethanolamine

<sup>26</sup> ND = results are not detected at the limit of detection (LOD)

<sup>27</sup> Mitoxantrone was not analyzed for during the 2018 site visit

<sup>28</sup> HEPA = high efficiency particulate air



Figure 1. BSC in Chemotherapy Preparation Room (Photo Credit: NIOSH)



Figure 2. Special Procedures Room; several wipe samples were collected in this room including floor by examination table and door front cabinet (Photo Credit: NIOSH)



Figure 3. Kennel (Photo Credit: NIOSH)



Figure 4. I.V. bag with bag adapter CSTD attached for intravenous chemotherapy (Photo Credit: NIOSH)



Figure 5. Chemotherapy drug, doxorubicin, being administered to patient via catheter (Photo Credit: NIOSH)



Figure 6. TSI® VelociCalc™ Plus Model 9555-P thermal anemometer (Photo Credit: NIOSH)



Figure 7. Qualitative smoke test with Wizard Stick Smoke Generator (Photo Credit: NIOSH)



Figure 8. Patient on floor with veterinarian technician about to receive chemotherapy treatment (Photo Credit: NIOSH)

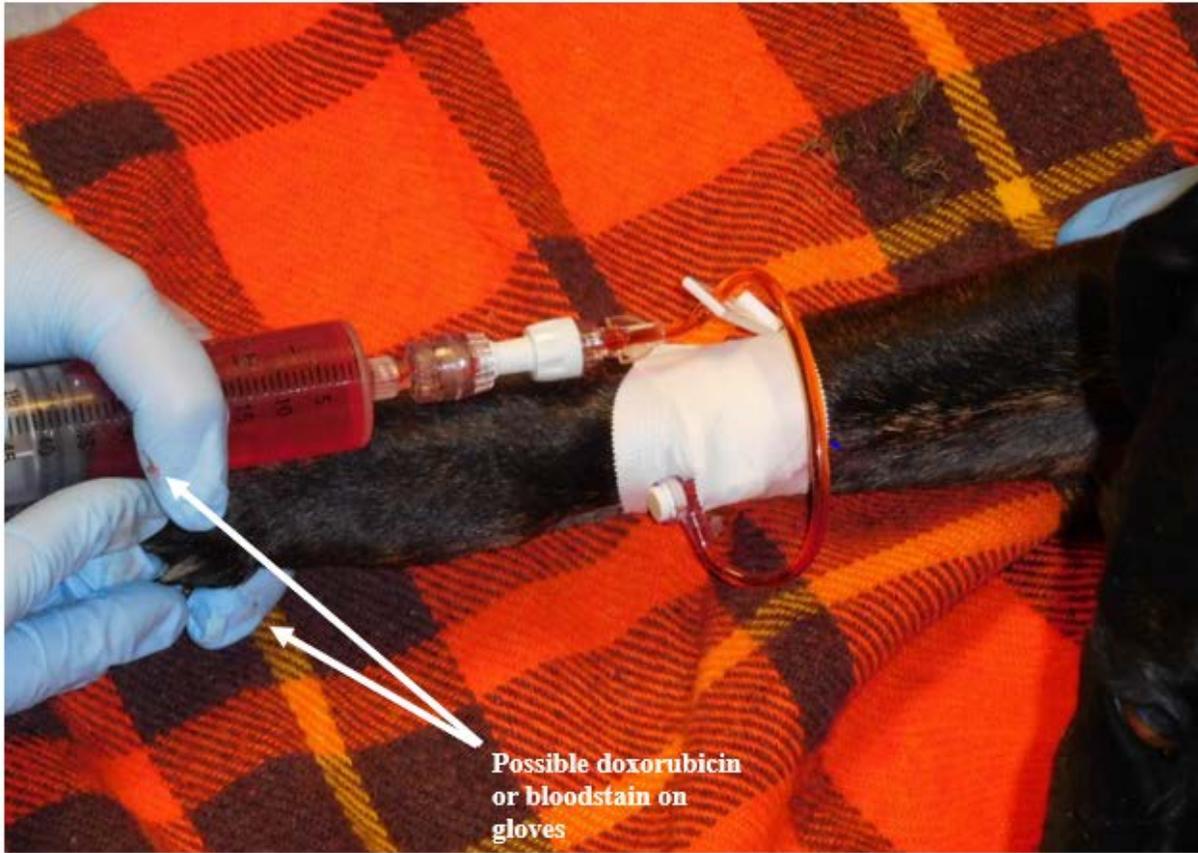


Figure 9. Possible doxorubicin or bloodstain on veterinarian technician's glove in special procedures room (Photo Credit: NIOSH)

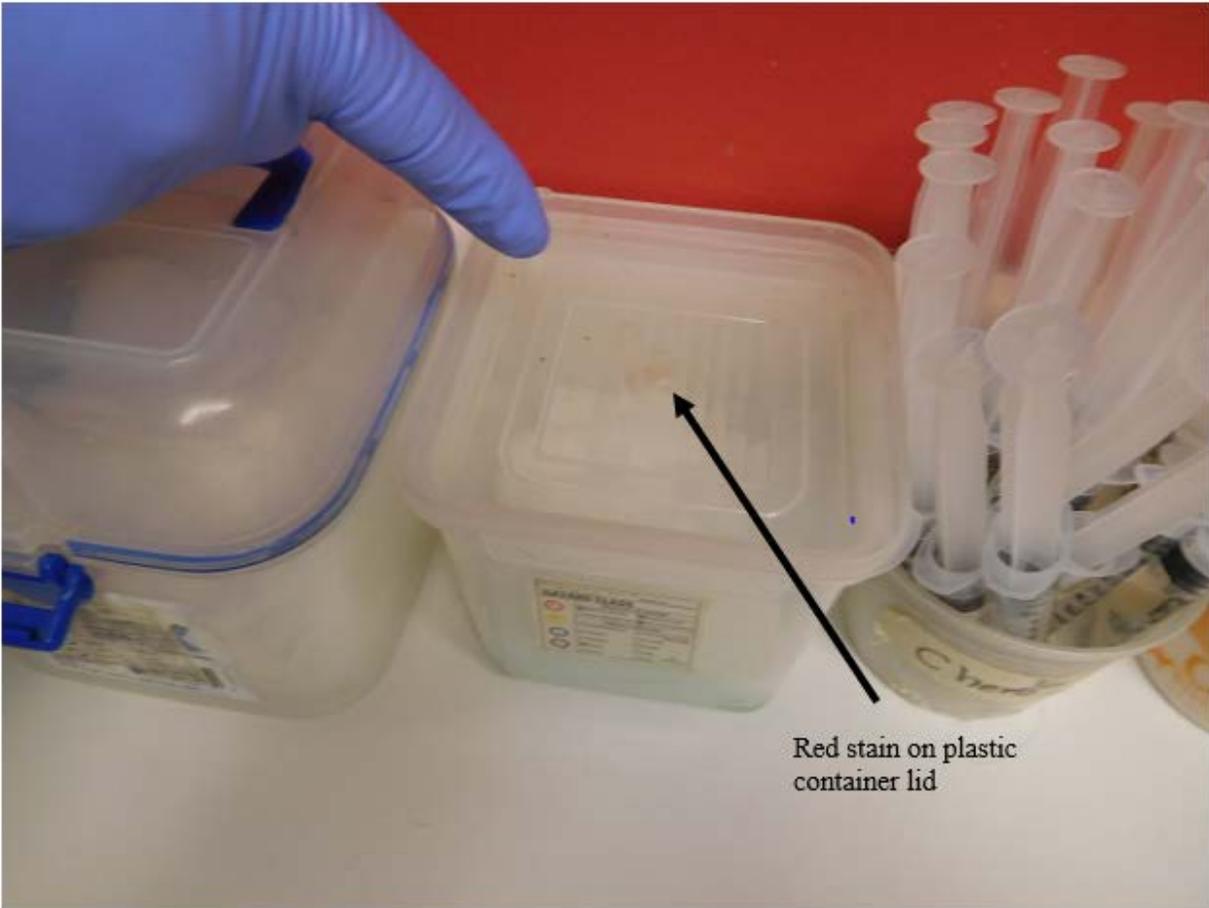


Figure 10. Possible doxorubicin or bloodstain on plastic container's lid in special procedures room (Photo Credit: NIOSH)



Figure 11. Safety glasses and drug refrigerator in the chemotherapy preparation room (x-ray processing equipment is also shown) (Photo Credit: NIOSH)



Figure 12. Smoke detector (Photo credit: NIOSH)



Figure 13. Prepared chemotherapy treatment in small white tray (Photo Credit: NIOSH)



Figure 14. Examination table base in kennel room (Photo Credit: NIOSH)



Figure 15. Floor by water bowl inside of kennel (Photo credit: NIOSH)



Figure 16. Litter boxes in kennel room (Photo credit: NIOSH)



Figure 17. Examination table in kennel room (Photo credit: NIOSH)



Figure 18. Examination room's floor (Photo credit: NIOSH)



Figure 19. Wipe sample collected on BSC's switches (Photo credit: NIOSH)



Figure 20. Wipe sample collected on horizontal surface near outlet of BSC (Photo credit: NIOSH)



Figure 21. Wipe sample collected on HEPA filter box surface (Photo credit: NIOSH)

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