Received: 18 January 2018 | Revised: 22 January 2018 | Accepted: 22 January 2018

DOI: 10.1111/jvim.15077

CONSENSUS STATEMENT

Journal of Veterinary Internal Medicine Open Access

ACVIM American College of Veterinary Internal Medicine

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ACVIM small animal consensus statement on safe use of cytotoxic chemotherapeutics in veterinary practice

Annette N. Smith[1] | **Shawna Klahn**[2] | **Brenda Phillips**[3] | **Lisa Parshley**[4] | **Peter Bennett**[5] | **Andi Flory**[3] | **Rosemary Calderon**[6]

[1]Department of Clinical Sciences, Auburn University College of Veterinary Medicine, Auburn, Alabama

[2]Department of Small Animal Clinical Sciences, Virginia–Maryland Regional College of Veterinary Medicine, Virginia Tech, Blacksburg, Virginia

[3]Oncology Veterinary Specialty Hospital of San Diego, San Diego, California

[4]Oncology Olympia Veterinary Cancer Center, Olympia, Washington

[5]Oncology University Veterinary Teaching Hospital Sydney, University of Sydney, Sydney, Australia

[6]Blue Pearl Veterinary Partners, New York, New York

Correspondence
Annette N. Smith, Department of Clinical Sciences, Wilford & Kate Bailey Small Animal Teaching Hospital, 1220 Wire Rd, College of Veterinary Medicine, Auburn University, AL 36849-5540.
Email: smith30@auburn.edu

The purpose of this report is to offer a consensus opinion of ACVIM oncology diplomates and technicians on the safe use of cytotoxic chemotherapeutics in veterinary practice. The focus is on minimizing harm to the personnel exposed to the drugs: veterinary practitioners, veterinary technicians, veterinary staff, and pet owners. The safety of the patient receiving these drugs is also of paramount importance, but is not addressed in this statement. Much of the information presented is based on national recommendations by Occupational Safety and Health Administration, National Institute for Occupational Safety and Health, United States Pharmacopeia, and other published regulations. These directives reflect an abundance of caution to minimize exposure to medical personnel, but large-scale studies about the consequences of long-term occupational exposure are not available in veterinary medicine. Challenges in the delivery of optimal treatment safely and economically to veterinary patients in general practice without access to a veterinary oncologist or other specialist, because of costs or proximity, remain.

KEYWORDS
cancer, drugs, NIOSH, safety

1 | DEFINING THE PROBLEM

As use of cytotoxic chemotherapy in veterinary practice increases,[1–3] there is a greater risk of cytotoxic exposure in the workplace and the patient's home environment. Increasing popularity in the use of continuous low-dose PO chemotherapy ("metronomic" chemotherapy) and

Abbreviations: BSC, biologic safety cabinet; CSTD, closed-system transfer devices; HD, hazardous drugs; NIOSH, National Institute for Occupational Safety and Health; OSHA, Occupational Safety and Health Administration; PPE, personal protective equipment; SDS, safety data sheets; RCRA, Resource Conservation and Recovery Act; USP, United States Pharmacopeia.

Work presented in part at the 2013 ACVIM Forum, Seattle, WA.

daily or every-other-day small molecule inhibitor treatment also increases the risk of exposure to clients.

Handling of cytotoxic drugs has been classified as an occupational health hazard according to a National Institute for Occupational Safety and Health (NIOSH) alert, first published in 2004 and most recently updated in 2016.[4] Such drugs are carcinogenic, mutagenic, teratogenic, abortifacient, and increase the risk of stillbirth.[5–8] Some of this information has been derived from in vitro studies, animal studies, and from studies in pregnant women receiving chemotherapy for their own malignancies, but adverse effects still might be seen at lower levels of exposure. Compared to intermittent high-dose exposure, chronic low levels of cytotoxic chemotherapy exposure actually may have increased risk, because cytotoxic effects are less likely to occur with similar mutagenic effects.[9] Veterinary small molecule inhibitors, although often not considered "classical" chemotherapy agents, carry similar risks, according to package inserts (https://www.zoetisus.com/products/dogs/palladia/index.aspx). Current targets are associated with angiogenesis, and treatment with these agents could harm a growing fetus. They should be handled as other cytotoxic drugs.

Human healthcare workers (eg, pharmacy employees, nurses) handling chemotherapeutics have been found to have variably increased chromosomal aberrations compared to the general population,[9–16] as well as urinary excretion of these drugs or their metabolites,[17,18] which could lead to similar reproductive complications found in cancer patients treated with cytotoxic drugs.[19–23] In fact, some large studies[5] and a meta-analysis[24] have shown an incremental increased risk of infertility and early pregnancy loss with occupational exposure to chemotherapeutics. Chromosome changes appear to be exposure- and drug-dependent, with high-volume practice and alkylators being associated with the most abnormalities.[10] Additionally, the chance of developing some cancers might be increased.[21,23,25] As a caveat, most of the studies included in the meta-analysis were performed before the widespread use of closed-system transfer devices (CSTD). Various methods used to detect abnormalities, lifestyle factors, amount of exposure to cytotoxic drugs, and variable use of safety measures impact the usefulness of these studies in attributing causation to these health risks. The addition of protective measures such as biologic safety cabinets (BSCs), CSTDs, and personal protective equipment (PPE) markedly decreases, but does not always eliminate, evidence of drug contamination.[16,26,27]

In veterinary medicine, several studies have been performed to investigate occupational risk in reproductive outcomes and cancer development. However, chemotherapy use and exposure have not been specifically investigated related to these outcomes. A 1998 study of 3000 female veterinary graduates showed both a decreased risk of preterm delivery and a decreased risk for small-for-gestational age births compared to the general population.[28] In a review of several studies examining the cause of death in veterinarians, an increased risk was found for the development of multiple myeloma (6 cases out of 12 000), and a decreased risk for lung cancer, but overall there was a similar risk of cancer as in the general population and no conclusion about specific occupational exposures could be made.[29] Reportedly, 71% of veterinary practices in the United Kingdom use cytotoxic drugs, indicating that practitioners do need to be aware of the use of protective procedures when using chemotherapeutics.[30] In a 2009 survey of 93 practices in Hampshire,[31] half of which used cytotoxic drugs, 100% reported compliance with staff training, exclusion of pregnant workers, waste management, and instructions to clients about precautions. However, none had a designated BSC, and only 82% used PPE. In a survey of Canadian veterinary practice, 30% of general practitioners and 22% of academic veterinarians reported using chemotherapeutics.[32] Mixed or small animal practitioners made up 91% of the private practice population and equine practitioners 8.6%. In 8% of general practice veterinarians, accidental exposures to cytotoxic drugs were reported. Academic veterinarians using chemotherapeutics were mostly small animal or mixed practitioners (47%), although a larger proportion of equine veterinarians using chemotherapeutics was found in academia (35%). No accidental exposures were reported in this population. In the Netherlands, a 2006 study found frequent contamination of the veterinary practice environment, including gloves of personnel administering chemotherapy, surfaces of preparation and administration areas, floors, and door handles.[33] In a review of an American veterinary teaching hospital in 2010, surface contamination was found in 10% of swabs within the preparation area only, and 60%-70% compliance with safety procedures regarding the use of PPE was reported.[34]

The risk to clients while caring for their pets with cancer or administering cytotoxic drugs also is poorly defined. Some contamination of the environment, and potential exposure to family members or caregivers occurs when people are receiving chemotherapy.[33,35] Guidelines for safe handling of PO chemotherapeutics in human practice have been compiled, attempting to limit potential harms.[36] In veterinary medicine, some environmental contamination also has been documented,[37] and similar precautions should be taken by clients handling veterinary cancer patients undergoing chemotherapy and administering drugs at home to their pets.[38,39]

Because chemotherapy drugs usually have a low therapeutic index, inappropriate administration increases risks of exposure to personnel, as well as the risk of adverse events for the patient. Evaluation and suggestions in this regard are beyond the scope of this consensus statement, but some guidelines have been included that also impact the safety of those administering drugs. The European consensus statement on chemotherapy use recommends that these drugs should have proven efficacy before administration, recognizing that most are used in an off-label fashion. Acknowledging that practitioners other than oncologists do administer these drugs, at a minimum, consultation with a veterinary oncologist to determine the risks versus benefits to the patient is strongly recommended. The reader is referred to the following resources regarding patient safety:

Biller B, Berg J, Garrett L, et al. 2016 AAHA oncology guidelines for dogs and cats. *J Am Anim Hosp Assoc*. 2016;52:182–204.

Steffy-Morgan JD. Chemotherapy: chemotherapy administration. In: Henry CJ, Higginbotham ML, eds. *Cancer Management in Small Animal Practice*. MO: Saunders Elsevier Maryland Heights; 2010:114–118.

2 | FEDERAL AND STATE GUIDELINES

Several states now mandate that veterinary hospitals comply with NIOSH guidelines[40] regarding hazardous drugs (HD). The first was the state of Washington in April 2011, closely followed by California in 2013 and North Carolina in 2014. The United States Pharmacopeia (USP) has updated guidelines (Chapter 800) that are scheduled to be implemented in 2019.

Washington State Laws & Guidelines:
http://app.leg.wa.gov/RCW/default.aspx?cite=49.17.465

http://www.lni.wa.gov/Safety/Topics/AtoZ/HazardousDrugs/ProgramGuides.asp

California State Law & Guidelines:
http://leginfo.legislature.ca.gov/faces/billNavClient.xhtml?bill_id=201320140AB1202

North Carolina State Law & Guidelines:
http://www.ncga.state.nc.us/Sessions/2013/Bills/House/HTML/H644v5.html

USP chapter 800: Hazardous Drugs—Handling in Healthcare Settings
http://www.usp.org/usp-nf/notices/general-chapter-hazardous-drugs-handling-healthcare-settings

3 | EXPOSURE RISKS: GUIDELINES FOR MITIGATION

Exposure to cytotoxic drugs can occur at many time points. For staff, risks occur during handling, preparation, and administration of the drugs. Pet owners risk exposure when they administer PO medications at home and also when they are exposed to secretions and excreta from their pets. These latter exposure events also are risks to veterinary staff when patients are hospitalized after their treatments or admitted for treatment of adverse events. The routes of exposure include skin contact, skin absorption, inhalation of aerosols or drug particles, ingestion, and needle stick injuries.[41] The guidelines below are currently recommended practices, but they are being continually revised.

4 | PERSONNEL TRAINING

In human hospitals, the rate of compliance with chemotherapy safety guidelines varies from 68% to 80%. The attitude of oncology nurses to preventative measures is altered by their education and their belief in the risks posed.[42,43] Reasons cited for lack of use of PPE include: they are not comfortable, they were forgotten because of work pressures, and they were not believed to be necessary.[44] Complacency occurs with PO medications because people do not perceive them to be as toxic as parenteral medications.[45] Additional concerns in veterinary medicine include increased client costs and the perception that safety practices can decrease efficiency. Although there are costs associated with using appropriate safety equipment, their use does not impede workflow and educated veterinary technical staff are willing to use protective practices.[46] All of the aforementioned obstacles should be considered and addressed during training.

Only trained personnel should handle and administer chemotherapeutics, and training should be documented in staff personnel files and, for owners, in the medical records of the patients being treated, before the handling of any HD. A safety officer should be designated in each facility, with responsibility for training, documentation, and continual review (at least every 6 months) and updating manuals as needed when new guidelines become available.

Written policies and procedures for the safe handling of HD must be in place in any facility in which HD are handled.[47] A key element of the safety program is the availability of Safety Data Sheets (SDS, formerly called Material Safety Data Sheets [MSDS]). The Occupational Safety and Health Administration (OSHA) guidelines state that healthcare facilities in which HD are used must provide worker training, adequately label HD, and provide access to SDS for all HD used in the hospital. The updated Hazard Communication System requires that SDS will have a new common format and contain standardized information, such as proper handling, protective equipment to be used, steps to take in case of spills, first aid measures, and toxicological information (eg, routes and symptoms of exposure). Drug insert information sheets for every anti-neoplastic agent used in the hospital should be collected into a binder and kept available for review by staff.

All employees must be trained on the proper care and use of PPE and spill kits.[47] Workers should be trained to wear proper PPE during HD receiving, storage, preparation, administration, disposal, and in cleaning up waste from patients that have received HD.

PPE Recommendations for preparation, administration, spill and waste management, and inventory management

Chemotherapy-rated (ASTM International [American Society Testing Materials]) double-gloving

Long-sleeved coated impermeable gown with back closure
Shoe coverings

Shoe & hair coverings to maintain sterility (if needed)

Eye shield/Face shield if potential for splashing/aerosolization

Respirator (fitted)

Proper use of CSTD to ensure containment of HD during compounding and administration and methods of preventing aerosol formation and spread of contamination should be taught. Employees must also understand proper methods of drug transportation within the facility. Policies and procedures regarding drug spills should be established, and employees should understand how to recognize and manage a spill. Large spills should be handled by workers who are trained in handling

HD. Cleaning protocols, the appropriate cleaning products, and proper waste containers for disposing of HD should be available.

Medical management programs should be in place for workers who handle or may be exposed to HD. Training should occur at the time of hiring. At a minimum, employees should be encouraged to come forward with any concerns and should notify their supervisors if they are actively attempting to become pregnant, are pregnant, are lactating, or have a health issue that requires they consider alternative duties on the advice of their physician. Documentation of the amount of drug handling per shift can serve as a surrogate of potential drug exposure, and can be maintained in the employee's file if questions arise.[48] Workers who have health changes or substantial contact with HD, such as cleaning up a large spill, skin or eye contact, or a needle stick should have follow-up reviews after consultation with their physician.[40]

HD safety skills

Risks of handling HD

How to access written policies and procedures on HD, including MSDS

How to recognize HD (pictograms per the Hazard Communication System (HCS): http://www.osha.gov/dsg/hazcom/)

How to recognize areas in which HD are used

Methods of controlling exposure to HD

Proper PPE use

CTSD use

Recognize accidental release of HD into environment
Spill management

Management of personnel exposure to HD

5 | ALTERNATIVE DUTY

There currently is no recommended exposure limit for HD, and the safe level of exposure cannot be determined. Workers who are pregnant, breastfeeding, or attempting to conceive or father a child should avoid exposure or decrease exposure to as low a level as reasonably practicable. They should not assist in preparation or administration of HD, nor should they handle patients or clean cages or runs of patients that have received chemotherapy. These workers should be offered alternative duties if they choose not to work with cytotoxic agents. Employees' physicians should be involved in making the determination of whether or not to work with HD. The greatest time of risk is during the first trimester, and women may not be aware of pregnancy during this time. Clear guidelines on decreasing occupational exposure to all staff at all times are a critical component of chemotherapy safety for unborn children. It is the responsibility of the employee to alert management if she is pregnant or if she is trying to conceive.

6 | ENVIRONMENT

The environment in chemotherapy safety should be set up so as to limit direct exposure to HD and decrease the risk of indirect exposure by contaminated packaging, poor handling technique, and spills. The risk of exposure starts when HD are delivered to the facility. These drugs should be labeled as HD at entry to the facility to ensure that appropriate safety measures are followed. In testing of vials and packaging of cytotoxic drugs at arrival from the manufacturer, surface contamination is common, ranging from 0% to 100% of vials tested.[49–51] In 1 study, no contamination of vials had occurred when they arrived from the distributor, but frequent contamination of vials that had been stored in the pharmacy was identified, with a presumption of cross contamination from the preparation areas.[49] In areas receiving chemotherapy agents, such as a central supply facility, staff should, at a minimum, handle incoming drugs from suppliers with chemotherapy-rated gloves to prevent exposure from broken vials. Staff should be trained in how to manage spills and broken vials.

Storage should be carried out according to labeled recommendations (eg, refrigerated, room temperature, light-sensitive). The HD should be stored in a separate, labeled area. Refrigerated items should be stored in a dedicated, labeled refrigerator that is not used to store food or other drugs. In addition, areas in which HD are stored or prepared must be designated and clearly marked with appropriate signage. Eating, drinking, smoking, chewing gum, using tobacco, applying cosmetics, or storing food or drinks must be prohibited in areas in which HD are stored, prepared, or used.[40] Warning signs should be posted during preparation and administration to alert other personnel of the potential hazard of entering the area(s). The storage, preparation, and administration areas should include surfaces that are easily cleaned and decontaminated. Carpet and upholstery should be avoided. Work surfaces in preparation areas often are found to have traces of drugs present.[49,51] Contamination varies with the type of equipment used in the preparation procedures. Some studies have shown similar levels of contamination within the oncology wards of human hospitals as seen in HD preparation areas.[49]

All HD should be prepared and administered in a controlled area where access is limited to authorized personnel trained in chemotherapy procedures. Ideally, preparation and administration would occur in a negative-pressure room. Positive pressure rooms (such as surgical suites) should be avoided because of the potential spread of airborne contamination. The preparation and administration areas should be clutter-free and contain only necessary items and supplies. All needed supplies should be gathered before drug preparation and administration to minimize exiting and re-entering the work area(s). Whenever possible, tasks associated with preparation and administration should be coordinated to maximize efficiency and minimize worker exposure.

Chemotherapeutic agents should be prepared using primary engineering control, such as a BSC or compounding aseptic containment isolator. Employees must be trained on the proper use of these devices. Characteristics of ideal BSCs include: vertical laminar flow, which carries contaminated air away from the operator (horizontal flow only protects the drug and not the worker); High-efficiency particulate

arrestance filter; 100% ventilation to the outside; and, a continuously running fan. Current recommendations also allow for class II type A BSC with 30% recirculation. All BSC should be serviced and recertified according to the manufacturer's recommendations. Use of a BSC does not prevent contamination within the cabinet, and use of proper technique when working within the hood and following appropriate cleaning procedures are essential.[40,47]

Use of a CSTD is recommended during preparation and administration of chemotherapeutic drugs. A CSTD mechanically prevents the escape of a drug or vapor out of the system into the environment. A CSTD also should decrease the risk of needle accidents during administration. The typical device includes an adaptor for the drug vial, a piece that attaches to a luerlock syringe (needleless system), and adaptors to allow connection of the needleless syringe to the fluid lines. The risk of aerosolization is highest during transfer of the drug from the vial to syringe and from the syringe into a fluid line. A CSTD will decrease aerosolization of a parenteral drug during preparation and administration and prevent accidents during administration. Multiple studies have shown a decrease in environmental contamination with the use of CSTD.[52–59] A CSTD is not a substitute for the use of PPE or preparation in a ventilated cabinet.[40,47,60]

Many commercially available devices limit surface contamination during preparation and administration of chemotherapy agents. These devices take time to learn how to use properly and efficiently. Clinicians and technicians should acquaint themselves with a product by proper instruction. Once a degree of competency with the system has been reached, any of these devices appear to provide protection against contamination and accidents without slowing or hindering staff. Considerations that should be taken into account when choosing the appropriate device for a practice include: level of protection, ease of use, Food and Drug Administration (FDA) approval, and cost.

Chemoclave/Chemolock	ICUMedical
Equashield	Equashield
Onguard	BBraun
PhaSeal	BD

Commercially available CSTD

7 | PREPARATION AND TRANSPORT OF CHEMOTHERAPY DRUGS

Only personnel trained in the handling of HD and proper technique should prepare chemotherapy drugs. Orders and prescriptions should be independently calculated and verified by at least 2 separate individuals, but ideally including the prescribing clinician, a second person trained in handling HD, and the worker responsible for preparation. Full PPE should be worn during preparation. A plastic-backed absorbent pad should be placed under the preparation site, and should be replaced at least once daily, or anytime a spill occurs or the pad is contaminated. Only supplies essential to drug preparation should be placed in the BSC to avoid disrupting the efficiency of the BSC. Critical operations should be done at least 3 inches above the work surface. Splitting, opening, or crushing tablets or capsules should never occur. Fluid bags should be spiked and tubing should be primed with a compatible fluid before adding HD.

Outer gloves should be removed before final preparation and surface decontamination. The outside of the container should be wiped with gauze moistened with a deactivating substance before removal from the BSC. The work surface area in the BSC should be decontaminated and disinfected. A fresh pair of outer gloves should be donned before removing the product from the BSC. The final product should be clearly labeled as cytotoxic and sealed in a plastic bag that allows visualization of the product, then placed into the transport bag or plastic box. To our knowledge, no studies have evaluated contamination of the bags in which doses prepared for an individual patient are delivered, but bags to be used for transport should never be placed in the BSC to avoid inadvertent contamination of the outer surface of the bag. Gloves and PPE should be removed in such a manner as to avoid environmental contamination, and materials should be disposed of in an appropriate waste container. Transport of HD should occur by hand in a secondary container that allows clear visualization of the product. The worker responsible for transportation should, at a minimum, wear chemotherapy-rated gloves.

8 | DECONTAMINATION

Written protocols and supplies for cleaning should be available and readily accessible, and only trained staff should be involved in cleaning. A spill kit and hazardous waste container should be readily accessible in chemotherapy receiving, preparation, and administration areas, as well as in holding areas for patients receiving chemotherapy. Cleaning supplies used in the chemotherapy area should not be used in non-chemotherapy areas. Dedicated mops, buckets, and cleaning supplies should be identified and used. All surfaces associated with HD handling should be considered contaminated. All equipment, counters, and work surfaces should be cleaned with a deactivating agent and cleaning agent at the start of the day, before and after each activity, and at the end of the work shift.

Because no universal cleaner exists for all chemotherapy drugs, and no specific wipe-down procedures have been studied, no proven decontamination procedures exist. Most commonly used cleaning agents contain some form of detergent and hypochlorite solution. However, strong detergent and water may remove most drug residues when the directions as indicated on the container are followed. Repetition should provide increased effectiveness of decontamination. The use of alcohol for primary disinfection will not deactivate HD and may result in spread of contamination, although a final alcohol wipe is sometimes used to prevent corrosion of stainless steel surfaces. Directly spraying a surface is not recommended, because of the risk of aerosolization. Gauze, wipes, or paper towels should be sprayed directly, and then used to wipe the surface. Sprayers or pressure washers should not be used for initial cleaning of cages, kennels, or stalls used for housing patients treated with HD.

9 | SPILL MANAGEMENT

Spills must be contained and cleaned immediately, according to the extent of the spill. Cleaning always should proceed from areas of lesser contamination to those of greater contamination. One trained person should manage the spill by use of a properly maintained and easily accessible spill kit that includes: appropriate PPE; sufficient supplies to absorb a spill of 1000 mL; absorbent, plastic-backed sheets or pads; disposable toweling; at least 2 sealable, thick plastic, pre-labeled hazardous waste disposal bags; a disposable scoop for collecting glass fragments; and, a puncture-resistant container for glass fragments. Steps for managing a spill include: donning PPE, placing broken vials or other waste into a sealable bag, and absorbing liquid into absorbent pad or cleaning dry spills by wetting disposable toweling to limit creation of dust. The used bag and other supplies should be disposed of in a hazardous chemical waste container according to Environmental Protection Agency/Resource Conservation and Recovery Act (EPA/RCRA) regulations (https://www.epa.gov/rcra/resource-conservation-and-recovery-act-rcra-regulations#haz). The spill zone should be cleaned and disinfected after proper cleaning procedure. The PPE then should be removed and disposed of in the hazardous chemical waste container. Hands should be washed.

The spill should be documented by those involved in clean-up including: drug name; approximate volume spilled; how the spill occurred; spill management procedures; and, names of personnel, patients, and any others exposed to the spill. Documentation of exposures should be placed in the affected persons' personnel files. An analysis of the incident should prompt procedures to prevent recurrence.

10 | DISPOSAL

The EPA has been granted authority to enforce regulations set forth by the RCRA, which tracks hazardous waste from generation to disposal. The OSHA and ASHP recommend that hazardous waste be disposed of in a manner similar to that required for RCRA (https://www.epa.gov/rcra/resource-conservation-and-recovery-act-rcra-regulations#haz). All hazardous waste should be disposed of and stored separately from regular waste and according to federal, state, and local regulations. Trace wastes (<3% of original quantity) should be disposed of in chemotherapy waste containers (yellow in the United States). Waste containers should be clearly labeled, leak-proof, and covered with a foot-pedal operated lid to minimize respiratory exposure and contamination. Puncture-proof containers are needed for sharp or breakable items. Waste disposal should be carried out by licensed commercial waste disposal companies.

11 | CHEMOTHERAPY ADMINISTRATION

Safe administration of chemotherapy to veterinary patients requires a non-disrupted environment and cooperative behavior of the animal. If safe administration cannot be guaranteed, use of chemical restraint, or the decision not to treat an animal, is at the discretion of the prescribing clinician. Chemotherapy should be administered by 2 trained persons. The use of PPE is required. Work should be performed below eye level to minimize the potential for personnel contamination.

Chemotherapy drugs given PO should be intact; tablets should never be crushed or split and capsules should not be opened. Intralesional chemotherapy likely carries a high risk for environmental and personnel exposure, and additional precautions to prevent contamination such as a larger disposable administration pad for the table, cleaning the treated area on the patient afterwards and potentially covering it may be needed, depending on the amount of leakage that occurs. A full face shield is recommended. For injectable chemotherapy, an IV catheter should be placed in a suitable vein by experienced personnel. Catheter placement must be obtained by a "clean stick" to minimize the potential for extravasation and possible personnel exposure. The smallest gauge and shortest length of catheter to accommodate therapy should be used. Heparinized saline should never be used to irrigate lines or catheters because of possible precipitation of some chemotherapy agents and the potential for more extravasation risk because of local bleeding. An IV pump should be avoided where practical to prevent increased pressure on veins, decrease the risk of extravasation, and decrease the risk of disconnection and spills. The person restraining the patient should monitor the administration site for potential extravasation, and verify patency of the vein throughout administration. A syringe or infusion pump is acceptable for non-HD administration, such as monoclonal antibodies or bisphosphonates, and for long-duration infusions such as continuous rate infusion (CRI) of cytosine arabinoside and dacarbazine. Frequent observation of the patient to confirm patency and connection of the catheter is essential in this setting. Dedicated syringe and infusion pumps for chemotherapy administration should be stored in a dedicated chemotherapy administration area and not utilized for non-cytotoxic drug administration.

Before administration, the HD should be examined for leakage while it is contained in the transport bag. The patient's identification should be verified, as well as the drug name and dosage. If the HD appears intact and the dose correct, it may be removed from the transport bag. A plastic-backed absorbent pad should be placed under the administration area to absorb leaks and prevent drug contact with the patient's skin. The transport bag may be used as a containment bag for materials contaminated during administration.

After administration, the IV catheter should be removed with lines and tubing intact. The outer glove then should be removed, inside-out, with the IV catheter contained inside the glove. Administration materials should be properly disposed of and decontamination procedures followed. Gowns should not be worn longer than 3 hours to prevent permeation, and then should be removed and discarded after use, or earlier when soiled. Gloves should be discarded after each use and hands washed.[47]

12 | MANAGEMENT OF PATIENTS

The duration of excretion of cytotoxic drugs has not been established for most drugs in veterinary patients. Drug might be expected to be

found in urine, feces, saliva, vomitus, and sebum. In the studies that have been performed, detectable concentrations of drug have been found in the urine for days to weeks after administration, although concentrations are markedly decreased within 3 days.[38,61–63] Many drugs also are eliminated in the feces, and differences in PO bioavailability may result in drug excretion for 5–7 days post-administration.[38,47] The true level of risk from exposure to excreted products is not known. Information also is limited regarding the exposure of staff and owners after intralesional injection of drugs or electrochemotherapy treatments. Metabolites of HD also potentially retain cytotoxic attributes and, in most studies, these have not been measured or assessed. The default position should be to handle excreta from patients that have received injectable chemotherapy as contaminated for a minimum of 48–72 hours post-administration, and perhaps as long as 7 days after PO chemotherapy.

Chemotherapy excretion times in the dog

Drug	Excretion products studied	Days detected post-administration
Carboplatin[62]	Urine, feces, saliva, sebum, cerumen	21
Cyclophosphamide[60,61]	Urine	1–4
Doxorubicin[60,61]	Urine	21
Vinblastine[60,61]	Urine	7
Vincristine[60,61]	Urine	3

The number of personnel interacting with the patient should be minimized, and only trained personnel should handle patients or be involved in cleaning patient areas. Excreta from patients that have received chemotherapy should be handled with the same PPE as used for spills. At a minimum, safety glasses with side shields and chemotherapy-rated double gloves for cleaning and decontaminating work should be worn. Face shields should be used if splashing is possible. Gloves also should be chemically resistant to the decontamination or cleaning agent. Hands should be washed with soap and water after removing the gloves. Disposable towels should be used to clean kennels and excreta if possible, and materials should be double-bagged for disposal. All materials that have been in contact with the animal during the period of risk should be considered potentially contaminated and appropriate PPE should be worn when these materials are handled.

Dedicated cages, kennels, or stalls in a low-traffic area should be used for animals undergoing treatment with HD. All materials that might come into contact with the patient or bodily fluids should be disposable or easily cleaned. Metal or disposable bowls for food and water and disposable bedding should be used. Cages and runs should be labeled with a laminated, cleanable sign that includes verbiage indicating that the patient has received chemotherapy, the name of the drug administered, the major route of excretion, and the number of days PPE is recommended. Ideally, color-coded disposable collars should be used to identify animals recently treated with chemotherapy drugs.[38]

The patient should be allowed to urinate and defecate outside in a separate, designated, low-traffic area, if possible. Because ultraviolet light is believed to inactivate many drugs,[64,65] an area with sunshine exposure or an area that can be cleaned easily is recommended. Feces can be removed from the area by personnel wearing chemotherapy-rated gloves and disposed of as hazardous waste. Hands should be washed after handling excreta. Urine can be diluted with water from a low-flow hose or watering can.

13 | CLIENT SAFETY

When patients are discharged after chemotherapy administration, or HD are prescribed for clients to administer, written discharge instructions should include information about safe handling of the pet. Clients who are pregnant, attempting to conceive, or lactating should not be tasked with drug administration or cleaning of any patient excreta. Client consultation with their personal physician is recommended before initiating treatment to discuss any potential contact risks. The presence of small children in the home also should prompt a frank conversation about potential exposure to HD. Handling of pets after chemotherapy administration should be with caution; a pet's interaction with children in the home should be supervised, avoiding contact with excreta, and with thorough hand washing afterwards. If inadvertent direct contact with HD or contaminated urine or feces of a patient occurs, the skin should be rinsed with water and washed using dishwashing detergent for a minimum of 5 minutes, in accordance with recommendations for chemical exposure (https://ccohs.ca/oshanswers/chemicals/firstaid.html), and any additional instructions from a personal physician followed.

Chemotherapy-rated gloves should be dispensed with any HD for use by the client when giving medications, and hands should be washed after each administration. The pet's medications should not be stored with medications for humans, near food, or where accessible by children. Child-proof containers are recommended if there are small children in the home. Pills should not be split or crushed, capsules should not be opened, and swallowing of medications by the pet should be confirmed. Compounding of liquid medications should be discouraged, because of the potential for environmental contamination during administration. If a pet commonly spits out a pill after it has been concealed in food or a treat, the medication should be administered alone. Empty vials or syringes should be returned to the clinic for proper disposal.

Animals receiving chemotherapy should remain in a controlled environment and not be allowed to urinate or defecate in community areas, areas where children may be exposed, or areas that cannot be easily cleaned for at least 48 hours after drug administration. Ideally a low-traffic, sunlit area would be preferred for elimination. If excreta are found in the house, the area should be cleaned, and hands should be washed afterwards.

Recommendations for cleaning excreta include wearing gloves, avoiding high-pressure sprays, and using disposable towels. Solid items should be removed with gloved hands and double-bagged with

impermeable disposable bags for household wastes. Liquid wastes should be blotted dry. The area should be cleaned with dilute bleach once gross contamination is removed. Cat litter boxes should be cleaned daily and litter should be double-bagged and discarded with household trash. Any soft items (eg, bedding, towels, toys) should be washed twice, separately from other laundry, after exposure, and ideally bleached.[33,66]

14 | CHALLENGES

Currently, approximately 350 veterinary oncologists are listed on the ACVIM website, not all of whom are actively practicing. They are primarily concentrated in urban, high-population areas or at veterinary teaching hospitals. Many states have only 1 location with an oncologist available, and a few states have no oncologists within their borders. Although other specialists also administer chemotherapy, most are found in similar locations. Primary care veterinary practitioners often are requested by clients to administer chemotherapy to pets, either because of the perceived costs of specialty care or the time commitment and inconvenience in traveling to a specialty center. Suggestions (other than referral to a specialist) for these practitioners are to collaborate with a hospital pharmacy, create a group that can purchase appropriate safety equipment, or contract a company that can provide individual doses of chemotherapy drugs. Providing optimal patient care for our pets with cancer while also providing optimal safety for those people handling HD is a fine balance. The only known safe level of exposure to these drugs is none, and little information is available about increased risk to people who infrequently administer HD. Stricter mandates may limit the number of pets that can receive cancer treatment.

15 | COMMITTEE RECOMMENDATIONS

The committee encourages the formation of a central resource for veterinarians regarding chemotherapy use. Creation of standardized training materials, including slide sets, webinars, suggested documentation of personnel training in practice, and client and staff informational literature would be extremely helpful for practices that use chemotherapy drugs. Studies that evaluate risks in veterinary healthcare workers who handle chemotherapy drugs, especially information about levels of exposure, would help inform recommendations in practice. Further investigation of the risks to clients who own animals receiving chemotherapy also are needed.

CONFLICT OF INTEREST DECLARATION

L. Parshley: Member of Washington state's Hazardous Drug Advisory Committee. B. Phillips: Consulted for Pfizer Animal Health. Educator and key opinion leader for Palladia in 2010 and 2011.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Authors declare no IACUC or other approval was needed.

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How to cite this article: Smith AN, Klahn S, Phillips B, et al. ACVIM small animal consensus statement on safe use of cytotoxic chemotherapeutics in veterinary practice. *J Vet Intern Med*. 2018;32:904–913. https://doi.org/10.1111/jvim.15077