Most chemotherapeutic agents are both toxic and mutagenic. Alkylating agents have been associated with the highest risks to handlers. Organ damage and increased risk of fetal loss have been reported in persons handling and administering chemotherapy with inadequate attention to personal safety. This was first suspected in the 1970’s when chemotherapy drugs had already been in clinical use for 2 decades, and unfortunately (as in many other industries) many healthcare workers were exposed to hazardous substances that led to illness and even deaths among those workers.\(^1\)

In the US, the Occupational Safety and Health Administration (OSHA) investigated chemotherapy preparation practices in the early 1980’s and in1986 published guidelines describing the equipment, garments, and work practices appropriate to protect pharmacists and nurses from exposure to cytotoxic agents.\(^2\)

After the OSHA guidelines were implemented, concern about safety in handling chemotherapy was again reduced; however although the magnitude of risk was certainly greatly reduced by following the guidelines, new studies were published in the 1990’s showing that drug residues on work surfaces were a potential significant source of worker exposure.\(^3\)

One review pointed out that despite the use of precautions cyclophosphamide was present in the urine of health care workers in 11 of 12 studies.\(^4\) The presence of contamination outside of biological safety cabinets demonstrates that their protection is imperfect, and that manipulations such as reconstitution, transfer between containers, spiking and unspiking IV containers, priming IV tubing, and connecting or disconnecting syringes from injection ports cause leakage and contamination. In addition the contamination of the working environment is persistent, and other workers who are not directly involved in handling hazardous substances may be exposed.

**Regulatory Considerations**

Regression guidelines for employers whose workers are handling hazardous drugs including cytotoxic chemotherapeutics have been discussed and determined to some extent around the world, however in large part they are not legally binding. Overall, precautions are similar in any geographic location, but veterinarians are encouraged to check the specific guidelines and regulations for their location to ensure they are in compliance with any relevant regulations.

In the US, the relevant regulatory instruction is to be found in the OSHA Technical Manual, Section VI: Health-Care Facilities, Chapter 2. *Controlling Occupational Exposure to Hazardous Drugs*; which can be found online at: http://www.osha.gov/dts/osta/otm/otm_vi/otm_vi_2.html#5? While the OSHA guidelines are not in themselves law, they can be enforced under the general duty clause in the Code of Federal Regulations (CFR) which requires that employers provide a safe or healthful employment and places of employment, should OSHA be called in investigate a complaint. In addition, the Hazard Communication Standard is a federal regulation that requires employers to inform employees of the risks of all hazardous materials in their workplace; and the Access to Employee Exposure and Medical Records standard requires that employees who work with
toxic substances have access to workplace monitoring records as well as their employee medical records.

Additional extremely useful and more recent – but voluntary - guidelines can be found in NIOSH Publication No. 2004-165: Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings, to be found at: http://www.cdc.gov/niosh/docs/2004-165/.

While other specific requirements may exist, the OSHA and NOSH publications can also provide useful guidance for veterinary practitioners in other countries.

In addition, it is important to ensure that any cytotoxic-contaminated waste is disposed of according to any regulations. In the US, the Environmental Protection Agency (EPA) regulates the management of hazardous wastes, including several chemotherapy drugs according to the Resource Conservation and Recovery Act (RCRA). Two relevant EPA publications are Managing Hazardous Waste: A Guide for Small Businesses [EPA 2001] and RCRA Hazardous Waste Regulations [40 CFR Parts 260–279].

**Developing Safe Chemotherapy Handling Policies in Veterinary Practice**

Precautions should be taken during every phase of chemotherapy preparation, administration and disposal.

**Employers should:**
- Develop policies and procedures for the safe storage, preparation, administration, and disposal of cytotoxic agents.
- Seek input of workers on all policies and procedures that will affect them.
- Provide safety training for employees, including how to recognize and evaluate possible risks.
- Whenever possible, provide a work area that is designated for chemotherapy and is limited to authorized personnel.
- Whenever possible, provide a biological safety cabinet (below).
- Identify the hazardous drugs used in the practice and keep a written inventory up to date.
- Make Material Safety Data Sheets (MSDS) and other relevant information available to employees.
- Provide workers with proper personal protective equipment PPE (can include correct chemotherapy gloves, disposable gowns and sleeve covers, eye and face protection, and NIOSH-certified respirators (surgical masks do not provide adequate respiratory protection)) (these are generally available from chemotherapy drug suppliers), train workers in its use and require workers to do so.
- Prohibit eating, drinking, etc. in areas where cytotoxic agents are handled.
- Develop a spill management procedure.
- Develop a plan for medical surveillance of personnel handling hazardous drugs.
- Develop a policy regarding chemotherapy handling during pregnancy, conception, and breastfeeding. The Oncology Nursing Society recommends that “employers provide alternate duty to employees who request other assignments due to pregnancy, the desire to conceive, or breast-feeding”.
- Provide syringes and IV sets with Luer-Lok fittings for preparing and administering chemotherapy.
- Consider using closed-system drug transfer devices and needleless systems (below).
- Monitor compliance with safety procedures.

**Workers should:**
- Participate in training before taking on chemotherapy duties.
- Review guidelines and other documents for more information when needed.
- Consistently use personal protective equipment and follow recommended procedures.
- Wash hands after chemotherapy-related duties.
- Disposing of any contaminated waste in designated containers.
- Clean up any spills according to set procedures (above).
- Report and follow up on any accidental exposures.
**Safe Chemotherapy Handling**

There are 3 basic systems for safe chemotherapy handling:

The traditional gold standard is to use a vertical laminar flow biological safety cabinet (BSC) (or “hood”) for drug preparation. A BSC has vertical airflow that moves away from the worker, as opposed to horizontal airflow that moves away from the product toward the worker (which is used in cabinets designed to keep the contents of the cabinet sterile). However, as noted above, BSCs provide imperfect protection and should not be relied on solely. “Chemo-pins” (or the PhaSeal system) (both below) are used for preparing injectable chemotherapeutics in the hood. Both can be used as a multi-dispensing pin. Further, a disposable gown with closed-cuff sleeves and chemotherapy gloves should be worn.

A newer approach that appears to offer equivalent (if not better) safety and better convenience is to use a closed system drug transfer device, as suggested by the NIOSH guidelines published in 2004, discussed above. Several commercial systems are now on the market but the best developed and documented is the PhaSeal system, a component-based closed system drug transfer device that mechanically prohibits the escape of drug aerosols. Although a hood is not necessary, gloves should be worn. The components are relatively costly compared to regular syringes and needles, but much less costly than installing a hood. A major safety advantage over using a hood with traditional needles and syringes is that it provides protection during administration as well as preparation. As well as being safer, this also allows most clients (unless pregnant, see below) to remain with their pets during chemotherapy administration, which usually greatly reduces anxieties!

A third alternative is to prepare and administer drugs in a quiet, low traffic area using protective eyewear, a respirator mask, a disposable gown with closed-cuff sleeves and gloves during both preparation and administration. Further, when preparing injectable chemotherapeutics, it is preferable to use “Chemo Dispensing Pin” hydrophobic filters that insert into drug vials and prevent aerosolisation. If a filter is not used, alcohol moistened gauze should be wrapped around the vial top and needle when the needle is withdrawn. This option is only appropriate in situations where chemotherapy is being handled very infrequently.

**Further chemotherapy safety procedures include:**

- Whenever chemotherapy is to be administered, have ready a “SPILL KIT” containing personal protective equipment, disposable gown, over-shoes, chemotherapy gloves, protective eyewear, NIOSH-approved respirator; disposable absorbent material cleaner such as strong alkaline detergent, disposable mop head, approved container for cytotoxic waste and sharps, possibly a disposable brush and shovel should be available in case a glass container is broken, and potentially spill pillows for larger spills.
- Gloves should be powder free, nitrile or heavy latex (not vinyl), not exam or surgical gloves. If exam or surgical gloves must be used, they should be double-gloved.
- Gowns should be disposable, low-permeability, with closed front and cuffs, intended for single use.
- A plastic-backed absorbent disposable pad should always be used (“incontinence pads” are suitable).
- Luer lock syringes should always be used.
- Chemotherapy vials and syringes should be stored and carried in zipper-lock plastic bags.
- For drugs that are kept refrigerated, a designated small refrigerator is preferred; they at least MUST be kept in a separate refrigerator from that used to store food.
- Pills should never be split or broken.
- Chemotherapy waste (e.g. used syringes, gloves, empty bottles) should be managed separately from the main waste stream. Most hospital waste collectors can provide suitable containers.
- For practice staff handling body fluids (e.g. cleaning cages) from chemotherapy patients, routine protection should be taken against contact with excreta. Cages and runs must never be pressure-hosed.
**Premixed chemotherapy drugs**

Some veterinarians find it convenient to order custom-prepared individual chemotherapy doses; which can be ordered with PhaSeal components attached. This is more costly compared to purchasing multi-dose vials, but for practices that use chemotherapy infrequently it is more cost effective by saving on inventory, drug wastage and equipment costs. One disadvantage is that if chemotherapy administration is delayed the drug dose may not be able to be stored in the syringe, so is wasted.

**Oral medications**

Most chemotherapy safety guidelines focus on injectable medications, and guidelines for handling orally administered chemotherapeutics safely are sparse. For oral chemotherapy in smaller patients, it is often necessary to have drugs reformulated into smaller size capsules. This must only be done by a compounding pharmacist equipped for handling cytotoxic medications and must never be done in the veterinary practice.

**Pregnancy and Chemotherapy**

In the author’s opinion, despite all safety measures, veterinary staff who are, or are trying to become, pregnant or are breastfeeding, should not assist in chemotherapy preparation or administration, or clean cages of chemotherapy patients.

Pregnant pet owners should consult their obstetricians regarding whether they should have their pet undergo chemotherapy and how to manage aftercare. A general recommendation is that pregnant clients not be in the room during drug preparation and administration, and that aftercare be performed by another member of the family; however social contact such as petting is safe.

**Chemotherapy Safety At Home**

The main chemotherapy safety effort should be directed at the level of preparing and administering drugs, where higher levels of exposure to the drug occur, and often involve the same people repeatedly. However it is important to remember that clients will be taking chemotherapy drugs home - if not in bottles, then at least in their pets’ bodies – and will require instructions on safe handling.

If oral chemotherapy is dispensed for administration at home, medications should be placed in medication bottles (not paper envelopes or plastic bags) marked “CYTOTOXIC” and chemotherapy gloves should be provided.

Usually there is no significant risk to the owner of a pet receiving chemotherapy when routine hygiene is used. However, it is important to be aware of basic considerations involved. The two times pet owners need to take precautions are when administering medications, or when handling bodily wastes.

Many veterinary clients (and practice staff) are very concerned about handling excreta of chemotherapy patients. While it is appropriate to employ safety precautions, normal hygiene is largely adequate. Simply avoiding direct contact with urine and feces prevents the majority of exposure and most pet owners do this anyway. Weather conditions and contact with soil inactivate most active substances (remember how carefully most chemotherapy drugs must be stored to maintain potency) so pets should eliminate in an area where urine will drain into the soil. If solid wastes need to be picked up, gloves or an inside-out plastic bag should be worn and they should be put in a plastic bag and disposed of in the trash. If bedding is soiled it is preferable to dispose of than launder it if possible. The concentration of active substances in excreta is usually low so a single accidental exposure followed by washing should not be cause for panic. These precautions should be followed for approximately 48 to 72 hours following administration. However, specific guidelines for handling excreta are not well defined for most drugs in animals, so it is best to err on the conservative side. Recent reports showed that low levels of drug residues of some chemotherapeutics were detectable in the urine of dogs for days and in some cases weeks after therapy. For pets receiving frequent chemotherapy.
treatment (for example, on metronomic chemotherapy), the timing guidelines obviously need to be adjusted to the individual situation.

References
Table 1. An example of the type of instructions that should be given to pet owners following chemotherapy.

Most drugs (including chemotherapy) are excreted to some extent in the urine or feces as the actual drug, or metabolites which may be active, for approximately 24 to 48 hours. In particular, the platinum drugs (carboplatin and cisplatin) are highly excreted in the urine for about 48 hours after administration. So as a general rule, direct contact with these body fluids should be avoided for about 3 days to be on the safe side. Most people do this anyway. Here are some procedures for managing body wastes after chemotherapy:

- Any time you need to handle bodily wastes, wear latex gloves, “peel” the gloves off afterwards so they come off inside out and dispose of in the trash, and wash your hands.
- For cats that use a litter pan, consider using clumping litter. Wear latex gloves when scooping and wash your hands afterwards, peel the gloves off afterwards and dispose of in the rubbish, and wash your hands. Place waste in a plastic bag for disposal.
- If other cats in the household can be encouraged to use a different litter pan that is ideal, but if not possible then the next best arrangement is to keep the pan scooped as frequently as possible so the other cats are not continually getting the patients’ wastes on their feet and then grooming afterwards.
- If your pet relieves him / herself outdoors, try to have them do it in a quiet area, on soil where urine will drain away quickly, and drug and metabolites will be inactivated by sun and rain.
- If you need to pick up solid waste, you should wear latex gloves; put the waste in a plastic bag, and dispose of in the trash.
- At home, wastes can be put either in a plastic bag in the trash, or place in the toilet, close the lid, and double flush.
- If you need to clean up an “accident” in the home, wear gloves and use disposable absorbent materials like paper towels (or old towels that you don’t mind throwing away) and put them in a plastic bag in the trash. Bleach is the most effective cleaner for chemotherapy drugs but if that is not an option on the surface, other soaps or cleaners can also be effective.
- Any soiled bedclothes should be discarded rather than washed if possible.
- Other animals should not be allowed to consume the patient’s wastes (sorry, but it happens).
- Finally, if you, a family member, or another pet accidentally contacts body wastes; don’t panic, just wash it off with soap and plenty of water. Even with the drugs that are excreted in the highest concentration, it is over about 48 hours, so the amount in any single urination will be a fraction of the dose your pet received, and the amount that actually gets on your skin is a small fraction of that; and only a very small percentage could possibly penetrate the skin.

If you have chemotherapy tablets or capsules to give to your pet at home:

- Remember to keep bottles and waste well out of reach of children.
- Always wear latex gloves when handling these medications. Your veterinarian can provide these.
- The medications should not be handled in the kitchen; it should be done in another room such as a laundry room or bathroom (away from the toothbrushes). If medications need to be refrigerated, only place the tightly closed bottle in the fridge, and carry the bottle to another room before opening.
- Pills should not be split or broken, and capsules should not be opened.
- If you need to place the medications directly on a surface, use something disposable such a paper towel or piece of kitchen foil, and then dispose of it afterwards.
- Afterwards, “peel” your gloves off so they come off inside out, dispose in the trash, and wash your hands.

In addition to the procedures listed above, women who are or may be pregnant should:

- not be present in the room when chemotherapy is being administered
- never handle any chemotherapy medications that are dispensed to be given at home
- **never** handle the urine or faeces of a pet that has received chemotherapy within the past 3 days – these jobs should be delegated to another family member.

Very young children should also not be present when chemotherapy is being administered. There are no clear guidelines on whether it is safe for older children to be present when chemotherapy is being given to a pet, and this decision should be left to the judgment of the veterinarian and the parent.

These procedures may seem very detailed, but this is only because many people caring for pets receiving chemotherapy have lots of questions about safety. We want to be sure that all your concerns are addressed and prepare you for any eventuality. You’ll soon see that the times you need to be careful are really quite limited; most of the things you need to do are more or less the same basic hygiene that you normally use; and the additional things you need to do will become a simple routine.