Cytotoxic Drugs Guide

2021

Saskatchewan

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Introduction

Cytotoxic drugs include any drug that inhibits or prevents the function of cells. Cytotoxic drugs include drugs used to treat cancer and other medical conditions such as arthritis or autoimmune disorders (e.g., psoriasis). This guide explains the duty of an employer in a health care facility to protect workers who are likely to be exposed to cytotoxic drugs. Such worker exposure may occur at health care facilities such as:

- hospitals;
- special care and personal care homes;
- cancer and other medical clinics;
- in home care situations; and
- veterinary clinics and animal hospitals.

Reasons for concern

There is a potential for cytotoxic drugs to harm workers who are likely to be exposed to them. This includes workers who prepare, administer, or handle the drugs, waste products, contaminated surfaces or materials. The concern is based on:

- toxic side effects seen in patients treated with these drugs;
- evidence that these drugs can produce chromosome changes, cancer and reproductive abnormalities in animal experiments; and
- adverse effects in workers exposed to them.

Sources of exposure

Worker exposure occurs by inhalation of drug dust or aerosol, absorption through the skin, injection by accidental skin puncture and ingestion through contact with contaminated food, drink, or cigarettes. Exposure may occur through activities like:

- counting, crushing or breaking powdered tablets;
- mixing cytotoxic drugs into intravenous fluids;
- preparing or administering cytotoxic drugs. (e.g., while breaking open ampules, withdrawing needles from drug vials, transferring drugs with syringes or expelling air from a drug- filled syringe);
- handling any material that has been in contact with cytotoxic drugs like needles, syringes, IV bags, tubing, incontinence products, soiled linens, used personal protective equipment, drug packaging and waste, or;
- cleaning areas where cytotoxic drugs are used.

Responsibilities for controlling exposure

Section 31-5 of *The Occupational Health and Safety Regulations, 2020*, requires employers in health care facilities to take all practicable steps to minimize worker exposure to cytotoxic drugs or materials, or equipment contaminated with cytotoxic drugs.[1] Where workers are required to prepare, administer, handle, or use cytotoxic drugs or are likely to be exposed to them, the employer must prepare and implement a **written program**. The program includes written procedures and other precautions to ensure the health and safety of workers. The employer must train workers on the content of the program and its procedures when implementing the program.

Where workers prepare parenteral cytotoxic drugs on a **frequent and continuing** basis, the employer must provide and maintain an **approved** biological safety cabinet (BSC) and ensure it is used safely. The regulations also place duties on workers to co-operate with the employer and use the safe work procedures and protective equipment referred to in the written program.

Guidelines for controlling exposures

The following guidelines explain the employer's duties under section 31-5of the Regulations and are intended to assist the employer in developing the written program. The program is especially important because there are no established contamination limits for cytotoxic drugs. The goal of the written program is to keep exposures as low as reasonably achievable (ALARA) given the potential for severe health hazards associated with cytotoxic drugs.

The written program

The employer is required to consult with the occupational health committee when developing the written program. The program must include:

1. A list of all cytotoxic drugs that are used on site.
2. Identify workers that are at risk for exposure to cytotoxic drugs based on the work activities completed.
3. An explanation of how cytotoxic drugs, supplies and equipment contaminated with cytotoxic drugs will be:
   a) identified;
   b) stored;
   c) prepared, transported, administered, handled and used (including the means to minimize the risk of aerosolization);
   d) maintained (supplies and equipment); and
   e) discarded – this section must identify means to:
      - contain and label cytotoxic drug wastes;
      - describe how the wastes will be transported per the *Transportation of Dangerous Goods Regulations*; and

[1]"**Practicable**" means possible given current knowledge, technology and invention.

- identify the collection or disposal site, which must be approved by Saskatchewan's Ministry of Environment.

4. Emergency procedures to use:
   a) when a cytotoxic drug spills or leaks, (e.g., from a damaged package); or
   b) when a worker is exposed to cytotoxic drugs as a result of:
      - a skin puncture;
      - contact with intact skin;
      - contact with the eye;
      - accidental inhalation of drug dust or aerosol; or
      - swallowing a substance contaminated with a cytotoxic drug.
5. An explanation of how to maintain or dispose of equipment that becomes contaminated with cytotoxic drugs.
6. The use of:
   a) engineering controls (e.g., general or local exhaust ventilation);
   b) work practices;
   c) hygiene practices (e.g., personal hygiene standards). These standards should include a ban on eating, drinking, smoking, applying cosmetics or storing food in or near the preparation area;
   d) hygiene facilities (e.g., personal wash facilities);
   e) approved respiratory protective devices, approved eye or face protectors and other appropriate personal protective equipment; and
   f) decontamination materials and equipment that are appropriate in the circumstances.
7. The use of an approved BSC for preparing cytotoxic drugs and methods of maintaining the cabinet.

Once prepared, the program must be implemented. Workers must be trained on the program and a written copy of the program must be made readily available to workers. The program must be reviewed annually and revised as needed.

The following sections describe protective measures to minimize workers' exposure.

Receiving, Storage and Transport

All workers who receive deliveries of cytotoxic drugs should be trained on how to properly handle them. The integrity of the external package should be inspected upon receipt. If packaging is broken or damaged and likely to cause a leak or spill, the spill protocol developed as part of the emergency procedures must be initiated. Delivery containers should be taken immediately to the pharmacy department or other dedicated storage area. Since packaging can have high levels of contamination, there should be an unpacking area in the pharmacy to limit exposure risks. Workers should wear a protective gown and two pairs of gloves to unpack cytotoxic drugs. A receptacle for cytotoxic waste must be available in the unpacking area for the disposal of secondary packaging. Once unpackaged, all drug

containers should be cleaned to reduce external contamination. It is important to ensure that the cleaning process does not damage the container or make it difficult to read the label.

Areas where cytotoxic drugs are stored should be separated from regular storage and clearly marked. Engineering controls (e.g., locks, limited access card systems) should be in place to prevent unauthorized workers from entering the storage area. The list of the cytotoxic drugs on site should be kept in the room, along with instructions for cleaning spills. Where possible, other drugs should not be stored with cytotoxic drugs. Clear warning labels should be used to identify the cytotoxic drugs. The shelves should also be fitted with a lip or back slope that prevents the drugs from falling to the floor.

When a damaged container is found, it must only be handled by trained workers wearing appropriate personal protective equipment. Broken containers and contaminated packing materials must all be placed in the appropriate labeled puncture proof container and disposed of as cytotoxic biological waste.

Any transport of cytotoxic drugs must be done in containers designed to contain leakage and spills. The containers must be clearly labeled as containing hazardous drugs.

Preparation of parenteral cytotoxic drugs

Before preparing the written program, determine whether the facility will be equipped to prepare parenteral cytotoxic drugs.

The employer must make a determination of whether the health care facility will prepare parenteral cytotoxic drugs on a **frequent and continuing** basis. To make this determination, the employer needs to examine the present situation at the facility. Consider the size of the population being served the size of the facility, how frequently parenteral cytotoxic drugs have been prepared in the past and the location of the nearest facility with an approved BSC. The employer should also consider any intended changes to the current situation. For example, are there going to be changes in the size of the population being served or other reasons that might increase the frequency of cytotoxic (parenteral) drug preparations?

An **approved BSC** must be provided to workers when it is determined that parenteral cytotoxic drugs will be prepared on a frequent and continuing basis in the facility. If it is determined that parenteral cytotoxic drugs will not be prepared on a regular basis in the facility, the employer must make this intention clear to the occupational health committee and the workers and should also explain the alternate arrangements to clients.

An alternative arrangement may be made with another facility. These drugs could be prepared at a nearby facility that has an approved BSC and then transported to the facility where the drugs will be administered to patients. Alternately, the patient may travel to another nearby health care facility that is suitably equipped to prepare parenteral cytotoxic drugs.

Parenteral cytotoxic drugs may be prepared on an occasional or interim basis at a health care facility that does not have an approved BSC, where:

- exceptional circumstances arise;
- alternative arrangements prove impractical to use; or
- the employer has planned for, but not yet received, the BSC.

In such cases, the employer must determine what arrangements can be made in the facility to minimize worker exposure to parenteral cytotoxic drugs being prepared. The arrangement must include measures to protect the worker preparing the drug as well as other workers in the vicinity. The arrangement must also prevent the spread of drug contamination from the immediate vicinity of the preparation area.

Approved Biological Safety Cabinets (BSCs)

Class II BSC: B1, B2, or B3; and Class III BSC that meet the current standard of NSF/ANSI 49-2019 (See the *Resources* section) are **approved** for the purposes of preparing parenteral cytotoxic drugs. (More information can be found in the Centres for Disease Control and Prevention (CDC) publication *Biosafety in Microbiological and Biomedical Laboratories (BMBL) 6th Edition*, which can be downloaded at no charge from the CDC. Relevant information from that publication can also be found in Appendix 2 of this guide.)

Class II Type A BSCs exhaust HEPA-filtered cabinet air into the workroom. They are also approved if:

A. they are used with a canopy or thimble hood that captures air released from the BSC and exhausts the air out of the building; or

B. there are means to ensure that the HEPA filter is functioning effectively before each use (e.g., by reading a properly installed pressure differential gauge) and the exterior surface of the HEPA filter is protected from damage.

Option A is the recommended approach.

Preference should be given to Type B-BSCs, which do not exhaust any cabinet air into the workroom.

See the *Resources* section for more information on BSC.

Using and maintaining the Biological Safety Cabinet

The BSC must be inspected and certified by a competent person at least annually and when the cabinet is moved. The BSC must be cleaned, maintained, and used according to the manufacturer's recommendations.

The exhaust blower on the BSC should be operated continuously — even when the BSC is not in use. The cabinet should be cleaned daily with 70 percent alcohol and decontaminated weekly or whenever spills occur. Decontamination should consist of surface cleaning with an alkaline detergent followed by thorough rinsing. Personal protective equipment as described later in this document should be used while decontaminating the cabinet. The ductwork attached to the cabinet should be labelled to reflect its hazardous content.

If a risk assessment determines that a BSC is not required, designate a centralized area for

the preparation of cytotoxic drugs. The area should be a work area that is quiet, uncluttered, and well ventilated. The ventilation system, fans or air conditioning unit should not blow air directly at the preparation area. The area should be clearly posted with a sign identifying it as a cytotoxic drug preparation area.

Respiratory protection

Approved respiratory protection must be provided by the employer and worn by workers who may be exposed to cytotoxic drug dusts or aerosols. This type of exposure may occur when workers:

- prepare cytotoxic drugs on a counter or some other place that is outside of an approved BSC;
- clean up spilled cytotoxic drugs; or
- decontaminate a BSC that has the sash raised.

Approved respiratory devices

Approved respiratory protective devices include a reusable facemask with filter cartridges, or a disposable filter mask. The filter cartridges or the filter mask must provide high efficiency particulate air (HEPA) filtration and carry the National Institute for Occupational Safety and Health (NIOSH) label with either the N100, P100, or R100 rating.

These respirators are available from most safety equipment suppliers. Surgical masks are neither suitable nor adequate to protect the worker.

Use and maintenance of respirators

Workers must be trained to use their respirator properly. Training should include how to ensure a proper fit and how to prevent the contamination of the inner surface of the respirator. Workers must also be fit tested to ensure the respirator is the right size and will provide effective protection. Employers must ensure that workers can make an effective seal to their facial skin (e.g., clean shaven) during every use. Reusable facemasks must be cleaned and inspected after each day's use. The cartridge must be replaced according to manufacturer's recommendations. When not in use, respirators be stored in a dust-proof, sanitary location.

Other personal protective equipment

Personal protective equipment must be provided for and used by workers preparing or administering the drugs. The equipment must include well-fitted disposable gloves, an appropriate protective gown, shoe covers, face and eye protection. Workers must also be trained in the proper donning and doffing of protective equipment to ensure that they do not contaminate their skin, clothing or the work environment.

If an accidental spill or splash occurs, contaminated clothing and personal protective equipment should be removed immediately. Contaminated skin or eyes should be flushed immediately with copious amounts of running water to effectively cleanse the area. Specific emergency response information can be found on the safety data sheet for the drug(s) being used.

Gloves

The gloves used to handle cytotoxic drugs should meet with ASTM standard D-6978-05 (2019) *Standard Practice for Assessment of Resistance of Medical Gloves to Permeation by Chemotherapy Drugs* and be powder free. Nitrile, polyurethane or neoprene gloves are recommended. Vinyl gloves should not be used. Latex gloves are not recommended as they are known to cause latex allergies in workers. It is recommended that workers wear two pairs of gloves for additional protection. The first pair of gloves should be put on prior to donning the gown. The second pair should fit over the cuff of the protective gown. Hands must be washed both before and after gloving.

Gloves should be changed frequently (approximately every hour). They must be removed and changed immediately if they are punctured, cut, torn or visibly contaminated with a cytotoxic drug. Great care should be taken in the removal of gloves to prevent the contamination of the skin. Double gloving is recommended for cleaning up spills. Potentially contaminated gloves must not be worn outside of the work area.

Protective gown and shoe covers

Gowns used for handling cytotoxic drugs should:

- be disposable;
- be made of lint free and low-permeability fabric;
- have long sleeves with tight fitting cuffs; and
- fasten in the back.

Gowns must be changed in the event of contamination, spillage, or rips, as well as at the end of the procedure. Avoid touching the outside of the gown when removing it to prevent contamination of the hands. Potentially contaminated gowns must not be worn outside of the work area.

Disposable shoe covers should be worn to prevent contamination of the workers' shoes. They should be worn in the sterile preparation room or in the event of a spill. Shoe covers must be removed immediately when leaving the sterile preparation room to avoid contamination of other areas.

Face and eye protection

Eye protection, such as a face shield or splash goggles, must be made available for use in any situation where there is a risk of splashes, sprays, or aerosols onto the face or into the eyes. Face or eye protection must also be used when cleaning up spills. A risk assessment by a competent person is required to determine the level of protection required to ensure adequate worker safety.

Supplies and equipment for drug preparation, administration, waste disposal and spills

Preparing Cytotoxic Drugs

Standard operating procedures for parenteral preparations should be documented and emphasize the need to:

- contain excess drug solutions and air when priming;
- use techniques that avoid the generation of pressure differentials; and
- avoid using cytotoxic drugs supplied in glass ampoules. If glass ampoules must be used, open with an ampoule breaker or a low-linting swab.

Tablets, capsules and topical creams should be prepared under the same conditions as parenteral cytotoxic drug preparations.

Specific additional standard operating procedures for non-parenteral preparations include:

- using purpose-dedicated equipment;
- making mixtures by dispersing tablets in water;
- not crushing tablets in an open mortar;
- not counting tablets or capsules by machine; and
- cleaning equipment immediately after use.

Specific handling techniques and procedures incorporating suitable equipment (designed to reduce the risk of exposure) should be used and include:

1. Drug preparation equipment

Equipment used for preparing drugs should incorporate a closed system where possible, and reduce the potential for generating high pressure.

Note: Closed systems are not an acceptable substitute for appropriate ventilation or engineering controls (e.g., class II or III biological safety cabinets) used along with personal protective equipment. Specific methods of control may include:

- use of Luer-lock syringes and fittings to keep connections together;
- use of Luer-slip syringes (only if Luer-lock connections are incompatible) such as intrathecal needles;
- use of syringe-to-syringe connectors when transferring solutions from one syringe to another;
- use of wide bore needles to reconstitute and draw-up cytotoxic drugs;
- use of filter needles only when the cytotoxic drug has been removed from a glass ampoule, or if particulate matter is visible, for example if coring of a vial rubber has occurred; and
- use of air-venting devices to equalize pressures and to prevent the passage of powder, aerosols and liquids.

2. Waste disposal

Plastic bags that are 2 mm thick (if polypropylene) or 4 mm thick (if polyethylene) should be used to collect potentially contaminated materials. The outer container or bag must be colour coded and labeled with a cytotoxic warning label. All sharps should be placed in puncture-proof containers. All workplaces where cytotoxic drugs may be present should have a policy for segregating waste materials resulting from cytotoxic drug preparation and administration.

Housekeeping staff should be trained on how to safely handle waste materials and wear protective gloves while handling waste containers. Cytotoxic waste must be handled differently than regular garbage and must be disposed of according to provincial regulations at facilities approved for cytotoxic waste disposal.

3. Spill kits

A spill management kit should be available in all areas where cytotoxic drugs are stored, transported, handled and administered. All staff should know where the kit is located and the names of individuals who are trained to clean a spill. Spills must be cleaned by workers who have received appropriate training and have appropriate protective equipment. Others should vacate the area as soon as it is safe to do so and should not return until the spill is cleaned. They should remove any clothing or personal protective equipment that may be contaminated. All spills should be marked with a warning sign to prevent exposure to others. Glass must never be handled by hand, only with a scoop.

The spill kit should contain the following items:

- procedure for spill clean-up;
- protective disposable gowns (preferably lint free, low permeability fabric), hair and shoe covers;
- goggles/face shield;
- at least two pairs of chemotherapy gloves or thick quality disposable gloves such as nitrile or neoprene;
- approved respirator (when there is risk of inhaling drug aerosols);
- absorbent backed sheets or spill pads;
- decontaminating agent;
- puncture-resistant container labeled for cytotoxic waste;
- scoop;
- warning signs;
- any additional items identified by a risk assessment of the facility; and
- incident report forms.

Work procedures

Written safe work procedures or specific instructions are a part of the written plan. They should be formulated or otherwise adapted from existing written/published procedures. The employer must implement and train workers on the procedures and make them available to all personnel involved in the mixing and/or administration of the drugs. There are several written/published procedures available such as the U.S. Occupational Health and Safety Administration Guidelines, Center for Disease Control and Prevention and The National Institute of Health, etc. One or more of these documents should be obtained and adapted to the workplace (See the *Resources* section).

Training

The employer must ensure workers are:

- informed of the hazards of cytotoxic drugs and risks of exposure;
- instructed on proper precautions;
- trained on safe work procedures; and
- supervised to make sure they follow safe work procedures.

Pre-job training must be given to all personnel involved in the mixing and/or administration of cytotoxic drugs.

The training must include housekeeping, laundry, and janitorial staff. They must receive training on the potential hazards of handling laundry, excreta, etc., contaminated with cytotoxic drugs, and safe work procedures when handling these materials.

The training should be continually assessed and reinforced.[2] The written program must address how training will be developed, delivered and evaluated.

Additional protection for pregnant workers

A pregnant worker who may be exposed to hazardous amounts of cytotoxic drugs may notify the employer that they are pregnant. In this situation, the employer must minimize this worker's exposure (section 21-7of the Regulations), or, on the worker's request, the employer must transfer a pregnant worker to duties that do not involve handling cytotoxic drugs, where such duties are available.

A policy covering any personnel who are actively trying to conceive a child and breast-feeding workers should also be established.

[2] "**Train**" means to give information and explanation to a worker with respect to a particular subject-matter and require a practical demonstration that the worker has acquired knowledge or skill related to the subject-matter.

Resources

CAREX Canada

CAUT Cytotoxic Drugs Health and Safety Fact Sheet

Occupational Health and Safety Administration, (2016, August 1). Controlling Occupational Exposure to Hazardous Drugs.

Primary Containment for Biohazards: Selection, Installation and Use of Biological Safety Cabinets. Center for Disease Control and Prevention and The National Institute of Health. PHONE: (404) 639-3311.

Safe Handling of Cytotoxic Drugs in Home Chemotherapy. Seminars in Oncology Nursing (502), Suppl. 1, 1989, pp 15-20.

Safe handling of Hazardous Drugs in Healthcare

Safe Handling of Parental Cytotoxics: Recommendations for Ontario. American Society of Clinical Oncology. September 2009.

NSF/ANSI 49-2019 Biosafety Cabinetry: Design, Construction, Performance, and Field Certification Informative Annex 1 (formerly Annex E)

Appendix 1: Antineoplastic drugs classified by the International Agency for Research on Cancer (IARC)

Antineoplastic or anti-cancer drugs are used to treat cancer. Most antineoplastic drugs are also cytotoxic.

The following is a list of antineoplastic drugs that have been classified by the International Agency for Research on Cancer (IARC) as known, probable, or possible **cancer-causing agents**.

It is not a complete listing of all carcinogenic antineoplastic drugs, since not all antineoplastic drugs have been reviewed and classified by IARC.

Some of the following antineoplastic drugs that are classified as potentially carcinogenic are not cytotoxic. Despite this, the precautions outlined in this guide and guides on antineoplastic drugs should be used.

Group 1 – Drugs which are carcinogenic (sufficient human evidence of carcinogenesis)[3]

- Arsenic trioxide
- Azathioprine (Imuran)
- Busulfan (Myleran)
- Methoxsalen, plus UV radiation (Oxsoralen, Oxsoralen-Ultra, UltraMOP)
- Chlorambucil (Leukeran)
- Cyclophosphamide (Cytoxan, Procytox)
- Etoposide
- Melphalan (Alkeran)
- Thiotepa
- Tamoxifen citrate (Apo-Tamox, Gen-Tamoxifen, Nolvadex, Nolvadex-D, Novo-Tamoxifen, Tamofen, Tamone)
- Diethylstilbestrol sodium diphosphate (Honvol)

Group 2A – Drugs which are probably carcinogenic to humans (generally, limited human evidence, but sufficient animal evidence)[4]

- Adriamycin
- Azacitidine
- Certain combined chemotherapy for lymphomas: (e.g., procarbazine, vincristine, prednisone and nitrogen mustard)
- Bischloroethyl nitrosourea or carmustine (BiCNU)
- Carmustine
- 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea or lomustine (CeeNU)

[3] Source: IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Supplement 7, 2000.

[4] Source: IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Supplement 7, 2000.

- Cisplatin (Platinol)
- Doxorubicin (Adriamycin)
- Lomustine
- Nitrogen mustard (Mustargen)
- Procarbazine (Natulan)
- Teniposide

Group 2B – Drugs which are possibly carcinogenic to humans (generally, limited human evidence, but absence of animal evidence)[5]

- Amsacrine
- Bleomycin sulfate (Blenoxane)
- Dacarbazine (DTIC)
- Daunomycin
- Mitomycin (Mutamycin)
- Mitoxantrone
- Streptozocin (Zanosar)
- Daunorubicin (Cerubidine)
- Medroxyprogesterone acetate (Alti-MPA, Depo-Provera, Provera) – cancer, hormone

Drugs with evidence of carcinogenicity which, at present, are not used clinically in Canada

- Chlornaphazine (Group 1)
- 1-(2-chloroethyl)-3-(4-methylcyclohexyl)-l-nitrosourea or Methyl-CCNU (Group 1)
- Treosulphan (Group 1)
- Aminouracil mustard or Uracil mustard (Group 2B)
- Nitrogen mustard, n-oxide (Group 2B)
- Azacitidine (Group 2A)
- Chlorozotocin (Group 2A)
- Trichlormethine (Group 2B)

[5] IBID.

Appendix 2: Class II and Class III Biological Safety Cabinets

This information was developed by The Centers for Disease Control and Prevention (CDC), The full publication *Biosafety in Microbiological and Biomedical Laboratories (BMBL), 6th Edition* is available as a free download from the CDC website.

This information is provided for educational and illustration purposes only.

The Class II BSC

The Class II (Types A1, A2, B1, B2, and C1) BSCs provide personnel, environmental, and product protection. Airflow is drawn into the front grille of the cabinet, providing personnel protection. In addition, the downward flow of HEPA-filtered air provides product protection by minimizing the chance of cross-contamination across the work surface of the cabinet. Because cabinet exhaust air is passed through a certified HEPA filter, it is particulate-free (environmental protection), and may be recirculated to the laboratory (Type A1, A2, and C1 BSCs) or discharged from the building through a canopy (formerly thimble) connected to the building exhaust.

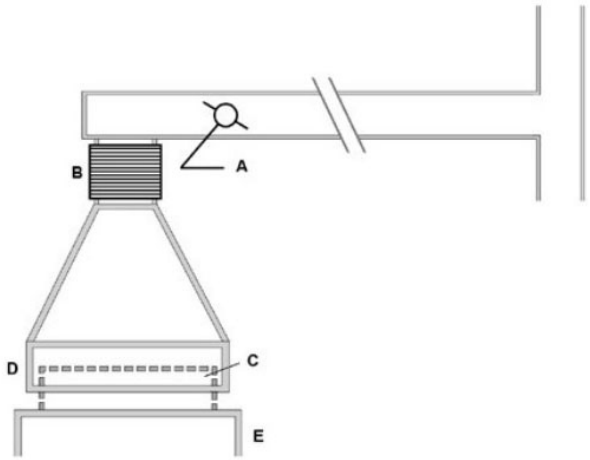
It is possible to exhaust the air from a Type A1, A2, or C1 cabinet outside of the building. When using volatile toxic chemicals, removal of the exhaust from the laboratory is required. However, it must be done in a manner that does not alter the balance of the cabinet exhaust system, thereby disturbing the internal cabinet airflow. The proper method of connecting a Type A1, A2, or C1 cabinet to the building exhaust system is through use of a canopy connection, which provides a small opening or air gap (usually one inch) around the cabinet exhaust filter housing (Figure 4). The airflow of the building exhaust must be sufficient to maintain the flow of room air into the gap between the canopy unit and the filter housing. The canopy must be removable or be designed to allow for operational testing of the cabinet and must have an alarm to indicate insufficient airflow through the canopy. Class II, Type A1 or A2 cabinets should never be direct-connected to the building exhaust system. Fluctuations in air volume and pressure that are common to all building exhaust systems can make it difficult to match the airflow requirements of the cabinet.

Type B cabinets must be direct-connected, preferably to a dedicated, independent exhaust system. Fans for laboratory exhaust systems should be located at the terminal end of the ductwork to avoid pressurizing the exhaust ducts. A failure in the building exhaust system may not be apparent to the user, as the supply blowers in the cabinet will continue to operate. A pressure-independent monitor and alarm must be installed to provide a warning and shut off the BSC supply fan, should a failure in exhaust airflow occur. Since this feature is not supplied by all cabinet manufacturers, it is prudent to install a sensor such as a flow monitor and alarm in the exhaust system as necessary. To maintain critical operations, laboratories using Type B BSCs should connect the exhaust blower to the emergency power supply.

HEPA filters are effective at trapping particulates, and thus infectious agents, but do not capture volatile chemicals or gases. Only canopy-connected Type A1, A2, and C1 or Types B1 and B2 BSCs should be used when working with volatile, toxic chemicals, but amounts must be limited.

Figure 4. Canopy (thimble) unit for ducting a Class II, Type A BSC

(A) balancing damper; (B) flexible connector to exhaust system; (C) cabinet exhaust HEPA filter housing; (D) canopy unit; (E) BSC. Note: There is a gap between the canopy unit (D) and the exhaust filter housing (C), through which room air is exhausted.



The mechanical design and air balance testing of the laboratory exhaust system for Class IIB BSCs must use Concurrent Balance Values (CBV) as published in the NSF/ANSI 49 Standard—a standard that describes the requirements for the construction and function of a Class II BSC. When a BSC is certified to NSF/ ANSI 49-2018, the standard method is to set the inflow velocities using a direct inflow measurement (DIM) hood. When the HVAC system air balance is set, it is typically done based on duct traverse air measurements taken at some point in the ductwork. The two groups are attempting to measure and set the BSC inflows, but each is using a different type of instrument and taking airflow measurements at different locations. There can be a difference in air volume measurements between the two. The CBV provides each discipline the information they require to properly test or certify the BSC.

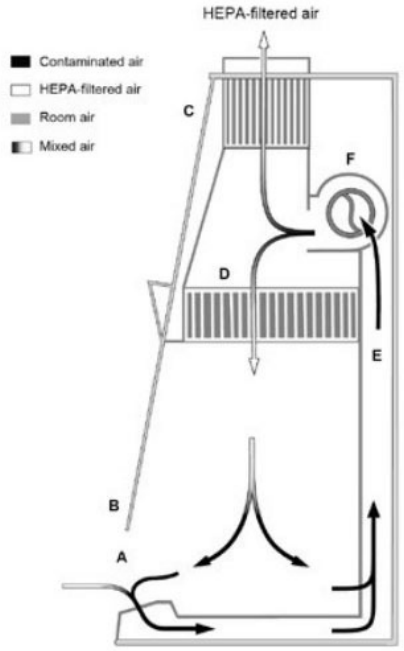
All Class II cabinets are designed for work involving microorganisms assigned to Risk Groups (RG) 1–4. Class II BSCs provide the microbe-free work environment necessary for cell culture propagation and also may be used for the formulation of nonvolatile antineoplastic or chemotherapeutic drugs. Class II BSCs may be used with organisms requiring BSL-4 containment in a BSL-4 suit laboratory by a worker wearing a positive-pressure protective suit. Maximum containment potential is achieved only through strict adherence to proper practices and procedures.

Class II, Type A1 BSC

An internal fan (Figure 3) draws sufficient room air through the front grille to maintain a minimum calculated or measured average inflow velocity of at least 75 lfm at the face opening of the cabinet. The supply air flows through a HEPA filter and provides particulate-free air to the work surface. Airflow provided in this manner reduces turbulence in the work zone and minimizes the potential for cross-contamination.

Figure 3. The Class II, Type A BSC

(A) front opening; (B) sash; (C) exhaust HEPA filter; (D) supply HEPA filter; (E) common plenum; (F) exhaust blower. Note: Since 2010 there is minimal difference between the Class II, Type A1 and Class II, Type A2 except for the inflow velocity.



The downward moving air splits as it approaches the work surface; the fan draws part of the air to the front grille and the remainder to the rear grille. Although there are variations among different cabinets, this split generally occurs about halfway between the front and rear grilles and two to six inches above the work surface.

The air is drawn through the front and rear grilles by the internal fan and pushed into the space between the supply and exhaust filters. Due to the relative size of these two filters, approximately 30% of the air passes through the exhaust HEPA filter and 70% recirculates through the supply HEPA filter back into the work zone of the cabinet. Most Class II, Type A1, and A2 cabinets have dampers to modulate this division of airflow.

Since 2010, a Class II A1 cabinet may not have a potentially contaminated positively pressurized plenum that is not surrounded by a negatively pressurized plenum. This change has minimized the difference between an A1 and A2 cabinet to the inflow velocity.

Class II, Type A2 BSC (Formerly called A/B3)

Only when this BSC (Figure 3) is ducted to the outdoors does it meet the requirements of the former Class II, Type B3. The designation Class II B3 is no longer used. The Type A2 cabinet has a minimum calculated or measured inflow velocity of 100 lfm. All positive-pressure contaminated plenums within the cabinet are surrounded by a negative air pressure plenum thus ensuring that any leakage from a contaminated plenum will be drawn into the cabinet and not released to the environment. Small quantities of volatile toxic chemicals or radionuclides can be used in a Type A2 cabinet only if it exhausts to the outside via a properly functioning canopy with exhaust alarm.

Class II, Type B1 BSC

Some biomedical research requires the use of small quantities of toxic volatile chemicals, such as organic solvents or carcinogens. Carcinogens used in cell culture or microbial systems require both biological and chemical containment.

The Class II, Type B cabinet originated with the National Cancer Institute (NCI)-designed Type 212 (later called Type B) BSC (Figure 5a) and was designed for manipulations of small quantities of toxic volatile chemicals with in vitro biological systems. The NSF/ANSI 49-2018 definition of Type B1 cabinets8 includes this classic NCI design Type B; cabinets without a supply HEPA filter located immediately below the work surface (Figure 5b); and those with exhaust/recirculation downflow ratios other than 70/30%.

Figure 5a. The Class II, Type B1 BSC (classic design)

(A) front opening; (B) sash; (C) exhaust HEPA filter; (D) supply HEPA filter; (E) negative pressure dedicated exhaust plenum; (F) blower; (G) additional HEPA filter for supply air. Note: The cabinet exhaust needs to be direct-connected to the building exhaust system.

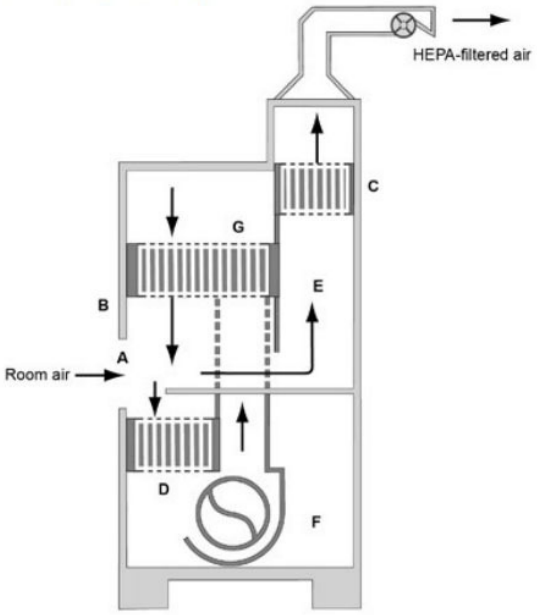
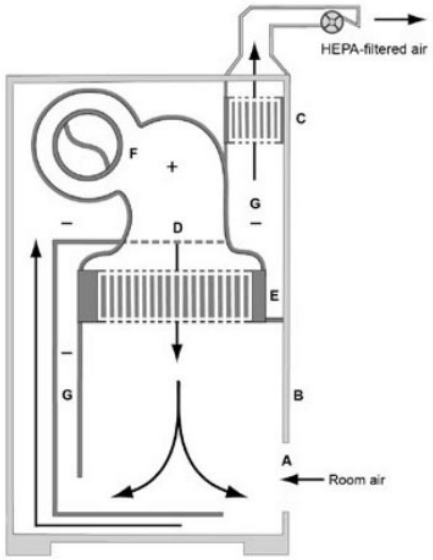


Figure 5b. The Class II, Type B1 BSC (benchtop design)

(A) front opening; (B) sash; (C) exhaust HEPA filter; (D) supply plenum; (E) supply HEPA filter; (F) blower; (G) negative pressure exhaust plenum. Note: The cabinet exhaust needs to be direct-connected to the building exhaust system.



The cabinet supply blower draws room air (plus a portion of the cabinet's recirculated air) through the front grille and through the supply HEPA filter located immediately below the work surface. This particulate-free air flows upward through a plenum at each side of the cabinet and then downward to the work area through a backpressure plate. In some cabinets, there is an additional supply HEPA filter to remove particulates that may be generated by the blower-motor system.

Room air is drawn through the face opening of the cabinet at a minimum measured inflow velocity of 100 lfm. As with the Type A1 and A2 cabinets, there is a split in the down-flowing air stream just above the work surface. In the Type B1 cabinet, approximately 70% of the downflow air exits through the rear grille, passes through the exhaust HEPA filter, and is discharged from the building. The remaining 30% of the downflow air is drawn through the front grille. Since the air that flows to the rear grille is discharged into the exhaust system, activities that may generate toxic volatile chemical vapors or gases should be conducted toward the rear of the cabinet work area.

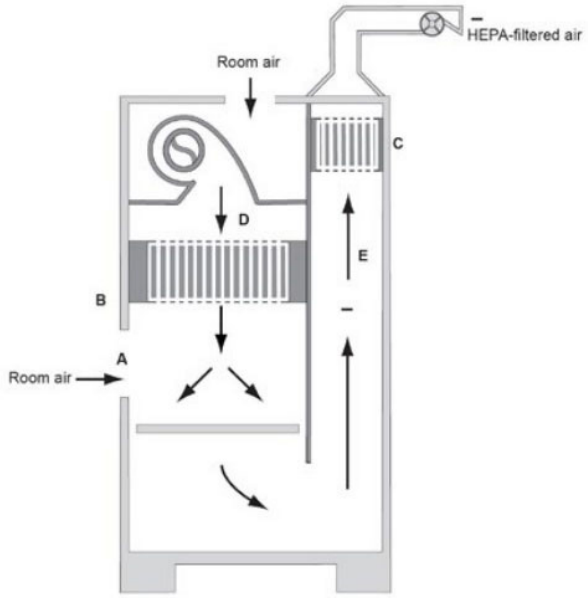
Class II, Type B2 BSC

This BSC is a total-exhaust cabinet; no air is recirculated within it (Figure 6). This cabinet provides simultaneous primary biological and chemical (small quantity) containment. Consideration must be given to the chemicals used in BSCs as some chemicals can destroy the filter medium, housings, and/or gaskets causing loss of containment. The supply blower draws either room or outside air in at the top of the cabinet, passes it through a HEPA filter and down into the work area of the cabinet. The building exhaust system draws air through both the rear and front grilles, capturing the supply air plus the additional amount of room air needed to produce a minimum calculated or measured inflow face velocity of 100 lfm. All air entering this cabinet is exhausted and passes through a HEPA filter (and

perhaps some other air-cleaning device, such as a carbon filter, if required, for the work being performed prior to discharge to the outside). This cabinet exhausts as much as 1,200 cubic feet per minute of conditioned room air making this cabinet expensive to operate. The higher static air pressure required to operate this cabinet also results in additional costs associated with heavier gauge ductwork and higher capacity exhaust fan. Therefore, the need for a Class II, Type B2 should be justified by the risk assessment of the research to be conducted.

Figure 6. The Class II, Type B2 BSC

(A) front opening; (B) sash; (C) exhaust HEPA filter; (D) supply HEPA filter; (E) negative pressure exhaust plenum. Note: The cabinet needs to be direct-connected to the building exhaust system.



Should the building exhaust system fail, the cabinet will be pressurized, resulting in a flow of air from the work area back into the laboratory.

Cabinets built since the early 1980s have an interlock system, installed by the manufacturer, to prevent the supply blower from operating whenever the exhaust flow is insufficient; systems can be retrofitted. Exhaust air movement should be monitored by a pressure-independent device, such as a flow monitor.

Class II, Type C1 BSC

This BSC is similar to a Type B1 BSC in that it has a special region of the work area intended for work with toxic volatile chemicals that are exhausted from the building (Figure 7a). However, it also has an internal exhaust blower that allows the BSC to be either room recirculated if no volatile toxic chemicals or vapors are present or canopy-connected with an exhaust alarm if volatile toxic chemicals are used. Room air is drawn through the face opening of the cabinet at a minimum measured inflow velocity of 100 lfm. The down-flowing air stream just above the work surface is split by a specific grille pattern with a portion of 70% to be exhausted and the remaining 30% recirculated. If the air that flows

over the specific region is discharged into the exhaust system, activities that may generate toxic, volatile chemicals or gases must only be conducted in that area of the cabinet work zone if connected to a properly functioning canopy with alarm (Figure 7b). If canopy connected during a building system failure, the BSC must be either interlocked with the cabinet blower(s) alarm to shut off the cabinet or, if using a sealed and tested duct system and if permitted by a chemical risk assessment, may continue to operate for up to five minutes pressurizing the duct and indicating the time remaining before the BSC is shut off.

Figure 7a. The Class II, Type C1 BSC (not connected to building exhaust system)

(A) front opening; (B) sash; (C) exhaust HEPA filter; (D) supply filter; (E) supply blower; (F) exhaust blower.

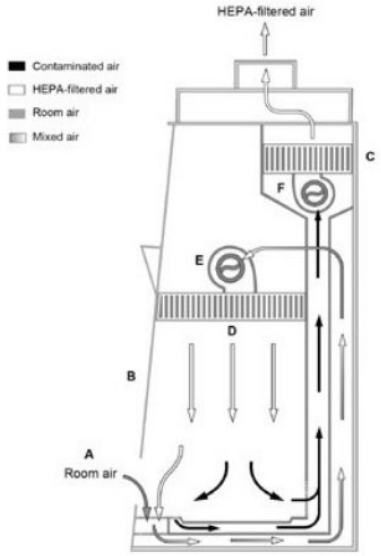
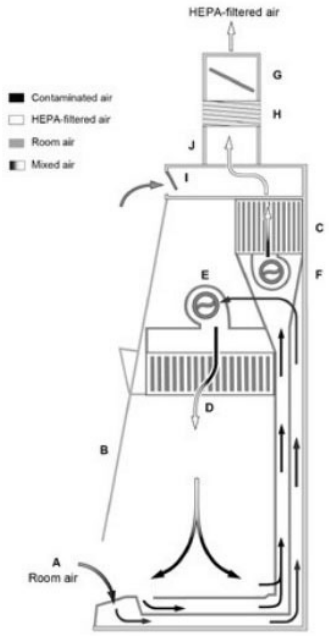


Figure 7b. The Class II, Type C1 BSC (connected to building exhaust system)

(A) front opening; (B) sash; (C) exhaust HEPA filter; (D) supply HEPA filter; (E) supply blower; (F) exhaust blower; (G) balancing damper; (H) sealed flexible duct (optional); (I) canopy opening/gap; (J) exhaust duct.



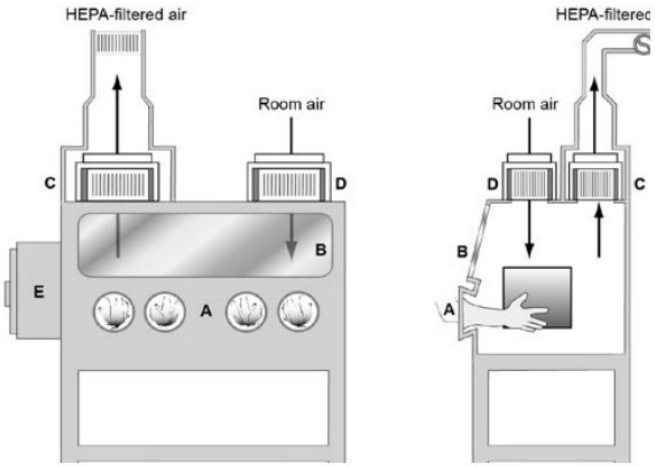
Special Applications Class II BSCs can be modified to accommodate special tasks. For example, the front sash can be modified by the manufacturer to accommodate the eyepieces of a microscope. The work surface can be designed to accept a carboy, a centrifuge, or other equipment that may require containment. A rigid plate with openings for the arms can be added if needed. Good cabinet design, microbiological aerosol tracer testing of the modification, and appropriate certification are required to ensure that the basic systems operate properly after modification.

The Class III BSC

The Class III BSC (Figure 8) was designed for work with highly infectious microbiological agents and the conduct of hazardous operations and provides maximum protection for the environment and the worker. It is a gas-tight (no leak greater than 1x10-7 cc/sec with 1% test gas at three inches pressure water gauge) enclosure with a non-opening view window. Access for passage of materials into the cabinet is through a dunk tank that is accessible through the cabinet floor or a double-door pass-through box (e.g., antechamber, autoclave) that can be decontaminated between uses. Reversing that process allows materials to be removed from the Class III BSC safely. Both supply and exhaust air are HEPA-filtered on a Class III cabinet. Exhaust air must pass through two HEPA filters, or a HEPA filter and an air incinerator, before discharge directly to the outdoors. Class III cabinets are not exhausted through the general laboratory exhaust system. Using a dedicated exhaust system reduces the risk of outside ventilation influences on Class III containment performance. Airflow is maintained by an exhaust system exterior to the cabinet, which keeps the cabinet under negative pressure (minimum of 0.5 in water gauge). This level of negative pressure is required to minimize risk and maintain containment if a breach occurs such as holes or tears in the glove system.

Figure 8. The Class III BSC

(A) glove ports with O-ring for attaching arm-length gloves to cabinet; (B) window; (C) exhaust HEPA filter; (D) supply HEPA filter; (E) double-ended autoclave or pass-through box; (F) exhaust HEPA filter. Note: A chemical dunk tank may be installed, which would be located beneath the work surface of the BSC with access from above. The cabinet exhaust needs to be direct-connected to an exhaust system where the fan is separate from the exhaust fans of the facility ventilation system. The exhaust air must be double HEPA-filtered or HEPA-filtered and incinerated.



Long, heavy-duty rubber gloves are attached in a gas-tight manner to ports in the cabinet to allow direct manipulation of the materials isolated inside. Although these gloves restrict movement, they prevent the user's direct contact with the hazardous materials. The trade-off is clearly on the side of maximizing personal safety. Depending on the design of the cabinet, the supply HEPA filter provides particulate-free, albeit somewhat turbulent, airflow within the work environment. Laminar or uniform airflow is optional but not a typical characteristic of a Class III cabinet.

Several Class III BSCs can be joined together in series to provide a larger work area. Such cabinet lines are custom-built; the equipment installed in the cabinet series (e.g., refrigerators, small elevators, shelves to hold small animal cage racks, microscopes, centrifuges, incubators) is generally custom-built as well.

Cytotoxic Drugs Guide

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