Technical note

Biosafety cabinets

An introduction to cytotoxic safety cabinets

Standards and use cases

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Introduction

When handling dangerous substances such as cytotoxic agents, it is vital to protect the person and their environment by using a safe and dedicated means of containment. One of the ways in which to do so would be the use of a cytotoxic Class II biological safety cabinet (BSC). These types of cabinets are also known as “triple-filter biological safety cabinets” or “cytotoxic safety cabinets”.

A cytotoxic safety cabinet is required when handling cytotoxic substances as laid out within DIN 12980 (1). Working with these hazardous materials within the cabinet can effectively prevent the materials from being contaminated by bacteria and particles during the preparation process, help ensure the safety and protection of the operator and others within the laboratory, and help protect the surrounding laboratory environment.

What are cytotoxic drugs and why are they hazardous?

Cytotoxic (CMR) or Hazardous Drugs are primarily used as anti-cancer medication because they are toxic to cells. While useful in the short term in treating cancer, chronic exposure has been associated with human cancers and are carcinogens.

CMRs are chemical substances that are Carcinogens, Mutagens or toxic for Reproduction.

- **Carcinogens:** Chemicals that, if they are inhaled or ingested or if they penetrate the skin, may cause, or increase the incidence of cancer.
- **Mutagens:** Chemicals that, if they are inhaled or ingested or if they penetrate the skin, may induce heritable genetic defects, or increase their incidence.
- **Toxic for Reproduction:** Chemicals that may produce or increase the incidence of non-heritable adverse effects in the progeny and/or impairment in reproductive capabilities.

Cytotoxic substances are used in a variety of settings and applications including hospitals, specialist oncology units, hospices, care homes, charitable organizations, and domestic homes. They may also be used in veterinary applications.

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How does exposure occur?

- Inhalation – drug dusts or droplets
- Absorption – via skin or mucous membranes
- Ingestion – via contact with contaminated food, drink, cigarettes, hands etc.

How does a cytotoxic safety cabinet work? (See figure 1)

Cytotoxic safety cabinets are very similar to Class II biological safety cabinets (BSCs). As with BSCs, air from the laboratory is drawn into the BSC at the front aperture. The air being drawn in at the front aperture must be ≥0.40m/s as per EN 12469 standard (2). This is the basis of containment, and this "inflow" air is what creates the air barrier at the aperture.

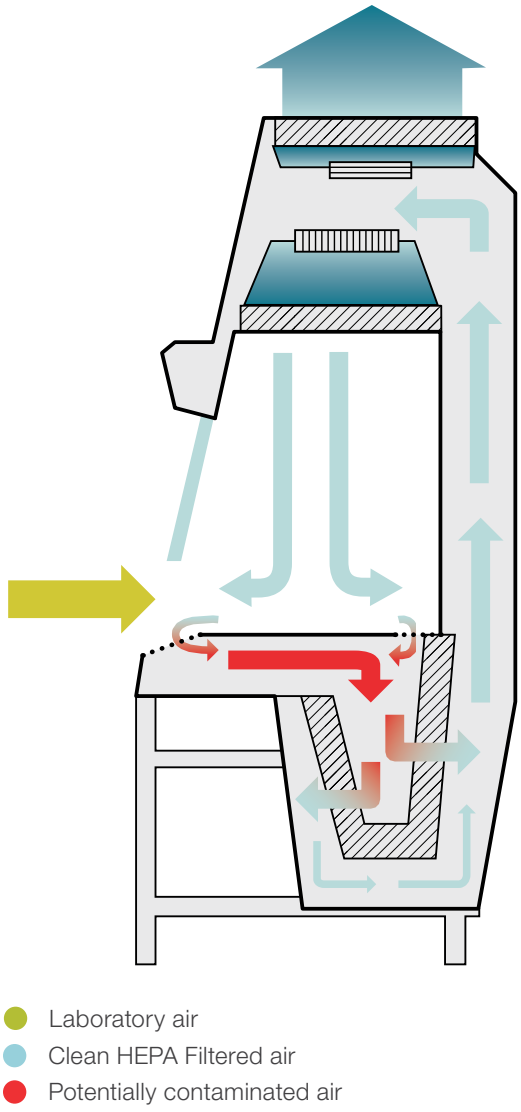
Downflow air is pushed through a HEPA filter by a motor/fan(s). This is known as unidirectional airflow. According to EN 12469, the average downflow velocity must be between 0.25m/s and 0.50m/s. This sterile air is what protects the product inside of the cabinet.

Once the downflow air hits the work surface it will split, with 50% going to the back grill of the work area, and the other 50% going to the front grill in the work area. One of the additional requirements for cytotoxic safety cabinets is the requirement for a safe method of replacing contaminated filters. In this cytotoxic safety cabinet all of this air will then pass through the primary set of H14 HEPA filters. These are situated directly underneath the work surface.

The air continues to the downflow plenum. It will then split, approximately 70% of the air will be "recycled" via the downflow fan and will be pushed back through the downflow HEPA filter. The remaining 30% will be pushed out through the exhaust HEPA filter.

This filtered exhaust air is then expelled back into the laboratory. Alternatively, it can be pushed into a ducted exhaust system to outside air. All the exhausted air is clean, filtered air.

Figure 1: Diagram demonstrating airflows of a triple-filter cabinet



Why the need for a specialist Class II BSC to handle CMR?

Important point: *Cytotoxic material cannot be inactivated by chemical decontamination.*

The primary HEPA filters are installed directly beneath the work surface. All cytotoxic powders/materials are contained and trapped in these "safe change" first stage primary H14 HEPA filters. This ensures plenums/fans/downflow and exhaust HEPA filters are not contaminated with a substance that cannot be decontaminated. If a downflow fan or downflow HEPA filter needed to be changed, this could be completed safely in the knowledge that the plenum and components have not been subjected to CMRs, because the primary HEPA filters would have captured the hazard.

If we did not have this primary bank of H14 HEPA filters the whole BSC carcass would be contaminated with hazardous material. This would be a big problem when there is a need to perform maintenance or replacement of parts internally.

Primary H14 HEPA filters

Thermo Scientific™ Maxisafe™ Biological Safety Cabinets (BSCs) include “V – type cartridge” H14 HEPA filters. The small, easy to handle cartridges have a snap in design which fit between steel supports in the base of the BSC. They are sealed in place with a tape sealant.

Figure 2 shows the HEPA being fitted at point of installation. Figure 3 and figure 4 depicts the snap in design that sits flush between the steel supports adding rigidity, then finally, sealed in place using a specialist sealant tape.

Figure 2

What happens when the primary HEPA filters require changing?

Once the primary HEPA filters are fully loaded, changing these filters within a Maxisafe 2030i BSC is straightforward. The removal of the loaded “contaminated” primary filter is completed within the BSC work area’s negative pressure environment whilst the BSC is still operating. Simply remove the filter and bag within the work area. Keeping everything contained inside the BSC under negative pressure. Once the filters are bagged and sealed within the BSC, they can be safely removed in much the same way as the traditional bag in bag out (BIBO) approach. It can then be disposed of responsibly following local regulations.

The small size of the primary HEPA filters makes them easy to handle and bag. A common method of disposal for the HEPA filters is by incineration.

Figure 3

Health and safety when removing contaminated primary HEPA filters

- This procedure should only be performed by a trained and competent engineer.
- Full instructions on the procedures are laid out within the service manual.
- When changing contaminated primary HEPA filters, personal protective equipment is required.
- The disposal of the contaminated filters is the customer’s responsibility and should be done responsibly and safely.
- Adhere to local regulations with regard to responsible disposal.

Figure 4

Information on standards

DIN 12980

DIN 12980:2016-10 is the German standard addressing safety cabinets and glove boxes for cytotoxic substances and other CMR drugs. It is frequently recommended and required in Europe and is the major standard directly addressing BSCs for work with cytotoxic substances and other CMR drugs.
This standard borrows heavily from EN 12469.

EN 12469: 2000

This European standard specifies basic requirements for biological safety cabinets.
Class I, II and III are covered, with respect to safety and hygiene. EN 12469 sets the minimum performance criteria for safety cabinets for work with microorganisms and specifies test procedures for biological safety cabinets with respect to protection of the worker and the environment, product protection and cross contamination.

Maxisafe 2030i BSC standards

- EN 12469 TÜV NORD certified
- DIN 12980 TÜV NORD certified
- EU GMP compliant (3)
- Minimum of ISO Class 5 air quality in the work area as per ISO 14644-1 (4)
- Optimized protection on downflow and exhaust filter. (Primary HEPA filter underneath work tray).

Four levels of safety

1. Safety for the operator. Aperture protection factor (APF) > 10^5
2. Safety for the environment. Triple H14 HEPA filter. Double exhaust filtration.
3. Safety for the product. Minimum of ISO 5 classification.
4. Safety for the engineers when changing the primary HEPA filter (bag-in bag-out procedure).

Other useful information

- **Exhaust systems** – DIN 12980 specifies that when cytotoxic safety cabinets are connected to exhaust air systems, it must be ensured that the system does not negatively affect the protection provided. DIN 12980 does not include a requirement to connect to exhaust air systems for all cabinets. The application and local regulations should be followed when deciding to install a BSC onto a ducted system.
- **KI Discus tests** – DIN 12980 BSC that are ducted, KI Discus is completed at commissioning and thereafter, annually.
  All other DIN 12980 BSC (recirculating type) require KI Discus test after initial commissioning only.
  If any DIN 12980 BSC is relocated, then KI discus test is required at commissioning.
- **Single piece work trays** – There is no specific section within the DIN 12980 standard stating this is a requirement/ mandatory. The only requirements are that the filters beneath the work surface are protected against liquid spills. In this case, if liquids are being used, then single piece work tray is the easiest way to achieve the protection. However, there are segmented work trays within the market that fulfill requirements.

Conclusion

If your application involves the handling of cytotoxic materials (CMR), consideration should be given to using a dedicated containment device such as a cytotoxic safety cabinet.

Unlike microbiological materials, cytotoxic drugs cannot be neutralized by normal methods of decontamination. Therefore, these types of cabinets are designed specifically for cytotoxic applications. They help protect the user of the cabinets, the service personnel performing maintenance and the environment.

The Maxisafe 2030i biological safety cabinet is manufactured and tested to the DIN 12980 standard that addresses this type of application. In addition, the Maxisafe 2030i BSC conforms to EN 12469 for Class II biological safety cabinets.

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