# Staying Safe When Weighing Hazardous or Sensitive Materials

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Many substances processed in today's working labs or production environments must be kept pure. Many of these substances also pose a risk to user safety, particularly in microbiological and pharmaceutical settings.

The right containments for sensitive and hazardous materials that pose a threat to human health yet require a highly clean environment are safety cabinets and specialised isolators. These enclosures provide a higher degree of protection than standard fume hoods or weighing cabinets, where turbulent airflow is a major drawback for weighing scenarios where aseptic or particle-free conditions are required.

Unlike fume hoods or weighing cabinets, safety cabinets and specialised isolators ensure that all air from the lab environment entering the weighing workspace is guided via unidirectional airflow through a high-efficiency particulate air or HEPA-grade purification system to remove contaminants in a practical manner.

The unidirectional system also provides a high degree of protection against exposure to vapours, aerosols or particles for the operator. However, it may be difficult to avoid exposure risk completely, particularly in the case of accidental minor or major spills. To further limit exposure risk, operators must adopt safe weighing principles including appropriate operational protocols (e.g. training, SOPs, hygiene management).


## Mandatory Personal Protective Equipment (PPE)

Even though the operating principles of safety cabinets and isolators are sound, PPE is always mandatory. This is due to potential toxicity or to the carcinogenic, mutagenic, reprotoxic (CMR) or teratogenic properties of many substances in use in the modern lab.

These PPE items, detailed in Table 1, provide an added level of protection in the event of unforeseen environmental circumstances or equipment malfunction. They should be part of your lab's SOPs and followed consistently for every weighing or service task.

*Table 1. Personal Protective Equipment (PPE) to ensure maximum operator safety.*

| Item | **Details, Use** |
|---|---|
| Safety Glasses | Protects eyes; can be worn over corrective glasses; must be certified according to EN166 and EN170. |
| Nitrile Gloves | Chemical Protects eyes; can be worn over corrective glasses; must be certified according to EN166 and EN170. protection; protection against cross-contamination; must be certified according to EN374; disposable. |
| Fine Dust Mask | Protects lungs and mucous membranes in the nose and mouth; standard FFP3 to avoid breathing vapours, mist or particulate matter; disposable. |
| 200 mL Eye Wash Bottle with Integrated Eye Bowl | Provides extra precaution in case of unforeseen exposure to chemicals or biological agents; disposable. |

## Safe Weighing in Specialised Enclosures

Uniform approaches towards substance-handling will make it easier to comply with SOPs on a consistent basis. This helps to ensure your safety, the safety of those using the enclosure after you, and the purity of the product you are handling.

In general, safe laboratory principles are the rule. This includes:

- Not eating or drinking in rooms where potentially weighing hazardous materials are present.
- Using mandatory PPE for every weighing.
- Adopting appropriate containment technology.

## Technical Principles of Safety Cabinets and Isolators

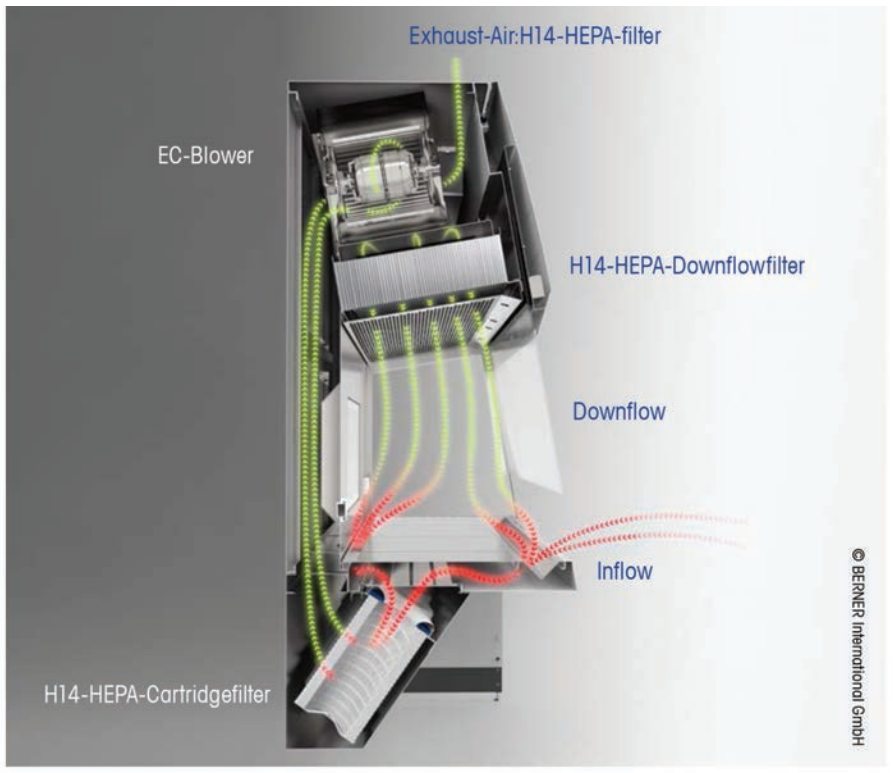


*Figure 1. Cross-section and functional principle of a safety cabinet for cytotoxics with 3 filter levels. ©Berner International GmbH*

After establishing the need for PPE and appropriate weighing protocols, we are ready to review the technical principles and benefits of a modern safety cabinet. These technical principles can be illustrated by the crosssectional example shown in *Figure 1*.

The high level of personnel and product protection provided by the safety cabinet is achieved by HEPA filtration, the interaction of downflow and inflow at the access opening, and the guidance of the air system itself. All factors combine to determine overall safety-cabinet performance.

The image itself is of a safety cabinet dedicated to the preparation of cytotoxics for individualised cancer infusions. In Germany, the requirements of safety cabinets and isolators used for such applications are defined in a relatively new version of a national standard called DIN 12980 established in 2017 [1].

Strict aseptic conditions according to GMP regulations [2] are required, as is the highest safety for the user because of cytotoxics' CMR properties. Safety cabinets for cytotoxics, according to DIN 12980, act as a model for many other applications in pharmaceutical, biotechnological and other laboratory settings.

## Air Guidance

As shown in Figure 1, the air path through the safety cabinet is driven by one or more energy-efficient EC blowers typically located in the upper area which is called the plenum. Lab air is sucked in at the front opening. The medial air velocity must be ≥0.40 m/s according to DIN 12980. The airstream is guided under the worktop through the front grid to the first and main H14-HEPA filter level and then through a double-walled backside up to the plenum. Here the total air volume is split into approximately 30% exhaust air and 70% recirculated air.

Exhaust air is directed to the outside through a second H14-HEPA filter to further protect the environment from potentially hazardous or infectious material. Through the largest and third H14-HEPA filter, which covers the

complete work space, clean recirculated air enters the work space as a uniform, downwards airflow, also called laminar airflow or downflow. The uniformity is important to prevent the spread of contaminants in a horizontal direction which can promote cross-contamination in the enclosure.

## HEPA Filtration

High or ultra-efficient particulate air filters (HEPA / ULPA) are basic elements of safety cabinets. Most are made from micro-glass fibre material and can separate airborne particles like dust, aerosols, spores, bacteria and viruses effectively.

According to international standards these filters need to fulfil defined requirements. In Europe, they must be at least class H14. That means they need to remove ≥99.995% of particles of the most penetrating particle size (MPPS) [3], typically in the range of 0.12 to 0.25 µm.

Safety cabinets for cytotoxics with three filter levels improve filtration significantly because the air passing into the workspace to create the laminar airflow and the exhaust air is filtered twice.

## Interaction of Downflow and Inflow

The personnel and product protection function is intensively evaluated during type testing of safety cabinets with internationally harmonised and defined microbiological test procedures. For proof, bacillus subtilis spores are set free in different settings to document either product protection or personnel protection. In the European standard EN 12469 for microbiological safety cabinets [5] to date, only the standard settings for inflow and downflow velocity given by the manufacturer are evaluated.

Other standards such as the US standard ANSI NSF49 [6] or the above mentioned new German standard DIN 12980 for safety cabinets for cytotoxics require more extensive evaluations. *Figure 2* shows the scheme for varying inflow and downflow according to DIN 12980:2017-05.

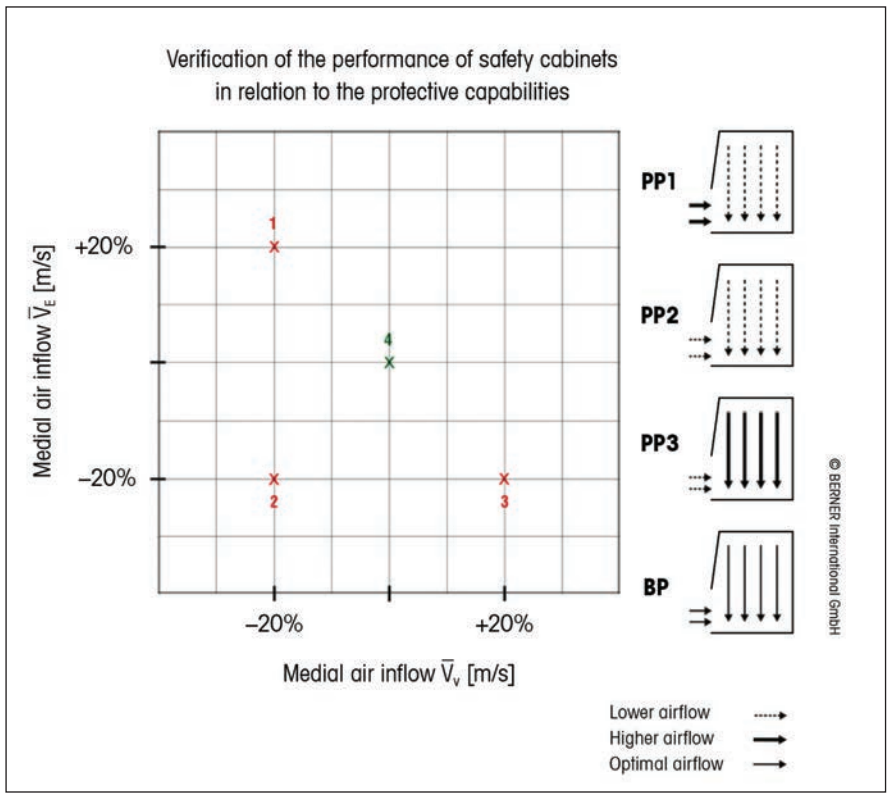


*Figure 2. Performance testing for safety cabinets for cytotoxics according to DIN 12980:2017-05. © Berner International GmbH*

## Addressing Challenges in the Weighing Process

The functional principle of a safety cabinet with the interaction of inflow and downflow is of high importance for understanding the challenges in weighing sensitive and hazardous materials.

The primary challenge is obtaining required accuracy in an environment where airflow is a constant presence to ensure safety. Airflow requirements coupled with balance technology that addresses the need for accuracy follow.

## Airflow Velocity and Its Effect on Weighing

Balances in direct combination with a safety cabinet face conditions which usually reduce the overall performance of the weighing equipment, including vibrations and pressure fluctuations caused by airflow. These are both typically in direct dependence to airflow velocity.

High-velocity airflow requires that the blower be run at high speed leading to a higher degree of vibration transmitted to the safety-cabinet housing and work surfaces. Therefore, all international standards during type-testing require measurement of work-surface vibrations expressed as the Root Mean Square Amplitude (RMS value) and must be ≤5 µm.

Increased downflow velocity is also accompanied by increased pressure fluctuations, which add directly to vibration applied to the balance. Taken together, this is why a balance in a safety cabinet under GMP conditions for pharmaceutical applications with a required medial downflow velocity of 0.45 m/s ±20% always operates at suboptimal conditions.

In practice, this will be expressed in a higher minimum operating range for balances that are used in safety cabinets in comparison to the theoretical minimum weight under best conditions. It is also possible that, in the worst-case scenario, the calibration of a sensitive balance will fail completely, especially for analytical, micro and ultra-micro instruments. This makes choosing the right balance critical.

## Achieving Accuracy and High Protection

Despite these difficulties, there are several countermeasures you can adopt to adequately operate high performance balances in a safety cabinet without giving up either the highest personnel or product protection.

These include:

- Use of a draft shield
- Solid worktops or enhanced integrated weighing segments.
- Solid weighing stones or specialised metal plates.

## Cable and Peripheral Options

Cables and connected peripherals such as power supplies or control boxes can also interfere with weighing performance. Connections between balance, peripheral devices and data-management interfaces should be kept as short as possible because space is limited inside a safety cabinet and because they increase spill risk. Connecting cables may also transfer vibrations, so any contact between cable wrappings and the balance must be avoided.

Peripheral devices can be positioned on the outside of the cabinet for reduced interference and good accessibility. They can also be integrated below the worktop or behind the back wall. Safety-cabinet manufacturers should be able to offer options that achieve short cable lengths along with integrated interfaces and connections.

## Fully Integrated Balances

The most challenging solution to vibrational interference is the full integration of a balance into a special worktop. This highly specialised solution - while currently only a vision for the future - could potentially provide a significant range of benefits including:

- Enhanced ergonomics to promote safe handling of potentially hazardous substances.
- Elimination of cables or peripheral devices, helping to provide a best-case scenario for cleaning and the avoidance of cross-contamination.
- Minimised interference with safety-cabinet airflow due to inherent design and elimination of cables and peripherals.
- Improved personnel and product protection through all of the above.

## External Influences

Finally, external factors can also have a strong influence on weighing performance, especially when using sensitive micro and ultra-micro balances. As noted above, these external factors can be caused by the cleanroom environment or the HVAC system and include temperature and pressure variations.

These influences can be limited through the application of weighing best practices, including appropriate placement of the safety cabinet and observing practices that limit drafts and changes in temperature and humidity.

## Summary

Particularly in pharmaceutical and biotechnological applications in GMP conditions, safety cabinets and isolators typically enable the highest personnel and product protection. When combined with appropriate PPE and safe operating procedures such as limiting contact with personal items and work surfaces, cross-contamination risk is practically eliminated.

This level of protection becomes necessary when hazardous and sensitive material is handled, and it is of the utmost importance when the product has CMR properties. GMP Regulations require laminar airflows for safety cabinets of 0.45m/s ±20%.

The high downflow velocity for safety cabinets that conform with GMP is a challenge in weighing processes, especially when using analytical, micro and ultra-micro balances. Due to resulting vibrations and pressure fluctuations, higher minimum operating ranges in comparison to the theoretical minimum weight or even failures in calibration routines can result without appropriate counter measures.

Ways to minimise the negative effects on weighing performance are:

- Use of solid worktops or special weighing worktops.
- Separate weighing stones or metal plates decoupled from vibration.
- Short cables to power supply and for interfaces.
- Avoiding contact between cable wrappings and the balance.
- Integration of peripheral devices or positioning them outside the cabinet.

Full integration of balances into the worktop is an interesting future goal for enhanced weighing and safety.
This type of solution will require excellent cooperation between the manufacturers of balances and safety enclosures.

Download the **Free White Paper**: **www.mt.com/labtec-safety-weighing** or scan here:

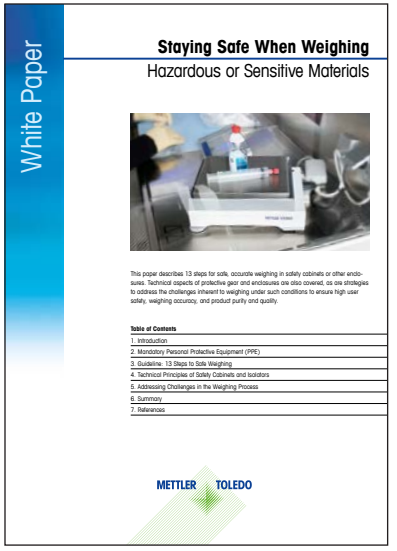


*Figure 3. Mettler-Toledo's white paper describes 13 steps for safe, accurate weighing in safety cabinets or other enclosures.*

## References

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