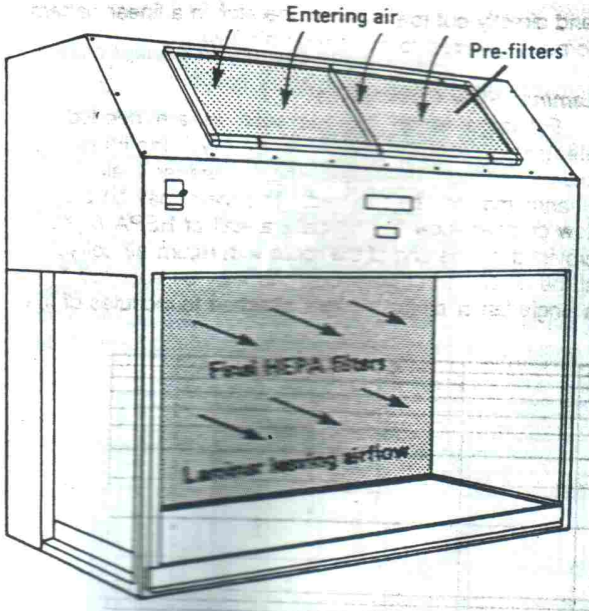


Fig. 6-60B Typical Laminar Flow Workstation (Courtesy Gelman Sciences Pty Ltd)

filters. Air quantities may be as high as 300 air changes per hour and is often returned via a full ceiling plenum. Outside air is provided to meet personnel requirements and to maintain the room at a positive pressure.

AS 1386.2 "Cleanrooms and clean workstations. Part 2: Laminar flow cleanrooms." details all requirements.

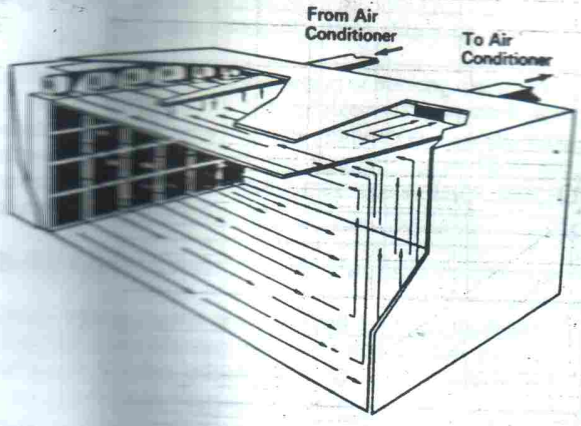


Fig. 6-60C Typical Laminar Flow CleanRoom

All pharmaceutical companies are required to comply with Code of Good Manufacturing Practice from the Therapeutic Goods Administration (TGA), (previously NBSL) [24]. These standards lay down strict requirements for the safe handling, manufacture and distribution of drugs and chemicals. In most cases the minimum requirement is for a non-laminar flow clean environment utilising terminal HEPA filters with laminar flow for critical activities such as dispensing. TGA requires regular on-site testing of installations, preferably by a NATA registered organisation.

Precautions are similar to the operating theatre application ie. the need to remove micro-organisms as well as inert particulate matter and also the need to regularly inspect, clean and decontaminate.

Non-laminar Flow Cleanrooms

Clean conditions of Class 3500 and class 350 can be achieved without laminar air flow being needed. The air handling system would have conventional distribution except that HEPA filters would be installed in terminal filter housings. Terminal units incorporating blowers to overcome filter resistance could also be used, particularly where an existing air-conditioning system is used to provide cleanroom conditions. A minimum of twenty air changes per hour is required for such a system. Class 3500 can even be achieved with lesser quality filters by increasing the air change rate.

The code requirements are detailed in

AS 1386.3
Cleanrooms and clean workstations. Part 3: Non-laminar cleanrooms - Class 3500. and

AS 1386.4
Cleanrooms and clean workstations. Part 4: Non-laminar cleanrooms - Class 350 and cleaner.

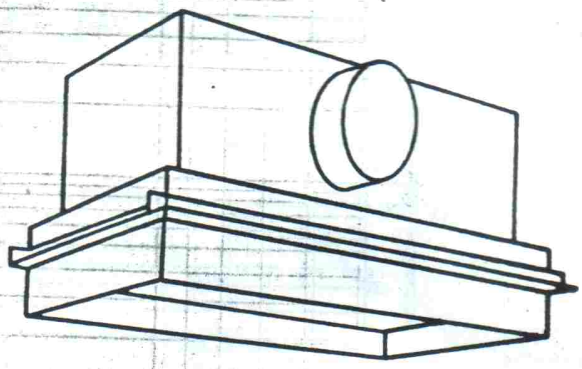


Fig. 6-60D Typical Terminal Filter Housing

6-70 Pathogen Free Facilities

The distinction between Particle Free Facilities and Pathogen Free Facilities is a little vague in some applications. Cleanrooms (or particle free facilities) for any biomedical activity, may be more concerned with micro-organisms than inert dust.

However some facilities are only trying to exclude pathogenetic organisms, such as bacteria, viruses, spores etc, eg. Animal Breeding Facilities and protective enclosures for people and animals susceptible to infection. These are called Pathogen Free Facilities or Specific Pathogen Free (SPF) Facilities. The main difference as far as the filtration system is concerned is the need to decontaminate or inactivate any organism on the filters before they are brought into service after the initial installation and any servicing that may contaminate the filter.

6-80 Containment Facilities

Containment facilities may be required for personnel, product or environmental protection.

A microbiologist responsible for, and familiar with, the use will need to determine the appropriate level of protection needed. Relevant standards are:

AS 2243.3 - 1985
Safety in laboratories - Part 3: Microbiology. (Under revision).

AS 2252.1 - 1981
Biological safety cabinets. Part 1: Biological safety cabinets (Class I) for personnel protection.

AS 2252.2 - 1981
Biological safety cabinets. Part 2: Biological safety cabinets (Class II) for personnel and product protection.

AS 2567 - 1982

Cytotoxic drug safety cabinets.

AS 2639 – 1983
Cytotoxic drug safety cabinets – Installation and use.

AS 2647 – 1983
Biological safety cabinets – Installation and use.

RDNA
Guidelines for large scale work with recombinant DNA. Recombinant DNA Monitoring Committee

Unlike Pathogen Free Facilities which are to stop micro-organisms entering, containment facilities are primarily to stop micro-organisms escaping. However some may have the additional function of also excluding particles. This time the main difference as far as the filtration system is concerned is that the filters are primarily needed on the exhaust air system and are generally to be decontaminated or sealed before being inspected, tested or removed.

Personnel Protection

Class 1 biological safety cabinets are designed to protect personnel by an inward flow of air through the work access opening thereby protecting the operator from the potentially contaminated work zone. They do not provide a sterile or aseptic internal environment. Potentially contaminated air from the work area is exhausted through pre-filters and a HEPA filter. AS 2252.1 requires that exhaust air be discharged into the laboratory to avoid wind effects on the discharge. Because the HEPA filter may be contaminated, it is necessary to decontaminate the equipment before any service work is carried out.

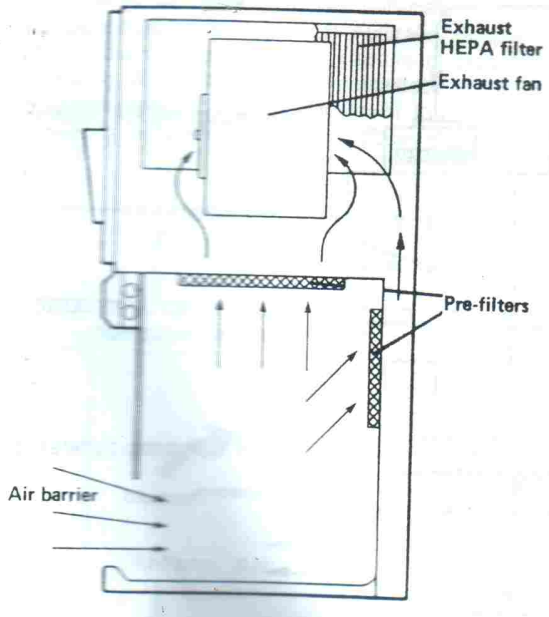


Fig. 6-80A Class 1 Biological Safety Cabinet
(Courtesy Gelman Sciences Pty Ltd)

Australian Standard AS 2252, Part I – Biological Safety Cabinets (Class 1) for Personnel Protection, describes this equipment in more detail.

Personnel and Product Protection

Class II biological safety cabinets are designed to protect personnel and to also protect the product or experiment from contamination. Air is forced down through HEPA filters above the work zone in a vertical laminar flow pattern and returned up a plenum at the rear of the cabinet for recirculation. Some room air is also

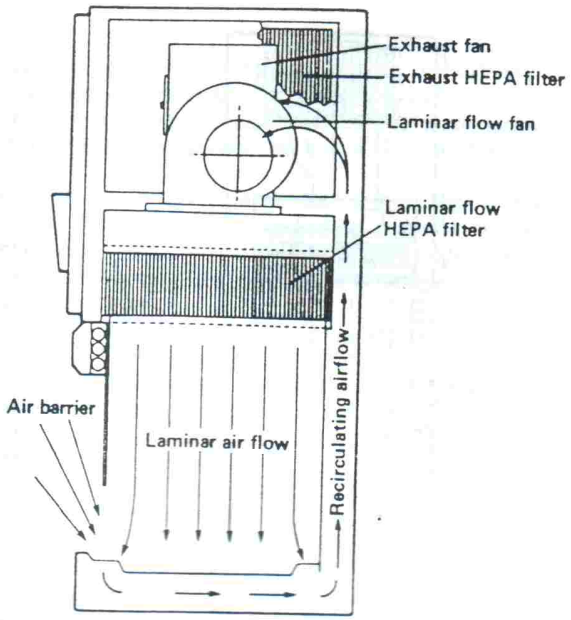


Fig. 6-80B Class II Biological Safety Cabinet
(Courtesy Gelman Sciences Pty Ltd)

drawn in through the front of the working face. The air pattern provides shielding between the operator and the work zone. Exhaust air arrangements are the same as for a Class I cabinet except that the quantity is less.

These units should be used whenever potentially hazardous biological material is manipulated, and where there is an added necessity to maintain sterility of the product. These applications include tissue culture, haematology, pathology, bacteriology and genetic engineering. Australian Standard AS 2252 Part II "Biological Safety Cabinets (Class II) Personnel and Product Protection.", describes this equipment in more detail.

To avoid disturbing the air patterns in Class I and Class II safety cabinets, the air velocity in their vicinity should be kept below 0.25 m/s. Cabinets should also be located away from disturbing influences such as doorways, high traffic areas or air-conditioning outlets. Provision should be made to exhaust decontamination gases from the cabinets directly to atmosphere.

Special Barrier Containment Facilities

Containment facilities for the handling of highly hazardous materials such as cytotoxic drugs, radioactive material and harmful micro organisms, may incorporate special cabinets, complete rooms, or a combination of both.

Cabinets would normally be totally enclosed with access via gloved ports; although there is no Australian Standard for such cabinets there are some in existence and they are generally called Class 3 Biological Safety Cabinets. Where the activity requires more space than a cabinet can provide a complete room can be treated to provide an appropriate level of containment. Manipulation of material may be undertaken by robotic arms or operators fully suited in protective clothing. Containment may be improved by enclosing cabinets or rooms within other rooms using the "box-within-a-box" principle to provide multiple barrier protection. The innermost room has the highest quality of treatment and system reliability and is called the Primary Barrier and must be at the lowest absolute pressure compared to surrounding rooms and the outside air.

Any ductwork between a HEPA filter and the barrier must be considered part of the barrier. It must be free from leakage and must be easily accessible for decontamination and cleaning. The filters may be housed

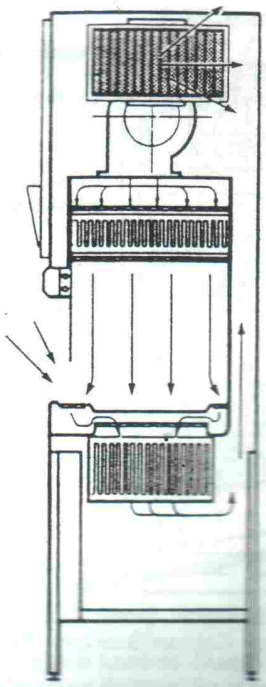


Fig. 6–80C Cytotoxic Drug Safety Cabinet
(Courtesy Gelman Sciences Pty Ltd)

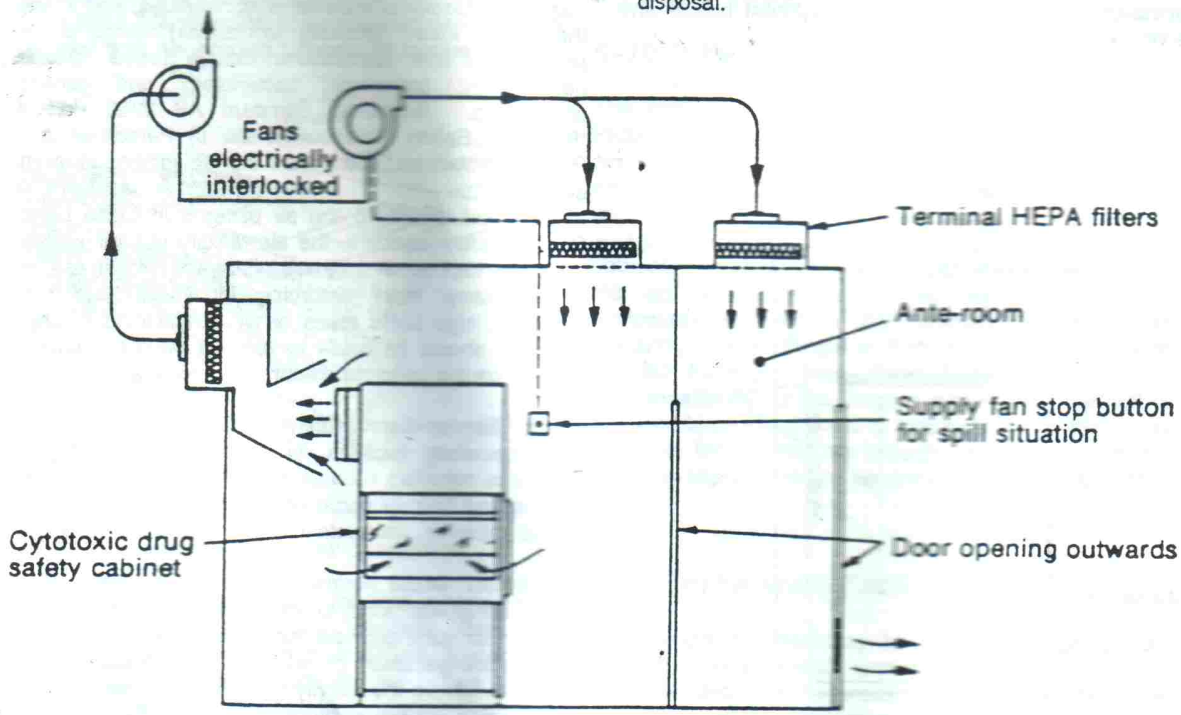
in individual containers each of which is capable of isolation with valves for decontamination (in the case of microbiological applications), inspection, testing or replacement. Filters used in the nuclear industry are housed in containers designed so that the filters can be removed directly into a sealed container for storage or disposal.

Special cytotoxic drug handling cabinets are available in Australia. These facilities are similar in operation to Class II biological safety cabinets but they include an additional HEPA filter beneath the work zone which is to protect the airways of the cabinet and so permits safe servicing of the cabinet. The exhaust system also incorporates an activated carbon absorber to remove odours and gases. Exhaust from the cabinet must not be connected directly to any other air handling system and the room in which the cabinet is located shall have HEPA filtered supply and exhaust.

For details of these cabinets refer to AS 2567 "Cytotoxic Safety Cabinets" and. AS 2639 "Cytotoxic Drug Safety Cabinets – Installation and Use."

Basic principles in the cytotoxic drug cabinet installation also apply to large laboratories handling dangerous micro–organisms or carcinogenic substances.

- All exhaust is through HEPA filters.
- Supply air may be through HEPA filters.
- Access to the outside for personnel and product is strictly controlled.
- Pressure gradients are maintained between spaces.
- Provision is made for in–situ decontamination of filters or safe removal for remote decontamination and disposal.



PRESSURE MODES:

Room

1. Normal operation, positive pressure.
2. Room product spill, pressure negative.

Annexe

1. Normal operation, positive pressure.
2. Room product spill, neutral pressure.
3. Annexe product spill, open inner door to obtain negative pressure.

Fig. 6–80D Incorporation of Primary and Secondary Barriers for Cytotoxic Cabinets.
Reproduced from AS 2639 with permission of SAA.

6–90 Hospitals and Health Care Facilities

Requirements for air filtration in hospitals and health care facilities vary widely. Air filtration needs to be considered for each of the various functional areas separately – sometimes down to an individual room where rooms of special function are involved in a department.

In general, consideration should be given to:

- The type of area, department or room concerned and its usage. In hospitals, usage varies form stores, car parks and workshops through offices, administration areas, records and pharmacies to wards, operating theatres, intensive care, laminar flow special theatres and cytotoxic drug preparation.
- The air filtration requirements of the different areas and rooms vary from a technical point of view such as degree of protection or sterility. For example much more stringent requirements apply to operating theatres than to administration areas.
  Note also that some areas require special filtration of exhaust air to provide hazard protection – cytotoxic drug preparation rooms and contagious patient isolation rooms are examples.
- Each State of Australia has an Authority having jurisdiction. These Authorities have differing requirements and a copy of the relevant regulations should be obtained and consulted.
- In the case of hospitals, whether the hospital is a public or a private hospital may be important as standards requirements may well differ. For special applications the hospitals Infection Control Officer should be consulted.
- Requirements set out in advisory publications from organisations such as Standards Australia, Hosplan (in New South Wales) and the Institute of Hospital Engineering Australia should be consulted.
- The preferences and requirements of the hospital Engineering Department (or planning committee in the case of a new hospital) should be established. Maintenance aspects such as makes of filter, replacement cost, service access space, location, use of pre-filters and service life are most important.

The air filtration requirements are one aspect which determine the number of air-handling systems; where special rooms have to be catered for within a department, a separate system may be required unless terminal filtration can be employed.

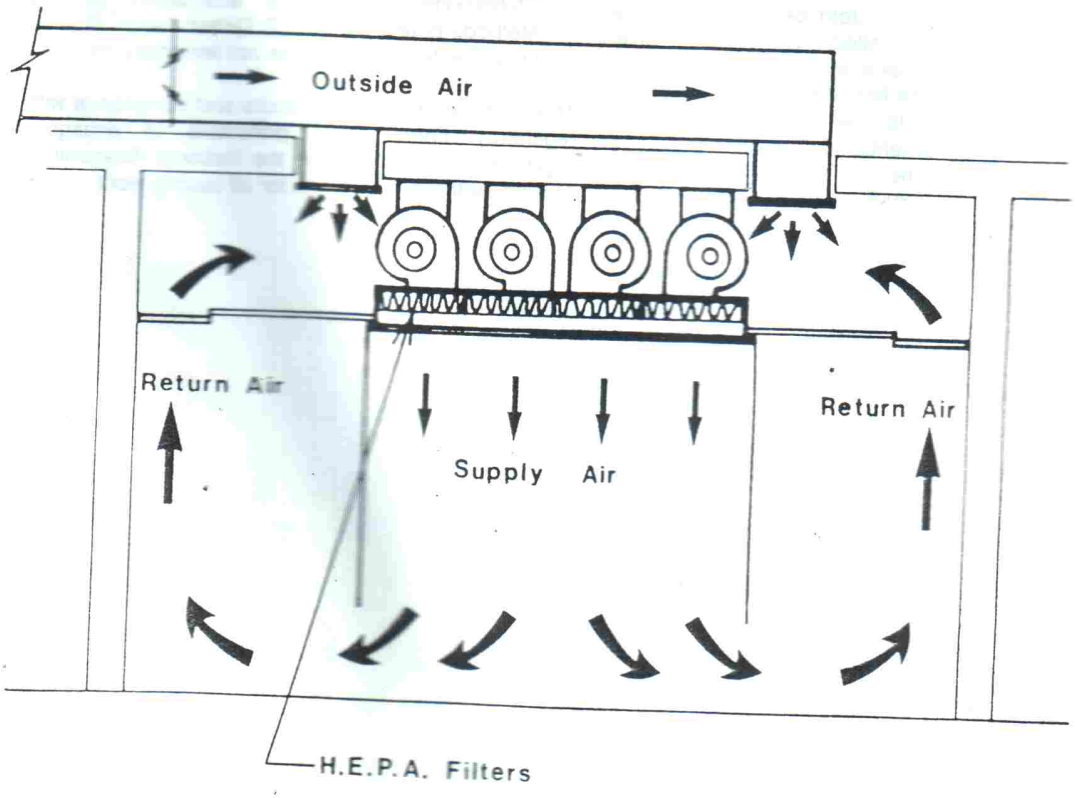
Terminal filtration is often inappropriate due to:

- maintenance having to be carried out within the area
- adverse effect on terminal air distribution
- filter pressure drop variation disturbing the system balance (unless special provisions are made).

Filters located centrally (in air-handling units in plantrooms) are generally preferred by maintenance departments. An exception are HEPA filters which may need to be installed in special boxes local to the room served. Special provision for access space for maintenance and testing is required in this case.

Many areas have particular problems which affect the choice of filter and its location. For example:

- Operating Theatres
  cleanliness, sterility, air pattern in relation to operating table, percentage of outside air.
- Intensive Care
  cleanliness, sterility, percentage of outside air.
- Isolation Rooms
  pressurisation (positive or negative), cleanliness, sterility and exhaust filtration.
- Cytotoxic Preparation & Radioactive Laboratories
  hazardous materials (refer Clause 6–80).
- Plaster Rooms
  dust extraction required.



g. 6–90A Typical Laminar Flow Operating Enclosure

- Linen areas
  fluff and lint removal.
- Workshops
  sawdust, fume removal.
- Animal Holding
  odour removal by carbon filters may be required plus roughing filters to remove hair, feathers, etc.

Operating Theatres

The type and location of filters for operating theatres is often subject to guidelines published by the various State Health Authorities and individual hospitals' infection control committee.

For general surgery theatres with 100% outside air supply, MEPA (EU8/9) filters, located either in the plantroom or local to the area served, are normally used. For critical situations HEPA filters are utilised.

Theatres, utilised for complex procedures such as open heart or orthopaedic surgery are often labelled as 'clean theatres' and employ customised laminar flow HEPA filter systems to filter particulate matter, especially micro-organisms that may infect the patients. In an operating theatre air is drawn from the room, passed through a bank of HEPA filters and discharged in a laminar flow pattern down over the patient, surgeon and persons attending at the operating table. Air supply systems covering only the table are totally unacceptable. This system is usually fully contained within the operating theatre and independent from the central air handling system (see Figure 6-90A). In this way very high air change rates are achieved and consequently the number of airborne micro-organisms is minimised. Important requirements in such applications are the need to inspect and, when necessary, decontaminate on the upstream side of the filter, the avoidance of crevices and the ability to regularly clean and decontaminate on the downstream side.

Code requirements are detailed in AS 2251 "Laminar Flow Enclosures for Protecting Hospital Patients."

6-100 On-Site Testing

The performance of a filter system depends to a large degree on how well it is installed. The pressure drop across the filter, particularly as it nears its final resistance, will cause air to by-pass the filter if any gaps exist. Prior to on site performance tests, the installation should be thoroughly inspected for potential leaks around frames or physical damage to filter media. An initial visual check can be made by shining a bright light through the filter bank and observing it from the other side. At this stage filters should be checked to ensure that they are installed with the air flow in the same direction as when the filters were tested.

A dirty filter condition can be simulated by covering part of the media with an impervious material. This technique can help verify fan performance, system integrity, pressure alarms and manometers where fitted. A particle counter may be used for testing air filters in-situ. In a typical particle counter, air is drawn through a chamber in which the interruption of a light beam is electronically monitored. These instruments can normally discriminate on the basis of particle size and can be used to assess overall system efficiency by taking measurements before and after the air filters. These tests should be carried out by trained personnel using properly calibrated and maintained equipment.

HEPA filters, biological safety cabinets and clean benches, should be tested when first installed and at twelve monthly intervals thereafter. They should also be tested after any maintenance work or relocation of cabinets. Leaks detected through media or via gaskets should be sealed and the system retested. AS 1807 details suitable testing procedures. On-site testing is required for TGA or NATA accreditation.

Cold DOP is commonly used to challenge HEPA type air filter systems on site. (See Clause 4-20). A cloud of Cold DOP is generated in known proportions before the air filter while air is passing through it in normal service. A photometer adjusted to sense DOP particles is used after the air filter to check for the occurrence of leaks. The method is detailed in the following Australian Standards:

AS 1132 - 1973
Methods of test for air filters for use in air-conditioning and general ventilation.

AS 1807.6 - 1988
Cleanrooms, workstations, and safety cabinets - Methods of test. Method 6: Determination of integrity of terminally mounted HEPA filter installations.

AS 1807.7 - 1988
Cleanrooms, workstations, and safety cabinets - Methods of test. Method 7: Determination of integrity of HEPA filter installations not terminally mounted.

To ensure repeatability of results and compliance with all regulatory codes it is preferable to engage an organisation registered by the National Association of Testing Authorities (NATA) for all testing work.

Referen

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    Filters.