

# UNIT-IV

## Design of Aseptic area



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- Designing of aseptic area
- Laminar air flow equipments

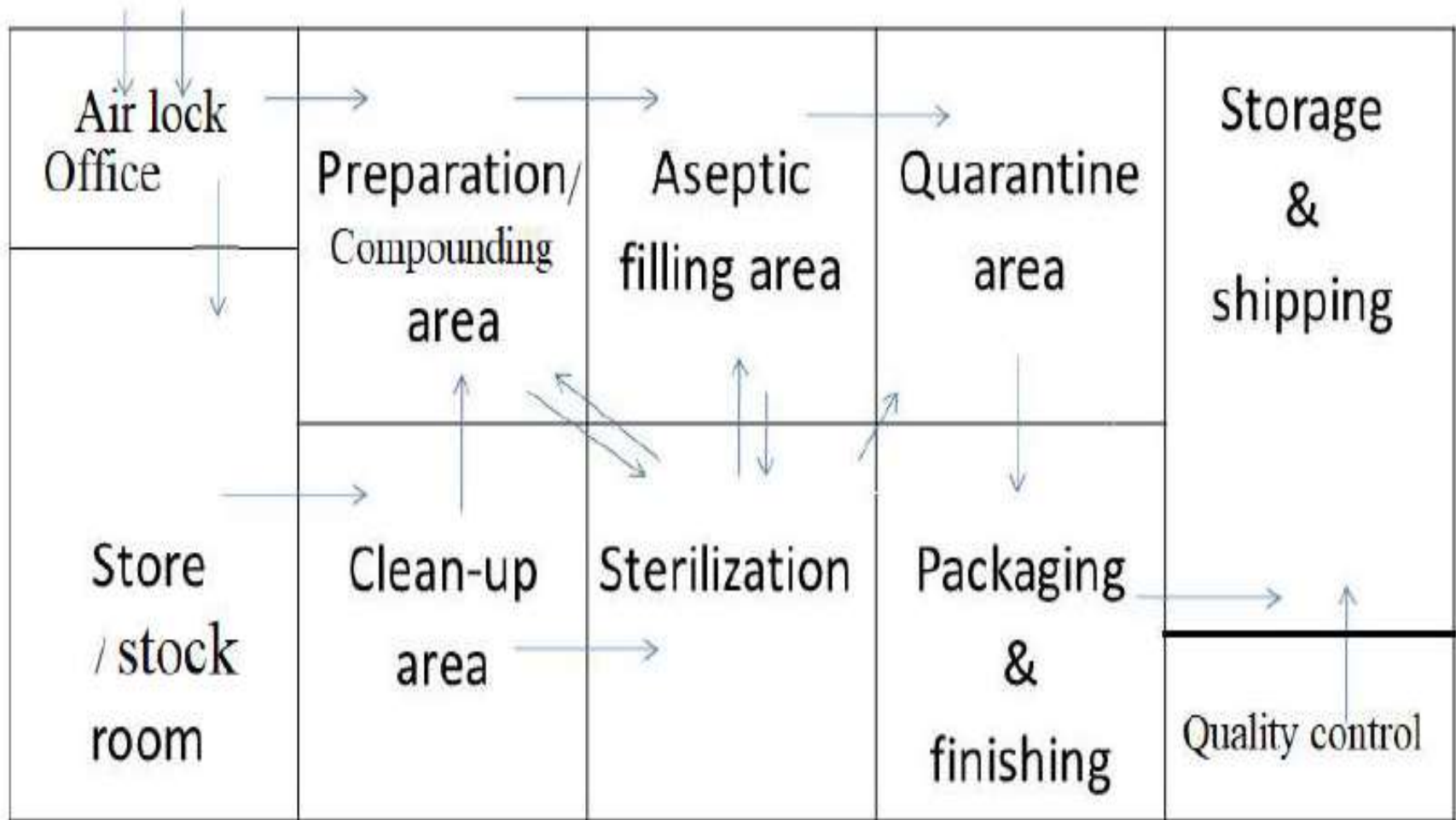
# Aseptic Area

- Aseptic procedures are used to safeguard ophthalmic and parenteral goods by preventing microbiological and particle contamination.
- To eliminate pyrogen and harmful bacterial products, microbial contamination must be avoided.
- The preparation of terminally sterilized products (those sealed in a container and then sterilized) takes place in clean areas, whereas the preparation of non-terminally sterilized products takes place under aseptic conditions using sterile materials, or by sterilization through filtration before being placed in sterile packaging.

- In an aseptic area, all the aseptic goods and products are manufactured.
- It is the room that is built, planned, utilized, serviced and more importantly it is kept clean to regulate and prevent all the microbiological contamination of the product.
- In contrast, **live or attenuated vaccines** are placed in separate areas when **they contain dead microorganisms, microbial extracts, or inactivated viruses, such as pharmaceutical items.**
- **Cross-contamination of Compounded Sterile Preparations is avoided in a controlled setting (CSPs).** Compounding should be conducted under engineering controls, such as **laminar airflow hoods (LAFHs)** or **biological safety cabinets (BSCs)** or a **compounding aseptic isolation chamber (CAI)** to **minimize contamination-related risks.**

# Designing of aseptic area

- Each stage of manufacturing is carried out individually by the **aseptic unit**.
- The unit should also maintain a **safe and well-organized workflow to reduce** the need for people to travel about the clean rooms.
- In order **to prevent contamination of the product**, the unit is constructed and the equipment positioned so as not to expose the product to contamination.



**Figure 4.1: Flow Diagram of Aseptic Area**

- The sterile production unit and the general manufacturing area within the hospital pharmacy or factory should be located separately. The sterile production unit should be buffered, i.e., unauthorized personnel should not gain access to this unit. The aseptic unit is designed to carry out each stage of production separately. The unit should also ensure a safe and organized workflow so that the need for personnel to move around the clean rooms is minimized. The unit is built and the equipment is positioned in such a manner that the product remains protected from contamination.

- The layout of aseptic area should be such that cleaning can be done easily and dust accumulation can also be reduced. Arrangement should be such that the risk of cross contamination (contamination of one product or material with another) is reduced.
- The filling area should be adjacent to the compounding area where the personnel assemble and prepare materials utilized by the staff in the filling area. In figure 4.1 the layout of areas and rooms for preparing terminally sterilized products (such as small or large volume injections) is shown.



# Design and Construction

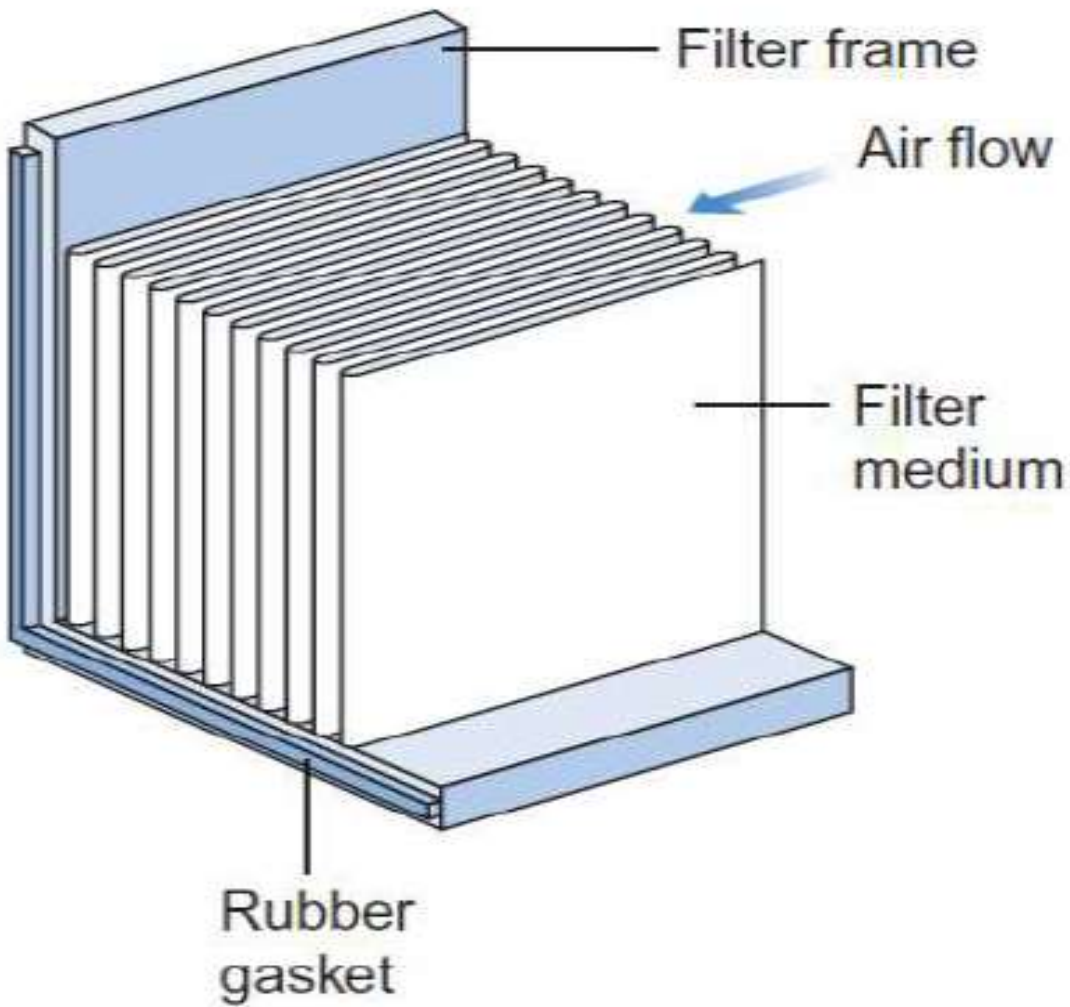
- Only authorized personnel can gain access to the clean and aseptic filling areas. The personnel enter the clean rooms by passing through the changing rooms where they put on and remove their clean room uniform.
- A pass-Over (or cross-over) bench extends across the changing room to form a physical barrier for separating the different areas for changing by the personnel.
- Special precautions are taken for preventing clean and aseptic filling areas from getting contaminated while materials are being passed through airlocks or hatchways. Thus, sterilizers and entry ports are fitted with double-sided doors, which are interlocked to prevent simultaneous opening of both the doors.

# Surfacing Materials

- The floor, wall, and ceiling surface of clean rooms **should be smooth, impervious, and unbroken to reduce the release and accumulation of contaminating particles and organisms.**
- The surface material **should be such that they can withstand the effects of cleaning agents and disinfectants.** The ceilings are **scaled so that the contaminants do not enter from the space above them.**
- Unclean-able recesses should be avoided within the clean rooms to minimize the accumulation of contaminating particles. Thus, **the wall and floor junction should be covered.** Minimum **shelves, ledges, cupboards, and equipment should be present.** **Non opening and sealed windows should be present to prevent the entry of contaminants.**

# Laminar Flow Equipment (Laminar Airflow Hood)

- A Laminar Airflow Hood (LAFH)/ Laminar Aseptic Hoods, or a workbench, is a primary engineering control device which provides the following services during aseptic compounding
  - 1) Clean air to the critical sites (immediate aseptic compounding area),
  - 2) Constant flow of air out of the work area to prevent the entry of room air, and
  - 3) Outward flow of air from the hood that suspends and removes contaminants which have been introduced in the work area by personnel.



**4.2: Section through a Mini-Pleat High-Efficiency Filter**

- A High Efficiency Particulate Air (HEPA) Filter is the most important part of a LAFH.
- The air within the room is taken into this filter and **passed through a pre-filter which removes the gross contaminants (lint, dust, etc.)**.
- The air is **then blown at a uniform velocity through the hood and HEPA filter in a unidirectional (laminar flow) manner over the critical sites (immediate aseptic compounding area)**.
- HEPA filter is a **particulate filter which traps the airborne particles and microbes; but allows the gases to pass through**.
- HEPA filter **should be fitted either at or near to the clean room inlet**.
- A **pre-filter is fitted upstream of the HEPA filter**, thus extending the final filter's life.
- **A fan is also fitted which pumps the air through the filter.**

- The filter medium used in HEPA filters is made up of pleated fiberglass paper. Parallely arranged pleats not only increase the filter surface area but also the air flow through the filter (figure 10.2). This parallel arrangement of filter medium also allows the filter to retain a compact volume. In the traditional type of HEPA filters, aluminium foil was used as spacers, which are no longer used in the modern mini-pleat type of filter (now widely used). The minipleat filters have a shallower depth in construction than the traditional HEPA filter. The filter material is sealed to an aluminium frame within the filter (figure 10.2). One side of the filter is protected with a coated mild steel mesh. HEPA filters provide:
  - 1) A high air flow rate,
  - 2) A high particulate holding capacity, and
  - 3) A low-pressure drop across the filter.

- HEPA filters remove larger, medium, and smaller particles from the air by inertial impaction, direct interception, and by Brownian diffusion, respectively.
- The HEPA filters are least efficient in removing particles of about 0.3 $\mu$ m size.
- However, its efficiency of removing particles is affected by air velocity and filter packing.
- It removes larger and smaller particles with more efficiency.
- The LAFH works on the principle that twice-filtered laminar layers of aseptic air continuously sweep the work area within the hood to prevent the entry of contaminated room air.

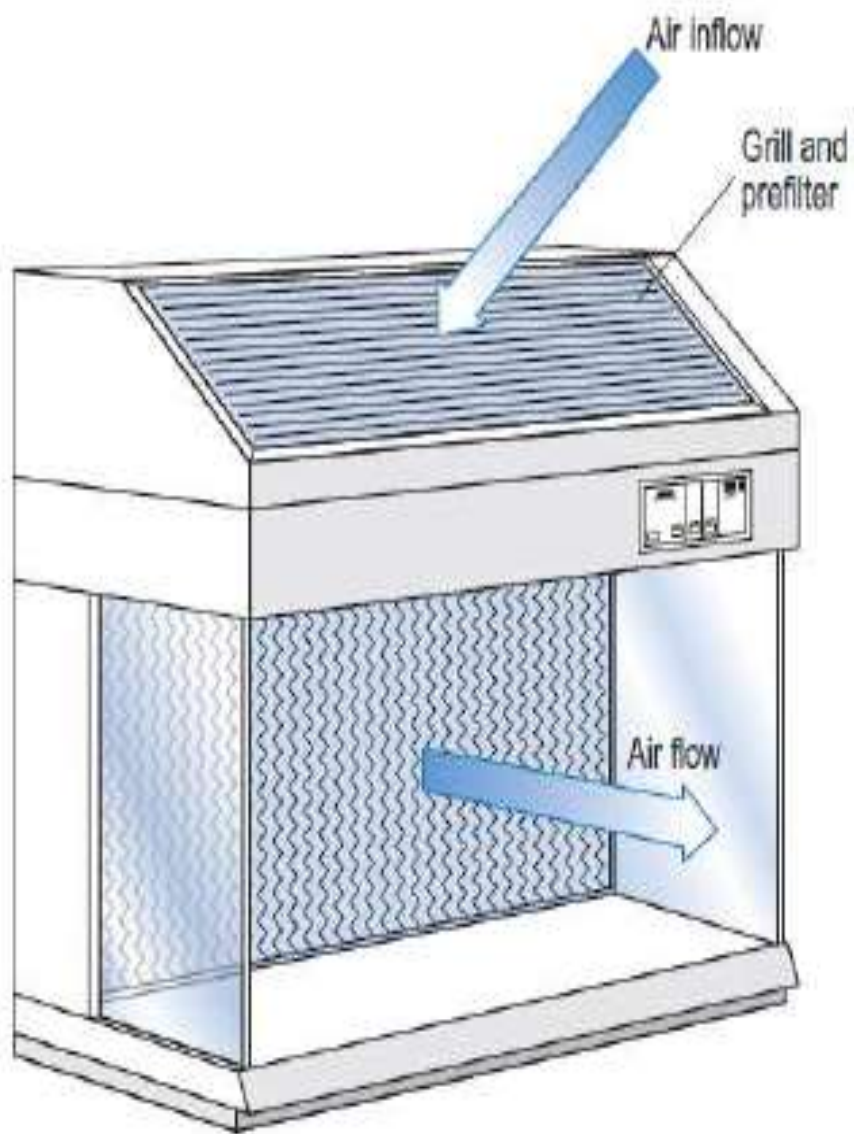
**Types:** A laminar air flow hood is of two types:

- 1) Horizontal Airflow Hoods:** These hoods sweep the filtered air from the back to the front of the hood. An electrical blower draws the contaminated room air using a pre-filter (similar to a furnace filter), to remove gross contaminants. The pre-filter demands timely cleanliness and replacement. The air after passing through the pre-filter is accelerated (but not pressurised) so that a consistent airflow distribution reaches the final filter (HEPA filter), present at the back portion of the hood's working area.
- HEPA filter removes 99.97% of  $0.3\mu$  or larger sized particles, thus removing most of the  $0.5\mu$  or larger sized airborne microorganisms.

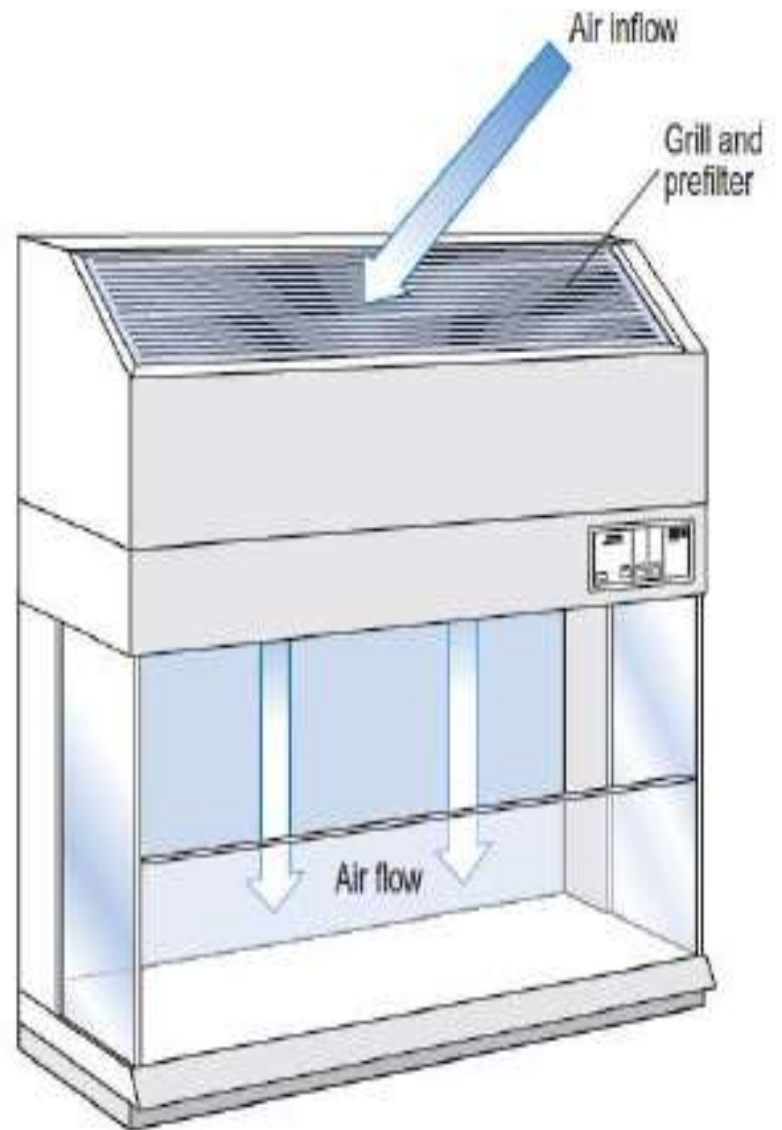


## 2) Vertical Airflow Hoods:

- These hoods sweep the filtered air vertically.
- The air passing through HEPA filter merges from the top and passes downward through the working area.
- The vertical airflow hoods work on the principle that the air flow between the HEPA filter and the component used for CSPs preparation should not be interrupted.
- When a foreign object comes in between the sterile object and the HEPA filter, the wind turbulence (zone of turbulence) in the critical area increases, and foreign contaminants are carried to the sterile work surface, thus contaminating the injection port, needle, or syringe.
- For ensuring complete sterility, nothing should pass behind a sterile object in a horizontal airflow hood; and in case of vertical airflow hood, nothing should pass above the sterile object.
- The materials within the compounding work area interrupt the pattern of air blowing from the HEPA filter.



**Figure 4.3: Horizontal Laminar**



**Figure 4.4: Vertical Laminar**

# Operating Principles

A Laminar Air Flow Hood (LAFH) operates on the following general principles:

- 1) It should be placed away from traffic, doors, air vents, or anything that can produce air currents, to avoid entrance of contaminants.
- 2) It should remain on for 24 hours otherwise, non-filtered, non-sterile air occupies the compounding work area. Thus, when again it is turned on, it should be left for 30 minutes for disinfection and then used. This also allows the hood to eliminate the non-sterile air from the compounding work area.
- 3) Before using the LAFH, its interior working surfaces should be disinfected using 70% isopropyl alcohol (or other suitable disinfecting agents) and a clean, lint-free cloth. Cleaning should be done efficiently beginning from the HEPA filter in a top-to-bottom and back-to-front motion, to completely remove the contaminants.

- 4) Cleaning should be done after every compounding batch and also when the work surface becomes dirty. Some materials on the surface are insoluble in alcohol (e.g., dextrose and amino acids), thus sterile water is used initially. After wiping the water from the surface, it is then cleaned using alcohol. Plexiglas sides present in some types of LAFHs, should not be cleaned using alcohol but with warm water and a germicidal detergent (e.g., Lysol IC, Vesphene, or LpH).
- 5) HEPA filter grill (protective grill) should be cleaned in such a way that it does not get wet.
- 6) Objects essential for aseptic compounding should be placed in the hood. Paper, pens, labels, or trays should not be placed in this area.
- 7) HEPA filter should not be brought into contact with cleaning solution, aspirate from syringes, and glass from ampoules (should not be opened towards the filter)
- 8) The operators during compounding should not wear any jewelry on hands or wrists since they affect the integrity of personnel clothing (gowns and gloves).
- 9) The operators should minimize talking and should cough away from the compounding work area.

- 10) The operators should avoid or reduce the unnecessary movement within or around the LAFH to minimize the airflow turbulence.
- 11) Smoking, eating, gum chewing, and drinking are strictly prohibited in the aseptic environment.
- 12) The objects should be arranged to get full benefit of the laminar air flow. Critical items should be placed close to the air source. The objects in horizontal hood should not be placed closer than 3 inches from the back of the hood (ensuring that nothing should be in direct contact with the filter). The pharmacist in some cases, may stack a few objects (such as IVPBs), but from lower to higher starting from the back of the hood. Also, the stack should contain only 3- 4 objects.

- 13) The aseptic procedures should be carried out 6 inches away from the sides and front edge of the hood to prevent contamination.
- 14) Testing of primary engineering controls (e.g., LAFHs, BSCs, and CAIs) should be carried every 6 months by qualified personnel. Testing is also required whenever the device is moved, or the filter is damaged. Specific tests are used for the certification of integrity of airflow velocity and HEPA filter.

## Uses:

- Given below are the uses of a laminar air flow hood:
- 1) It has various applications, especially where an individual clean air environment is required for smaller items, e.g., particle sensitive electronic devices.
- 2) It is used for special operations in laboratories.
- 3) It can be tailor made to the specific requirements of laboratories and are also used for general lab work, especially in medical, pharmaceutical, electronic, and industrial sectors.

# Advantages

- Given below are the advantages of a laminar air flow hood:
  - 1) The sterile area is spacious.
  - 2) Since the sterile area does not become hot, the plant material can stay for a longer duration.
  - 3) Bigger flasks having wide lids can be used.



## Limitations

- The airflow velocity can be overcome easily without any strict work practices and aseptic technique, thus an area of turbulence is created which can introduce room contaminants (particles and microorganisms) into the critical work area.
- A laminar air flow hood should remain on for 24 hours. If it is turned off; it should be left on for at least 30 minutes for its disinfection before use.