

UNIT-IV

Source of contamination in aseptic area



CENTURION
UNIVERSITY
*Shaping Lives...
Empowering Communities!*

RASMITA JENA
ASSISTANT PROFESSOR
SoPLS, CUTM, BBSR

- Study of different sources of contamination in an aseptic area
- Method of prevention

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.**

Different Sources of Contamination in an Aseptic Area

There are various contamination sources in an aseptic area, which are discussed below:

1) Personnel: Those supervising, performing, or controlling drug manufacturing are a potential source of microbial contamination, due to the following reasons:

- i) Inadequate training,
- ii) Direct contact between the hands and starting materials, primary packaging materials, and intermediate or bulk products,
- iii) Improper hygiene,
- iv) Unauthorized personnel entering the production, storage, and product control areas,
- V) Insufficient gowning and protective equipment, and
- vi) Eating, drinking, or smoking within the storage and processing areas.

2) Buildings and Facilities: These are also important contributors to microbial contamination due to the following reasons:

- i) Inadequate size and organization of the space, which lead to selection errors (such as mix ups or cross-contamination between consumables, raw materials, in-process materials, and finished products),
- ii) Poor filth and pest controls,
- ii) Rough floors, walls, and ceilings,
- iv) Absence of air filtration systems,
- v) Inadequate lighting and ventilation systems,
- vi) Poorly located vents, ledges, and drains, and
- vii) Improper washing, cleaning, toilet, locker facilities, sanitary operation, and personal cleanliness.

3) Equipment and Utensils: These are used during processing, holding, transferring and packaging. They are the common sources of microbial contamination due to the following reasons

- i) Unsuitable design, size, corrosion-causing materials, static material accumulation, and/or adulteration with lubricants, coolants, dirt, and sanitizing agents,
- ii) Inadequate cleaning and sanitization,
- iii) Inefficient cleaning and maintenance due to their designing
- iv) Inappropriate calibration and irregular service, and
- v) Using defective equipment.

4) Raw Materials: These are used during production and are considered a potential source of contamination due to the following reasons:

- i) Improper storage and handling, which leads to mix-ups or selection errors,
- ii) Microbial or chemical contamination,
- ii) Degradation due to extreme environmental conditions (like heat, cold, sunlight, moisture, etc.),
- iv) Wrong labeling.
- v) Incorrect sampling and testing, and
- vi) Using materials not meeting the acceptance criteria.

5) Manufacturing Process: During the manufacturing process, microbial contamination of raw materials, intermediates or packaging materials can widely occur due to the following reasons:

- i) Absence of facilities required for manufacturing of a single product,
- ii) Improper cleaning between batches for minimizing the amount of product changeovers,
- ii) Use of an open manufacturing system for exposing the product to the room environment,
- iv) Improper zoning,
- v) Lacking an area line clearance (as per the approved procedures) after each cleaning process and between each batch, and
- vi) Lack of cleaning status labeling on all equipment and materials used within the manufacturing facility.

- A HVAC (Heating, Ventilation, and Air Conditioning) System: An inappropriate HVAC system is a possible source of microbial growth and also disperses the contaminants throughout the manufacturing unit.

This occurs due to the following reasons:

- i) Organic materials accumulate in or near HVAC air intakes,
- ii) Inadequate air filtration system,
- iii) Inadequate magnitude of pressure differentials, which causes flow of reversal,
- iv) Incorrect ratio of fresh air to re-circulated air,
- v) Incapability of accessing ventilation dampers and filtering from outside the manufacturing areas, and
- vi) Non-directional airflow within production or primary packing areas.

Methods of Prevention of Contamination

- The steps by which microbial contamination of products can be prevented in aseptic areas are discussed below:

1) Personnel: They can take the following measures:

- i) Access to production areas by the unauthorized personnel should be restricted, and only trained ones should be allowed to enter.
- ii) Adequate personnel hygiene should be maintained.
- iii) The personnel should be given proper and regular training with respect to hygiene as well to ensure that their activities do not hamper the product quality.
- iv) Personnel entering the manufacturing area should wear protective clothing (overgarments, hair cover, beard or moustache cover, and overshoes).
- v) Personnel should avoid touching with naked hands the exposed products or any part of equipment in contact with the product.

2) Facility Design: This includes the following measures:

- i) In aseptic rooms, the differential air pressures should be higher than the adjacent controlled areas.
- ii) Air filtration and air change rates should be set to attain the defined clean room class.
- iii) Unidirectional (laminar flow) air flow should be maintained over critical areas at sufficient velocity to sweep particles away from filling/closing area.
- iv) Ambient temperature and humidity should not be very high.
- v) The ventilated cabinets, RABS (Restricted Access Barrier System), isolators systems, etc. should be used depending on the facility/product risk assessment results in order to achieve an absolute or partial barrier to contain microorganisms at their point of use
- vi) The areas of unequal risk are separated by UV air locks and door barriers.

- vii) All open-container processing should be performed within the isolator/RABS.
- viii) The air pressure of the changing room should be negative with respect to the manufacturing area corridor, but positive with respect to the external adjacent areas.
- ix) The ventilation dampers, specially designed filters, and other services should be positioned such that they can be accessed from outside the manufacturing areas (service voids or service corridors) for maintenance purposes.
- X) An impermeable barrier should be used in appropriate areas to prevent cross- contamination between two zones, such as closed systems, pumped, or vacuum transfer of materials.
- xi) HVAC air distribution components should be used for preventing the spreading of contaminants generated within the room.
- xii) All rooms and surfaces should be maintained and monitored for viable and non-viable particulates and this facility should be re-certified on a semi-annual basis. Facility and equipment design cannot eliminate microbial contamination completely but good risk assessment and consequent hygienic design can reduce these risks several times. For example,
 - i) Flow of man and material should be uniform,
 - ii) Equipment having smooth surfaces of appropriate material can facilitate effective cleaning, and
 - iii) Closed Material Transfer Systems.

3) Access to Areas: This includes the following measures:

- i) Access to production, packaging, and QC areas by unauthorized personnel should be restricted.
- ii) Personnel should gain access to these areas only via changing rooms.
- ii) Materials should be accessed via specific routes (generally air locks).

4) Building Requirements: This includes the following measures:

- i) Smooth, crack-free, and easily cleanable floors, walls, and ceilings should be used as they facilitate easy and effective cleaning.
- ii) Windows or viewing panels should be closed (non-opening), fixed with wall panels, and sealed to prevent accumulation of dust and microbial contaminants.
- iii) The designing of pipe work, ventilation, and light points should be such that Creation of recesses which are not easily cleanable is avoided.
- iv) Sinks of stainless steel should be present within the production areas.

5) Cleaning and Disinfection: This includes the following measures:

- i) Time-to-time cleanliness and disinfection of the areas should be done.
- ii) Adequate hygiene should be maintained in every aspect of the drug product manufacturing.
- iii) Cleaning agents of proper grades should be used for minimizing health risks.
- iv) Contact time, application, temperature, mechanical action, and the chemistry of cleaning agents should be considered during the cleaning process.
- v) The cleaning agents should not be directly applied on the product.
- vi) The cleaning practices should be validated to prove that the process effectively controls microbial contamination.

6) Utilities: This includes the following measures:

- i) Water of pharmaceutical grade, microbiologically controlled and monitored should be used in the manufacturing of products.
- ii) Clean and additive-free steam should be used for cleaning and sanitisation of production tools and equipment, and to supply for autoclaves and humidification.