PARENTERAL PRODUCTION

INTRODUCTION:

parenteral preparations are sterile, pyrogen-free liquids (solutions, emulsions, or suspensions) or solid dosage forms containing one or more active ingredients, packaged in either single-dose or multi-dose containers.

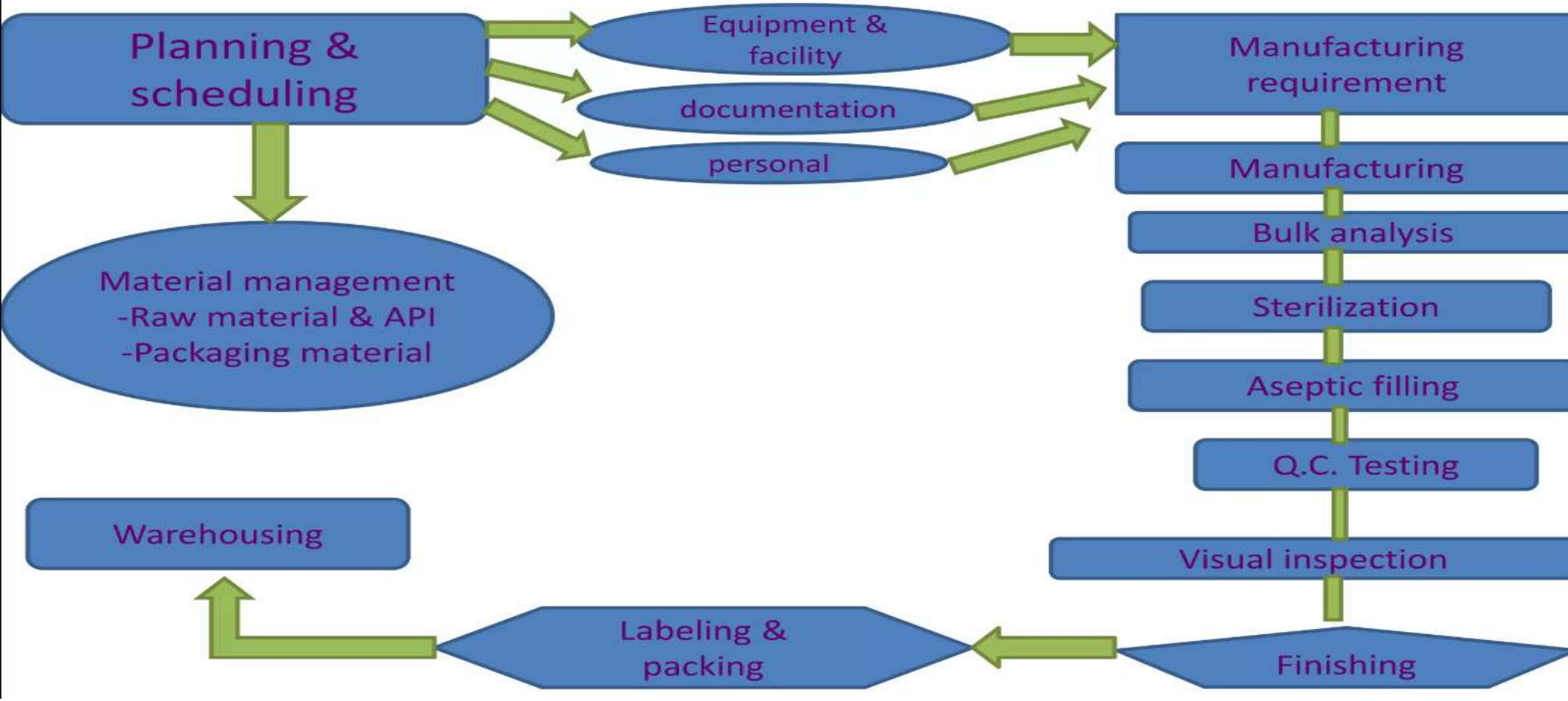
They are intended for administration by injection, infusion, or implementation into the body. Parenteral drugs are administrated directly into veins, muscles or under the skin or more specialized tissues such as the spinal cord.

TYPES: there are four main forms of parenteral preparations:

- injections,
- intravenous infusions (large volume parenterals),
- powders for injections, and
- implants

certain injections and intravenous infusions may be presented in the form of sterile concentrated solutions, which must be suitably diluted before use.

OVERVIEW OF MANUFACTURING PROCESS OF PARENTERALS



FLOW OF MATERIALS:-

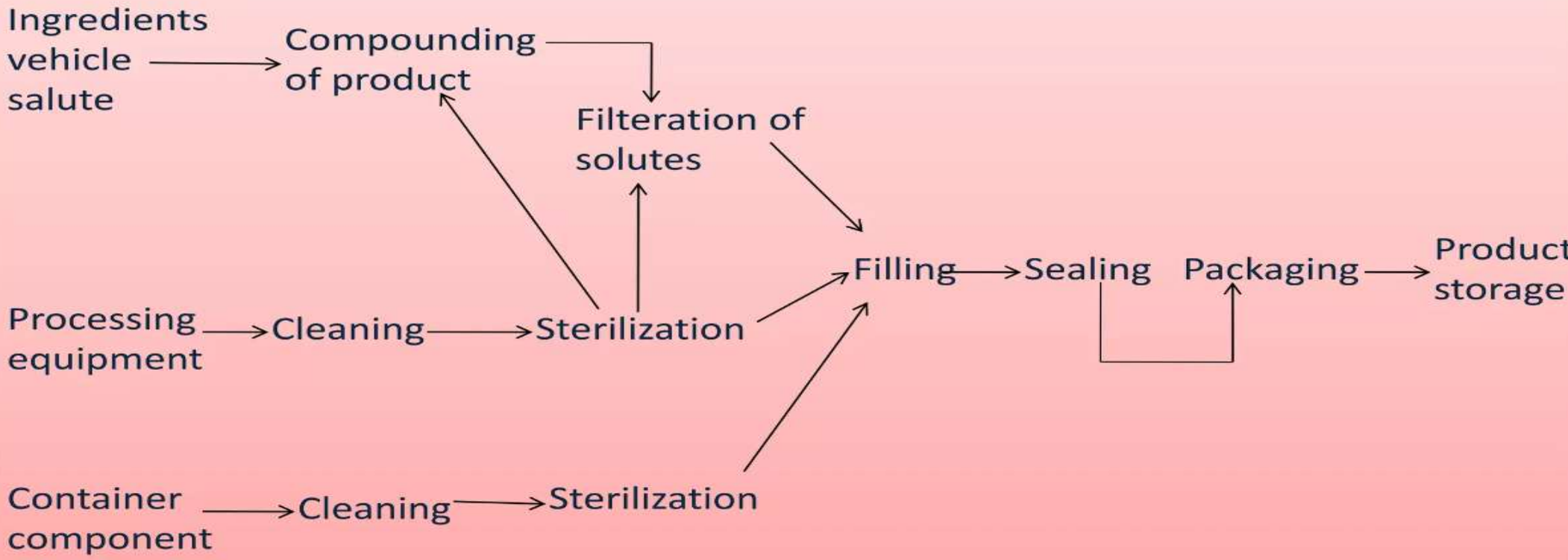


Diagram of flow of materials through the production department

[QUALITATIVE LAYOUT OF PARENTERAL MANUFACTURING]

Function	Area	
	Square meter	Percentage
Production	11,094	45.1
Warehouse	7,606	30.9
Utility	1,716	4.1
Quality control	1,716	7.0
Administration	1,018	4.1
Maintenance	1,014	4.5
Employee services	1,014	4.1
Security	39	0.9
Total	24,607	100.0

1.AREA PLANING AND ENVIRONMENTAL CONTROL:-

Area planning may be addressed by functional groups ground this critical area with particular attention given to maintaining cleanliness.

Functional groupings:-

Warehousing:-

- The storage of spare parts, air filters, change parts, water treatment chemicals, office supplier, janitorial supplies, uniforms, an so on may be handled as central storage or individually by department.
- Finished product and certain raw materials need special environmental storage conditions, such as, temperature and humidity control.

Administrative areas :-

1) Administrative area planning requires careful analysis of the direct and indirect administrative requirements of a particular plant.
2) Successively higher levels of supervision are usually provided successively larger office areas.
3) Some offices are individual, while some are grouped in an “open area concept”,

ZONES AS PER GAZZETE OF INDIA:

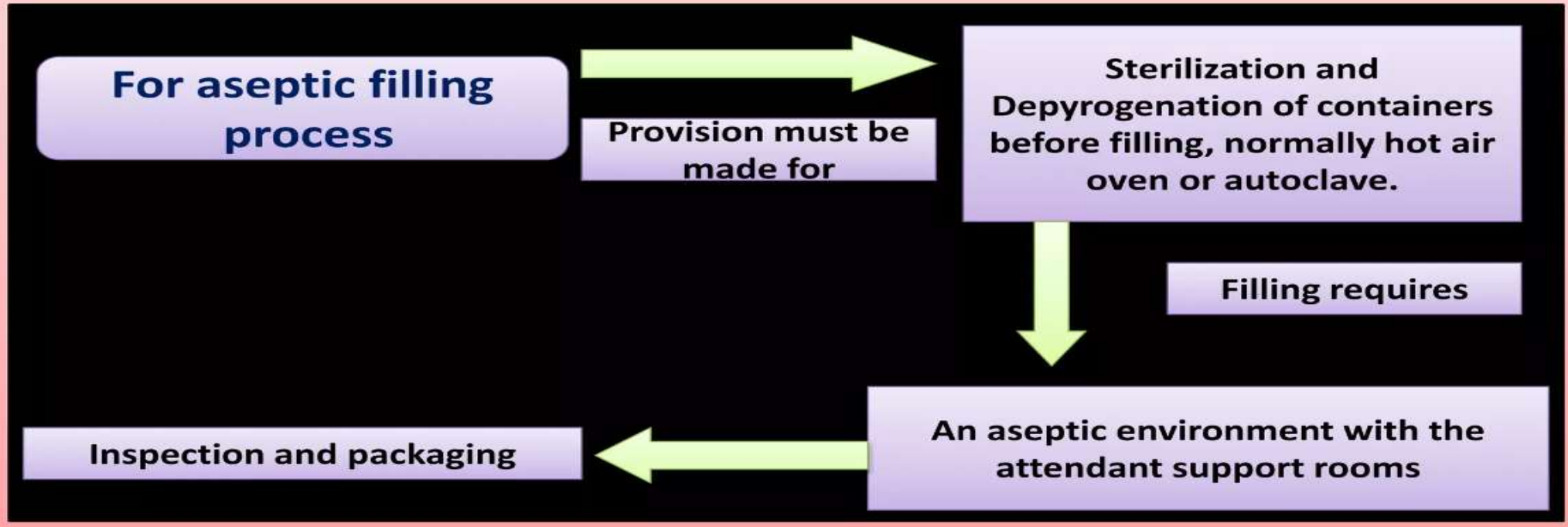
1st.zones as per gazette of India

- White zone:- final step (filling of parenteral)
- Grey zone:- weighing, dissolution & filtration.
- Black zone:- storage, worst area from contamination view point.

ENVIRONMENTAL CONTROL ZONE GROUPING :-

Zone 7:- filling line:-

The walls of the filling area are the last physical barrier to the ingress of contamination, but within the filling area a technique of contamination control known as laminar flow may be considered as the barrier to contamination.



Zone 6:- filling area:-

Zone 6 is a distinct zone of the controlled environment area for an aseptic filling process but may not be distinct zone for non-aseptic filling process.

Zone 5:- weighing, mixing, and transfer area:-

Zone 5 encompasses activities of "weighing, mixing, filling or transfer operations" addressed by c GMP section 212.81 which are not handled as zone 6 but which require a controlled environment.

Zone 4:- clean area:-

Activities in this may include washing and preparations of equipment or accumulation and sampling of filled product.

Zone 3:- general production and administration area:-

The third zone of environmental controls is formed by the periphery of the general production area.

Only essential materials-handling equipment and personnel.

Zone 2:- plant exterior:-

It is a base point from which to work in determining the requirements for the various control barriers.

Control zone 1 might include the maintenance of sterile areas around the facility.

2. WALL & FLOOR TREATMENT:

The design of filling areas or more generally, controlled environment areas involves attention to many seemingly minor details. The basic cleanlability requirement includes smooth, celanable walls, floors, ceilings, fixtures, and partition exposed columns, wall studs, bracing, pipes, and so on are unacceptable.

The need for cleanability also eliminates the open floor system commonly used in the microelectronics industry for laminar airflow rooms.

The goal of the designer, when creating the details for the architectural finishes and joining methods, is to eliminate all edges or surfaces within the room where dirt may accumulate.

All inside walls must be finished;

Example: common methods of finish are block, plaster, or gypsum board.

3. LIGHTNING FIXTURES :

Lighting fixtures should be reduced flush with the ceiling. Areas having a full HEPA ceiling obviously cannot accommodate recessed lighting fixtures. In these areas, fixtures are of a special "tear drop" shape which minimizes disruption to the laminar airflow pattern.

4. CHANGE ROOMS :

Personnel access to all controlled areas should be through change rooms. Change rooms concepts and layouts vary from single closet size rooms to expensive multi-room complexes.

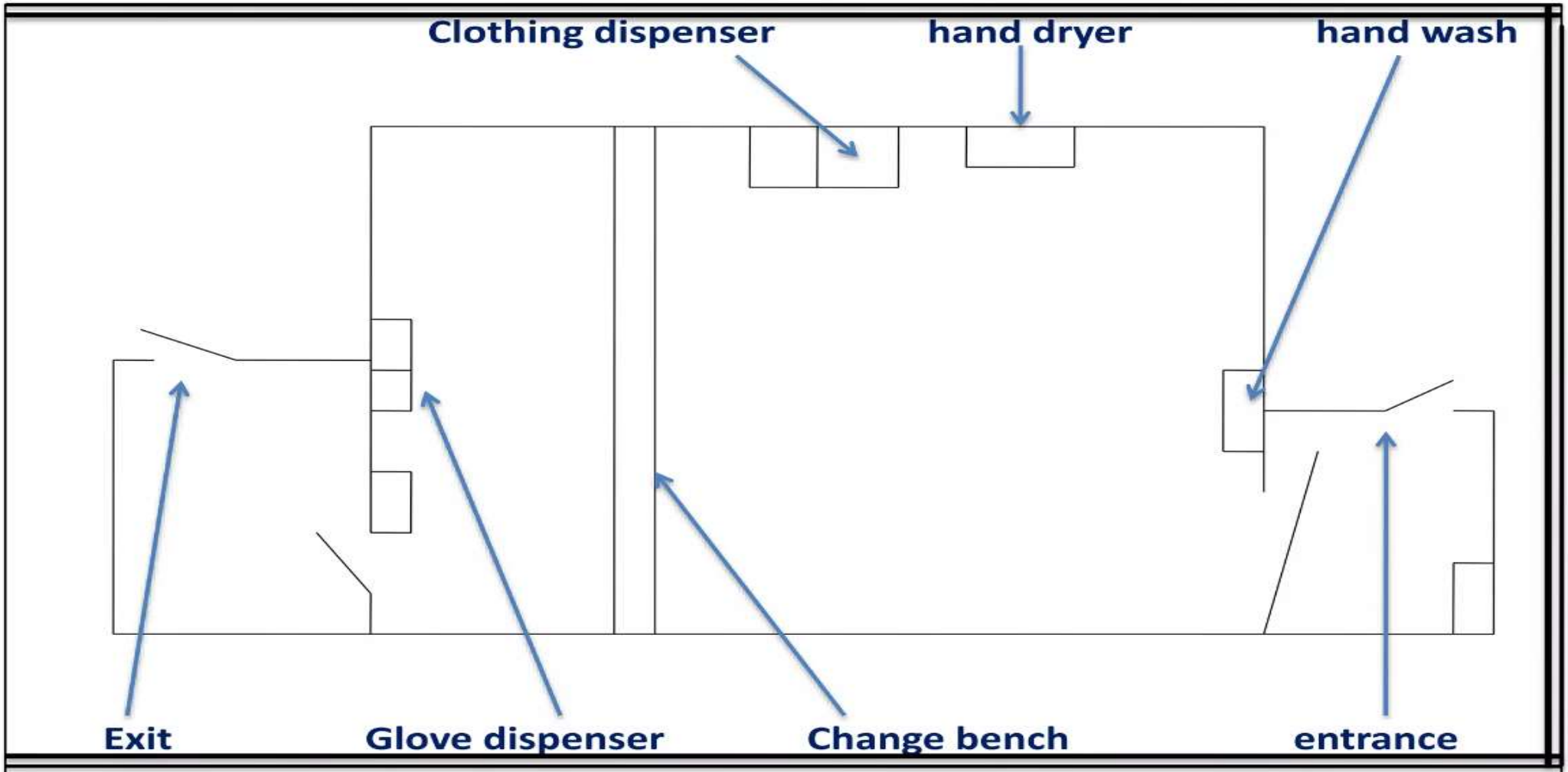
Entrance to a change area is normally through vestibules whose doors are electrically interlocked so that both cannot be opened simultaneously, thus maintaining the necessary air pressure differential to prevent the entry of airborne contamination.

Upon entry into the change room wash skins are provided for scrubbing hands and forearms.

Further control may be achieved by using filtered and heated compressed air for drying to reduce further particular potential.

After hands are dry, garments are taken from dispensers and donned while moving across a dressing bench.

As a final growing step, aseptic gloves are put on and sanitized. Exit from the change room to the controlled area is, like entrance, through an interlocked vestibule.

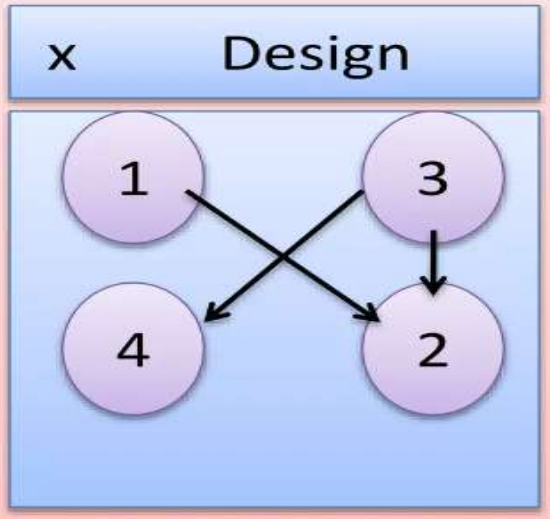

Clothing dispenser
hand dryer
hand wash
Exit
Glove dispenser
Change bench
entrance

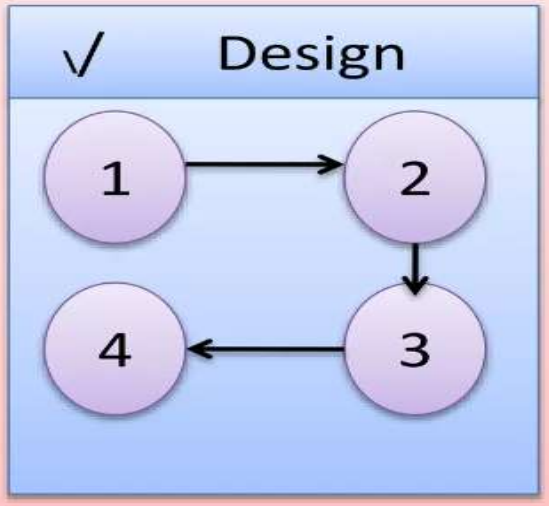
Change room

5. Personnel flow :-

The movement of personnel should be planned during the design of individual plant areas. Each individual production area may have a smooth and efficient personnel flow pattern, a discontinuous or crowded pattern may develop when several individual production area plants are combined.

The flow of material and personnel through corridors are inefficient and unsafe paths for moving materials, particularly if heavy forklifts are required.





Discontinuous and crowed flow patterns can decrease production efficiency, increase security problems, and increase the problem of maintaining a clean environment.

6. UTILITES AND UTILITY EQUIPMENT LOCATION :-

Utilities :-

Piping system in particular, must be initially and often periodically cleaned and serviced. Exposed overhead piping is not acceptable from a cleanliness or contamination stand point since it collects dirt, is difficult to clean and may leak. Buried or concealed pipe may require unacceptable demolition for cleaning or repair.

Utilities equipment location :-

Public utilities require space for metering. In addition to meeting, electrical power system require for switchgear and transformer.

Water systems usually require treatment to ensure consistent quality. Plant generated utilities typically require steam boilers, air compressors, and distillation, the typical "boiler room" approach. Proper equipment maintenance is difficult in foul weather, especially winter.

Heavy equipment may damage the roof-structure, particularly if the equipment location requires numerous penetrations through the roof which, coupled with equipment vibration, will invariable lead to leakage.

7.Engineering and maintenance :-

From an engineering stand point, even a location outside the plant can serve well if access to the production area by engineers for field work is not too difficult often particularly in small or less complex plants, maintenance or other plant service functions such as utilities or combined with engineering, making an in-plant location desirable.

Maintenance responsibilities cover all areas of the plant and can generally be grouped into two categories: plant maintenance and production maintenance.

1) production maintenance is a direct production support function and all the routine and recurring operating maintenance work. Production maintenance facilities are usually minimal, often only a place to store a tool box, and seldom have more than a small workbench.
2) plant maintenance operations, in contrast, are more diverse. They vary from heavy maintenance on production equipment to cosmetic work on the building exterior and often include plant service functions such as sanitation, ground sweeping, or waste disposal.

LIST OF EQUIPMENTS (as per schedule-M):

The following equipments is recommended:

a)Manufacturing area :-

1. Storage equipment for ampoules, vials bottles and closures.
2. Washing and drying equipment.
3. Dust proof storage cabinet.
4. Water still.
5. Mixing and preparation tanks or other containers.
6. Mixing equipment where necessary.
7. Filtering equipment.
8. Hot air sterilizer.

b) Aseptic filling and sealing room:-

9. Benches for filling and sealing.
10. Bacteriological filters.
11. Filling and sealing unit under laminar flow work station.

C) General room:-

12. Inspection table
13. Leak testing table.
14. Labeling and packing benches.
15. Storage of equipment including cold storage and refrigerators if necessary.