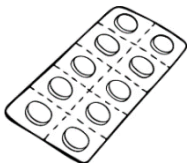
Part B – Health Facility Briefing & Design

256 Pharmaceutical Factories



iHFG

International Health Facility Guidelines

2024

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256 Pharmaceutical Factories

1 Introduction

This Functional Planning Unit (FPU) covers the requirements of Pharmaceutical Factories. The Pharmaceutical Factory is where pharmaceutical drugs are produced. The process involves various stages from raw material receipt, weighting, sampling and production to packaging, warehousing and dispatch. The staff working in different sections are required to follow different flow patterns such as initial changing, gowning and going through one or more ante-rooms.

The facility may have a single or multiple production runs, requiring one or several production rooms. The production rooms are regarded as clean rooms and subject to strict clean room construction standards as well as air pressurisation regimes. The exact pressurisation regime will depend on the type of products being produced, requiring either Positive or Negative Pressure systems.

This guideline covers a range of scenarios and facility configurations. Any other permutations of facilities should be based on the principles and examples provided in this FPU as well as the type, chemistry and science behind the products being produced.

2 Functional and Planning Considerations

Operational Models

The Pharmaceutical Factory models will take into consideration the following:

Type of pharmaceuticals manufactured

- Sterile products
- Radio pharmaceuticals
- Non-sterile pharmaceutical products
- Biological active
- Aerosols
- Medicinal gases
- Derived from human blood or plasma
- Herbal medicinal products
- Liquids, creams or ointments
- Chemotherapy and other hazardous products

Operational factors within the facility

- Quantity being manufactured
- Personnel flows
- Material flows
- Process requirements

Hours of Operation

- The factory will generally operate 5 days per week from 8 am to 6pm daily. The exact hours of operation should be determined by the Operational Policy, trade license conditions (if any) and operational licence granted (if any).
- Operational hours can also be adjusted considering production need and urgent requests.

Functional Zones

The Pharmaceutical Factory shall include the following main areas:

- Raw material receipt and store

- Sampling and Weighing
- Production
- Packaging
- Warehousing
- Staff Amenities
- Administration

The following standard rooms/areas are required:

- Entry/ Reception/ Lobby area
- Loading Docks for unloading raw materials and loading of finished products with a Control Room to supervise material movement
- Raw Material Warehouse, for storage of raw materials used for production
- Sampling area, to perform a quality check on the materials and primary packaging used during production
- Weighing area (optional), for dispensing of materials to be used during production of a batch
- Primary Staff Change Room, gender separated, where personnel will change from their outdoor clothing to their facility uniforms
- Production/ Clean Corridor (only required if multiple production rooms are provided)
- Airlock(s)/ Gowning Rooms (Gown-up and Gown-down)
- Production Clean Rooms
- Secondary Packaging Area
- Warehouse for storing of final packaged pharmaceuticals
- Administration / Office/ Support Areas:
  - Offices and workstations for key personnel, including Quality Assurance personnel and Service line managers
  - Meeting room
- Staff Amenities:
  - Staff Room
  - Locker area (may be shared with primary staff change room)
  - Toilets and Showers, gender separated (may be shared with primary staff change room)

The above zones are briefly described below.

Entry/ Reception/ Lobby Area

Personnel and visitors should enter and exit the factory via a lobby area. Staff within the reception area shall control the access of personnel and staff into the factory. Optionally, visitor and staff access may be separated, but both monitored by a reception or security counter with control over who enters the production areas of the facility.

Loading Docks

There will be a minimum of two loading docks:

- A dock for unloading the raw materials. This will be conveniently connected to the Raw Materials Warehouse
- A dock for loading the finished products and packaged pharmaceuticals from the Warehouse for distribution

Both docks will be monitored from a Control office to control and monitor the movement of the materials and products.

The two docks may be separate for maximum operational efficiency and quality control.

However, based on the design geometry, the two docks may be side by side with access off the same service road. However, the flows of goods through the two docks will be different following the diagrams in this FPU.

Raw Material Warehouse

Items from the loading dock will be transferred to the Raw Material Warehouse or Store.

- This area will be temperature and humidity controlled to maintain the viability of the raw materials.
- Raw materials should be stored appropriately depending on their individual requirements, whether at room temperature, in refrigerators or freezers etc.
- For Hazardous materials:
  - These must be unpacked from shipping containers in an environment that is at negative pressure relative to the surrounding areas.
  - They must be stored separately from other inventory and at negative pressure storage conditions to prevent exposure to personnel. Should the volume of the hazardous material be small, they can then be stored within the production room itself.
  - A refrigerator used to store hazardous materials should preferably have an exhaust installed next to the compressor or behind the refrigerator.
  - Storage of the material should ensure no spillage or breakage in the event of any natural disaster.
- The Warehouse or Store shall be security controlled.
- The temperature control for the warehouse should be alarmed. It should have both local and remote display and monitoring of the alarm.

Sampling Area

The Sampling Area is used to perform a quality check on the materials to be used during production including the primary packaging and the processing agents etc. A small quantity of a batch of the material intended to be used during production will be assessed.

- The Sampling Room provides a controlled clean environment to maintain the sterility and viability of the materials whilst being exposed to the environment during sampling.
- This area should be temperature and humidity controlled.
- The HVAC system for this area should have the same pressurisation classification as the production room where the material or products shall be exposed to the environment.
- The Sampling Room should prevent cross-contamination of the materials.
- The facilities should protect personnel during the sampling process.
- The transfer of material from the Raw Material Warehouse or store into the Sampling Room should be via a material airlock or two-door interlocking pass-through hatch.
- Warehouse staff should access the sampling room via a Staff Gowning Room with cross over bench.
- The Sampling Room shall have a laminar flow hood to protect the material from contamination during sampling.
- A clean up room for washing the equipment used during sampling should be available, either accessed from within the Sampling room or in close proximity to the Sampling Area.
- Lighting within the Sampling Room should be selected taking into consideration light-sensitive material that may be inspected.
- The materials can be transferred from the Sampling area to the Production Area via a Material Airlock or two-door interlocking pass-through hatch.

Weighing Area

The optional Weighing Area is where raw materials are weighed and transferred to clean containers for use in the production area. The requirement for a dedicated Weighing Area will

depend on the operational policy of the facility and product types. As an alternative Weighing may also occur in the Production Room.
The Weighing Area will have three main sections separated by material airlocks:

- Pre-staging

The external packaging of the materials to be weighed are removed here and the containers are wiped down. The pallet or cart is then moved to the material airlock by warehouse personnel that then exit the airlock. Weighing personnel then enter the material airlock, remove the material and transfer it to the weighing area.

- Weighing Room

The materials are weighed and dispensed here. This is done under a laminar flow hood. Any unused material is returned back to the pre-staging area and can be stored there or returned to the warehouse. Once dispensing is complete, the weighing personnel transfer the materials on a clean cart to the material airlock leading to the production area. The cart is then picked up by personnel to the post-staging area.

- Post-staging

Post-staging is recommended if multiple weighing areas are used for different product types. Materials are then transferred from the Post-staging area to the Production Room via the Production Room airlock. For small quantities and only a single weighing area, Post-staging may not be required.

The Weighing Area should also consider the following requirements:

- There should be a Unidirectional flow of materials.
- The area should be temperature and humidity controlled.
- Hazardous and non-hazardous material should be kept separate.
- The HVAC system for this area should have the same area pressurisation regime (negative or positive) as the production room where the material or products shall be exposed to the environment.
- During weighing, any dust produced shall be contained and the operator should be protected.
- A clean up room for washing the equipment used during weighing should be available, either accessed from within the Weighing Room or in close proximity to the Weighing Area.

Primary Staff Change Rooms

The Primary Staff Change areas are where staff change out of their outerwear (street clothes) into the factory uniform. The same Primary Staff Change Rooms may be used by all staff including administrative staff, production staff and support staff. The Primary Staff Change Rooms are separate from the Gowning rooms which are also required before entering certain areas such as the Production Room and Sampling Room.

The following apply to the Staff Change Rooms:

- Toilet facilities should only be present in the primary change rooms
- At least one shower per change room should be provided.
- Staff Change Rooms must be gender separated.
- Staff change rooms should have lockers for the secure storage of street clothes.
- It is recommended that visitors should have separate change rooms to staff, however this is not mandatory.
- Administrative staff may not require changing into uniforms unless they are required to periodically visit the Production Rooms or the Sampling Room.
- The Change Rooms for the Administrative staff may be separated for convenience, if preferred.

Production/ Clean Corridor

The Production/ Clean Corridor should be provided if more than one Production Clean room is required. The function of the Clean Corridor is to link the Raw Material Warehouse, Post Staging and Sampling areas to multiple Production Clean Rooms.

When the production involves the potential creation of dust, the Clean Corridor also serves to contain any dust produced in the Production Rooms. In such situations the corridor shall be at a higher pressure compared to the airlock leading into the Production Clean Room.

If only a single production room is intended, the provision of a Production Clean Corridor is not mandatory. In such situations, the Materials Airlock can be used instead of the Production Clean Corridor.

The Production/ Clean Corridor relative pressurisation against the Airlock/ Gowning Room will be Neutral pressure. Therefore, the Airlock/ Gowning Room may be either positive or negative compared to the Neutral pressure.

See below regarding the requirements for the air pressurisation of the Airlock/ Gowning Room.

Airlock/ Gowning Room

This Airlock/ Gowning Room is required for access to each Production Clean Room. It is located between the Production Clean Corridor or Materials Airlock and the Production Clean Room.

Based on the facility operational policy and the type of products being produced, either one or two Airlock/ Gowning Rooms is required per production clean room. One is to be used for Gowning Up and the other for Gowning Down. This, however, is not mandatory and for many production facilities a single Airlock for both Gowning Up and Down is sufficient. The Functional Relations Diagrams in this FPU indicate the separate Gown-Up/ Gown-Down Airlocks.

The Airlock/ Gowning Room requires the following provisions:

- Electronic interlock door system should be provided to prevent the opening of both doors in the Airlock at the same time.
- The staff should change into sterile gowns prior to entering the Clean Room.
- The staff should remove the sterile gowns after exiting the Clean Room.
- There should be no toilets or showers within the Airlock/ Gowning Room. Hand wash basins are optional but must be located at least one metre away from the entrance of the production room. Hand sanitizer dispenser is mandatory.
- Airlocks used for personnel should be separated from those used for material. If this is not physically possible, then the use of the same airlock should be time-separated.
- The HVAC should be appropriately designed to achieve the pressurisation regime required for the Production Clean room connected to the Airlock and described below.
- Positive Pressure Regime - If the Production Room is required to be under positive pressure, to protect the products from possible contamination, then the Airlock should also be positive pressure but at a level lower than the Production room. Therefore, it should be at relative negative pressure compared to the Production Room. The Airlock, in turn should be at a higher pressure than the Production / Clean corridor, which is at Neutral pressure. Therefore, any movement of air will be from Production Room to the Airlock and from Airlock to the Production / Clean corridor. This is referred to as a uni-directional flow of air towards the room with the lowest pressure.
- Negative Pressure Regime - If the Production Room is required to be under negative pressure to prevent any airborne toxic material or dust reaching other areas, the Airlock should also be negative pressure but higher than the Production Room. Therefore, it will be a relative positive pressure compared to the Production Room. The Airlock, in turn should be at a lower pressure than the Production / Clean Corridor, which is at Neutral pressure. Therefore, any movement of air will be from the Production / Clean Corridor to the Airlock and from the Airlock to the Production Room. This is referred to as a uni-directional flow of air towards the room with the lowest pressure.

Production Clean Room

The Production Clean Room is where the pharmaceutical products are manufactured. The Production Clean Room may be used for a variety of products, using different raw materials, machinery and processes. All permutations of the production cannot be anticipated or covered in these Guidelines. The Clean Room classification is dependent on the type of product being manufactured as well as the chemistry and science behind approved products. The common features of the Production Clean Room are as follows:

- The HVAC system and the air pressurisation regime should be appropriately designed to achieve and maintain the required cleanroom condition and uni-directional flow of air for the products being manufactured.
- The room should have temperature and humidity control with visible and audible alarms. To maintain the viability of the pharmaceutical the selected temperature and humidity must meet the requirements of the components and the final product.
- The room should contain laminar flow cabinets and/ or isolators for any sterile and/ or hazardous product manufacturing.
- A fixed window should be provided into the clean room from an adjoining corridor for viewing the processes and supervision of the full area without entering the room.
- Alternatively high-resolution CCTV cameras for remote monitoring should be provided.
- The facility to comply with room design and construction requirements in relevant Clean Room standards for pharmaceutical manufacturing of the specific products.
- Some products require manufacturing under Positive Pressure to protect the raw materials or finished products from contamination. However, some products require manufacturing under Negative Pressure to contain potentially hazardous materials or dusty material from being released to the external environment before the production is finalised and the products are stabilised and packaged. In the case of biologically active products, these are classified into four Biosafety Risk Groups; Group 1 – Organisms that are unlikely to cause disease is a healthy individual ; Group 2 – Organisms that can cause disease but under normal usage are unlikely to spread, and usually have an effective treatment available; Group 3- Organisms that can cause severe human disease and can spread but an effective treatment is available and ; Group 4 - Organisms that can cause severe human disease and can spread and an effective treatment is not available. Refer to the below table to determine the required Pressure Regime to be adopted based on the type of pharmaceutical being produced.

Pharmaceutical Type	Pressurization Regime*	Notes
Aerosols	Negative	
Biologically Active	Negative Pressure for Biosafety Risk Group 3 or 4 organisms	For Biosafety Risk Group 3 and/ or 4 organisms - Air should not be recirculated to any other area in the facility and should be exhausted through HEPA filters. Inactivation of the pathogen in the exhaust air is mandatory Biosafety Risk Group 4 organisms – a dedicated non-circulating HVAC system is required
Chemotherapy and other hazardous products	Negative	
Derived from human blood or plasma	Positive	Where blood products are handled, these areas should be completely separated, physically, from areas where non blood products are being handled
Herbal medicinal products	Positive	
Liquids, creams or ointments	Positive	
Medicinal gases	Negative	
Non-sterile pharmaceutical products	Positive or Neutral	
Radio pharmaceuticals	Negative	Airborne or volatile radiopharmaceutical must be produced under a Negative Pressure regime

Pharmaceutical Type	Pressurization Regime*	Notes
Sterile products	Positive	
IV's	Positive	
Dietary Supplements	Positive	
Medical Devices	Positive	If the devices include chemical capsules, then follow the requirements of the chemicals

* Any other pharmaceutical type that is deemed to be of a hazardous nature must be produced under a negative pressure regime

- Once the pressurisation regime is determined, the pressurisation of two adjoining areas leading to the Production Room, being Production Corridor and Airlock/ Gowning should be progressively positive or progressively negative to create a uni-directional flow of air.
- Work benches are to be free-standing, preferably mobile, and in stainless steel. Stainless steel trolleys can be provided for minimal storage.
- The different operations within the production room need to be separated to prevent contamination and errors.
- Primary packaging of the product is done within the clean room.
- After manufacturing and primary packaging, the product is transferred to an exit air lock that leads to the Secondary Packaging area.

Secondary Packaging

Within the secondary packaging area, an outer packaging is applied to the primary packaged product for extra protection, and to prepare it for storage and transportation. From here the packages are sent to a bulk store or warehouse.

The Secondary Packaging area should have the following features:

- Shelving system for the temporary storage of the packages
- Benches for the preparation of secondary packages
- Optional conveyor belts for the transportation of the boxes within the Secondary Packaging area
- At least one open workstation or office for the management of the Secondary Packaging area
- Various machines and devices for labelling, tagging and quality control
- The Secondary Packaging should be temperature and humidity controlled
- The products should not be removed or exposed to the air

Warehouse

The finished product is stored within a warehouse or bulk store. The Warehouse should have the following features:

- The Warehouse should be temperature and humidity controlled.
- The conditions of storage should follow the product's specific requirements.
- Tertiary packaging, if necessary, can be conducted within the Warehouse before dispatch.
- The Warehouse requires security and controlled access.
- The Warehouse should be located with ready access to the loading dock area.
- A control office or open workstation should be provided to oversee the access to the dock and manage the loading of the products for delivery.

Equipment Clean Up

This area is where the items from the various areas, including the Production Room, Weighing Room and Sampling Room, are sorted, rinsed and disposed of prior to disinfection and when necessary, sterilising. It is essential that the risk of contamination of the equipment after sterilising is minimized. For further information on guidelines for this area refer to the Sterile Supply Unit FPU.

Staff Amenities

Staff Amenities such as Staff Room, Toilets and Showers shall be located prior to the Primary Change Area. Optionally the Staff Amenities for the Administration area may be separated from the production and support staff. The staff amenities include the following provisions:

- Staff Room and any dining areas
- Toilets, Shower and Lockers within the Primary Change Rooms

Administration

Administration area includes the normal function of facility management, accounting, payroll, HR etc. Its exact requirements are based on the type of facility and the management policy. A typical administration area will include the following:

- Management Offices
- Open workstations
- File store
- Photocopy/ supply store
- Meeting room(s)
- Optional separate staff toilets and staff room

3 Functional Relationships

A Functional Relationship can be defined as the correlation between various areas of activity whose services work together closely to promote the delivery of services that are efficient in terms of management, cost and human resources.

External

The components of the facility should be arranged on the site to achieve the required relationships described above and indicated in the Functional Relationship Diagrams below. The provided diagrams are not Architectural plans and can be stretched, rotated and moved whilst still achieving the connectivity and flows implied and required.

For example, there are planning solutions where the in-coming and out-going loading docks can be arranged side by side whilst achieving all the other relationships.

As Pharmaceutical factories may be vastly different and specialise in the production of different products, there may be one or more production rooms (or halls). It is assumed that a modular configuration may be preferred. The specific requirements of each production room and the immediate support rooms such as Air lock/ Gowning rooms form one “module”. If the facility has multiple product lines, running concurrently, then multiple modules can be added. This is also implied in the Functional Relationship Diagrams below.

To note, areas where blood products are being processed need to be completely separated physically from areas where non blood products are being handled.

The Warehouse and Raw Materials Store may be located in separate buildings on-site, but the preferred location is with direct access to the main Production building. They should be located with ready access to a receiving Loading Dock area.

Internal

The Internal planning of the factory should consider the unit’s functional areas/zones.

Access points provided for the following people should be carefully considered:

- Visitors to the Unit
- Administrative staff who will not normally enter the production facilities
- Pharmaceutical Factory Staff
- Supplies delivery (Unloading and Loading Docks)

The internal flows for the production staff progress from outside the facility through the entrance point, primary change, then Airlock/ Gowning and finally the Production Clean Room.

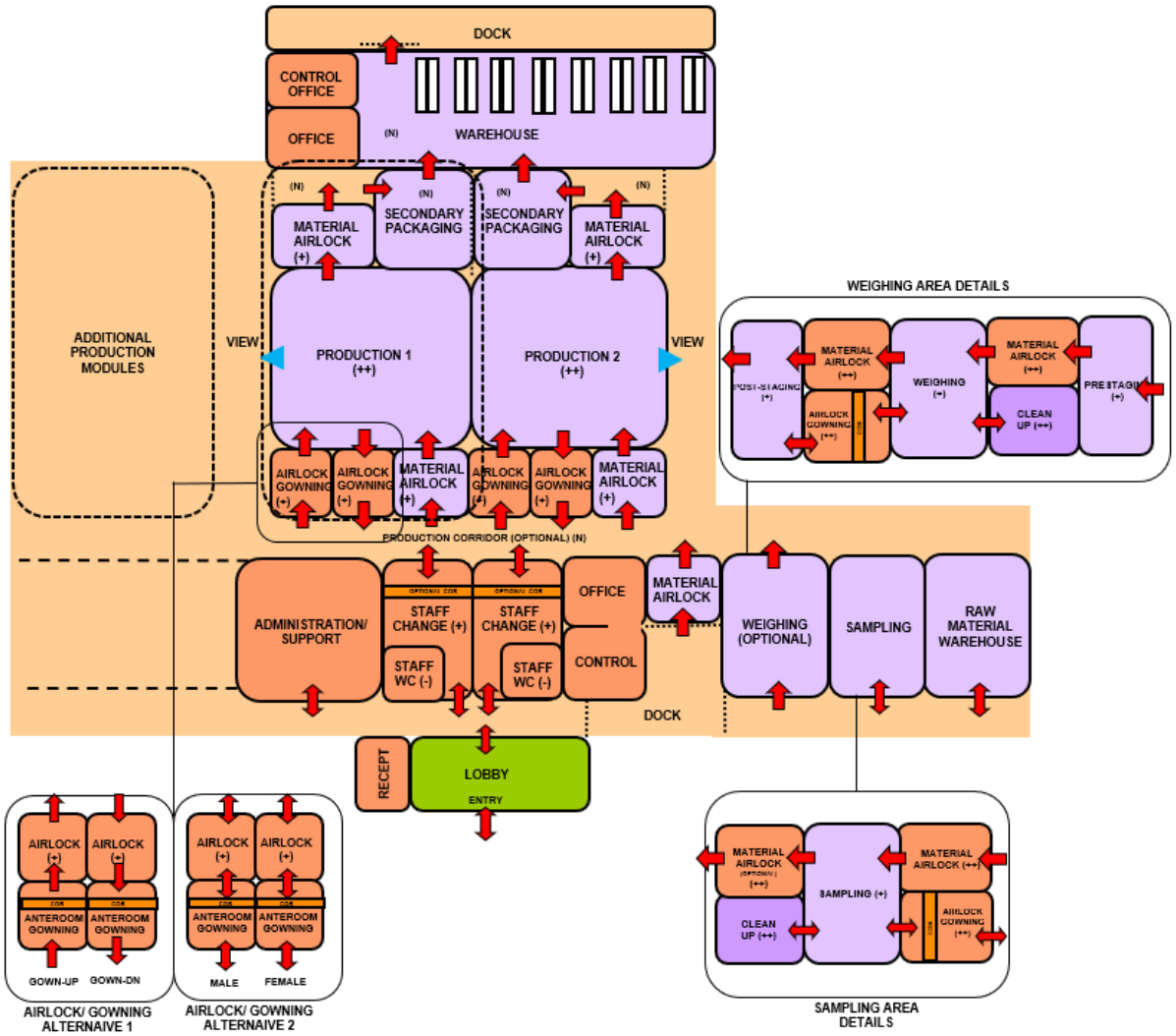
The products, but not the people, flow out of the Production Clean Room to the Secondary Packaging and finally to the Warehouse and dispatch loading dock.

Raw products arrive at the receiving dock and may be stored, sampled, weighed and transferred to the Production Clean Room via an air lock.

Functional Relationship Diagram

The Functional Relationship of a typical Pharmaceutical Factory either is best demonstrated in the diagram below.

Pharmaceutical Factory with Positive Pressure Clean Rooms



LEGEND

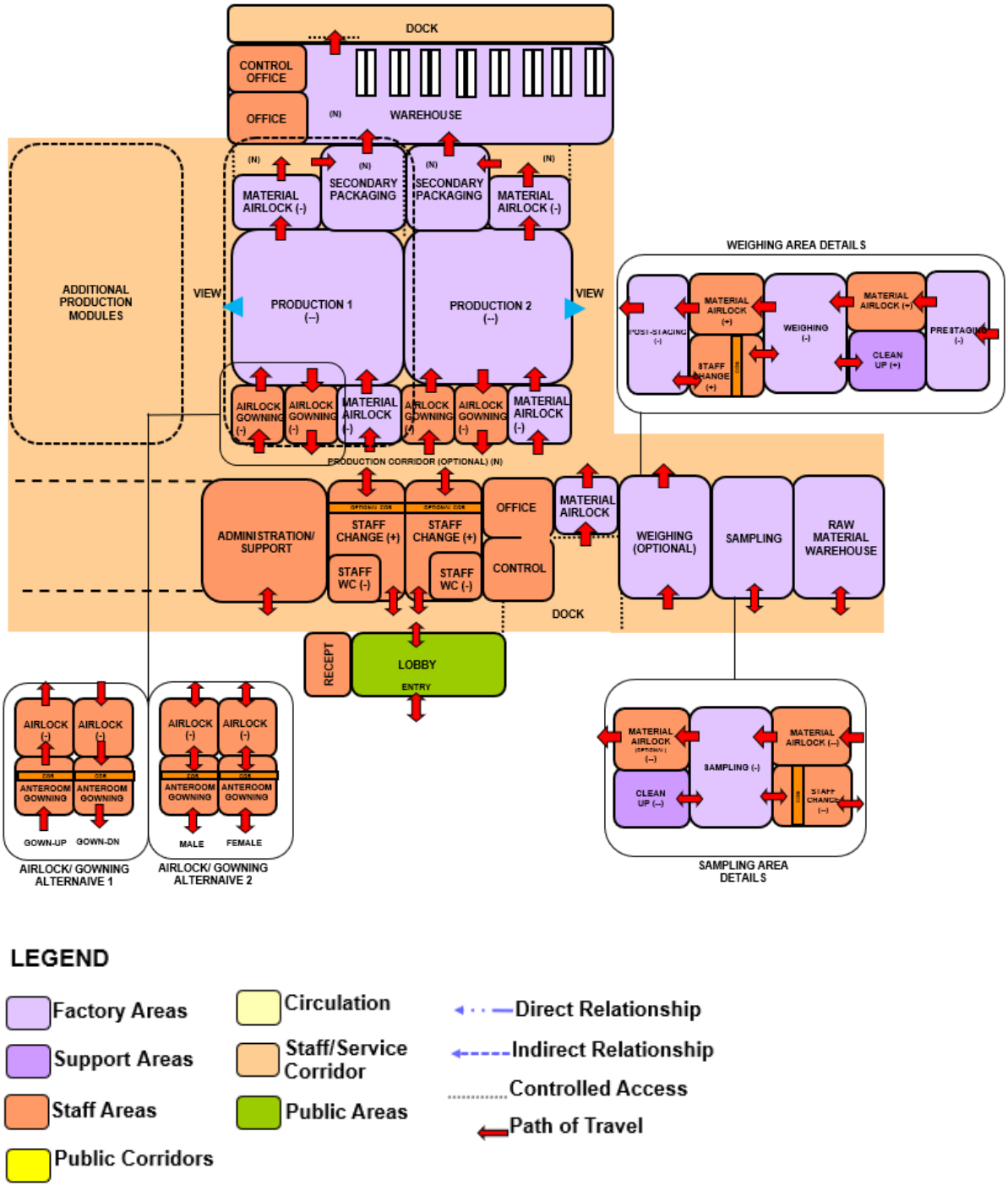
- Factory Areas
- Support Areas
- Staff Areas
- Public Corridors
- Circulation
- Staff/Service Corridor
- Public Areas
- Direct Relationship
- Indirect Relationship
- Controlled Access
- Path of Travel

Pressure Grading Symbols

Pressure Grading	Highly Negative	Negative	Neutral	Positive	Highly Positive
Symbol *	(- -)	(-)	(N)	(+)	(+ +)

* Each step within the pressure grading is a minimum of 2.5 Pascals. All pressures are relative between the rooms involved not compared to atmospheric pressure.

Pharmaceutical Factory with Negative Pressure Clean Rooms



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4 Design Considerations

General

Design of the factory should consider the need for security and sterility of the necessary areas.

Environmental Considerations

Operational Considerations

- Maintenance workshops, if provided, should be separated from production areas.
- Whenever parts and tools are stored in the production area, they should be kept in rooms or lockers reserved for that use.
- Storage areas should be of sufficient capacity to allow orderly storage of the various categories of materials and products with proper separation and segregation.
- Receiving areas should be designed and equipped to allow containers of incoming materials to be cleaned, if necessary, before storage.
- Highly active and radioactive materials, narcotics, other dangerous medicines, and substances presenting special risks of abuse, fire or explosion should be stored in safe and secure areas as per the requirements of the responsible Authorities.
- The production of certain other highly active products, such as some antibiotics, hormones, cytotoxic substances and certain non-pharmaceutical products, should not be conducted in the same production room/area.
- Quality Control (QC) laboratories (if provided) should be separated from production areas. Areas where biological, microbiological or radioisotope test methods are employed should be separated from each other. For Laboratories refer to the Laboratory Unit within these Guidelines.
- QC laboratories should be designed to suit the operations to be carried out in them. There should be separate air supply to laboratories and production areas.
- A separate room may be needed for certain instruments to protect them against electrical interference, vibration, contact with excessive moisture and other external factors, or where it is necessary to isolate the instruments.
- Rejected materials and products should be clearly marked as such and stored separately in restricted areas.
- Recalled products should be identified and stored separately.
- Provision should be made for the proper and safe storage of waste materials awaiting disposal. Refer to Waste Management Unit within these Guidelines.

Acoustics

For factories that utilise equipment that produce noise exceeding the maximum allowable levels, acoustic treatment may be required.

Natural Light/ Lighting

Natural lighting must be avoided, except within offices and administrative areas. This is to ensure the preservation of product viability and to minimise temperature variations.

- High quality general and task lighting is essential to ensure complex tasks can be safely achieved.
- Some raw materials are affected by the wavelength of light they are exposed to, degrading them and/ or impacting their usability. The type of light installed within the Sampling, Weighing and Production areas, or other areas where the raw materials are exposed to light, needs to take into consideration the requirements of the materials.

Accessibility – External

- There should be weatherproof loading and unloading docks to ensure protection of delivered

supplies and outgoing delivery of finished manufactured pharmaceuticals.

Doors & Clearance

- Corridors and door openings within the Warehouse and where materials are transported shall provide sufficient clearance for large items and equipment from bulk stores. The corridor should permit two-way traffic of bulky items.
- Configuration of factory benches, furniture, fixtures and equipment must not impede emergency access to an exit. A pathway, leading to the face of an exit must have the minimum width as required by the local fire services codes (not covered in these Guidelines).
- Sufficient space around production equipment for maintenance must be considered during the design phase.
- Doors to the Production Areas must be adequately sized to accommodate equipment located in the Production Clean Room such as fume hoods, automated equipment and the like.
- Door sweeps and door seals should not be installed at doors between the Production Clean Room and the Airlocks.
- Access doors to the Production Clean Room should be handsfree.

Ergonomics/ OH&S

- Ergonomics must be considered in the internal design of the Unit for staff health and safety. Heights and depths of benches need to allow staff to efficiently work from standing and seated positions. Consideration must be given to storage of supplies at suitable working heights.
- Consideration should be given to the need for manual handling devices such as dock levellers and lifters. A well-designed and equipped work area will eliminate injuries resulting from manual handling.
- Refer also to Part C – Access, Mobility and OH&S of these Guidelines for additional information.

Size of the Factory

- The size of the Factory is determined by the Service Plan establishing the intended scope and complexity of manufacturing.

Safety and Security

- The factory must be designed and constructed to prevent unauthorized access through doors, windows, walls and ceilings. All entrances and exits shall be secured. An Intrusion Detection Alarm System is required within the factory to allow for a 24-hour monitoring by a central security team on-site.
- An intercom or call bell should be located at the dock entrance area to announce deliveries when doors are closed.
- Where required, concave directional mirrors along corridors and bends should be provided to avoid collision of oversized trolleys, motorised transporters and staff.
- Security measures for consideration includes the following:
  - Electronic door controls
  - Movement sensors
  - CCTV cameras: CCTV cameras must be installed with an unobstructed view of the required areas
- Locking mechanism, where required in the Factory, can be in the form of controlled access cards, keypads or physical keys.
- Design of the Warehouse and Stores should ensure that storage areas are free from insects and vermin.
- Flammable liquids, chemicals and reagents used must be stored according to relevant local regulations.

- Storage, handling and disposal for radioactive and other such materials must be considered depending on the services provided.
- Radiation detection and measuring devices must be provided as per the relevant local authority requirements.
- Exhaust should be provided in rooms for storing and recharging of pallet jacks, motorised transporters and other equipment depending on battery type to avoid build-up of noxious gases.
- Any devices, equipment or rooms which must be controlled within strict parameters such as temperature must be alarmed. Such alarms must be both visual an audible and capable of monitoring from a remote area permanently manned by staff.

Refer also to Part C – Access, Mobility, OH&S of these Guidelines for additional information.

Finishes

Finishes within the Warehouse and Stores should consider the following:

- Door & wall protection shall be installed to prevent damage to walls caused by all types of trolleys, lifting/transport equipment and movement of large items. Sturdy wall protection such as rubber or timber wall protection is recommended to withstand impacts from trolleys, pallet jacks and other bulky transporting equipment. Solid core laminated doors with stainless steel door and door frame protection panels is recommended to avoid chipping and breakage. Alternatively, solid core doors with high quality enamel paint can be used with additional proprietary door protection on the leaf and frame.
- Floor finish is to be slip resistant, impervious, easy to clean and hardwearing. Movement of large equipment and lifting/ transporting equipment are to be considered when choosing appropriate floor finish.

In Clean Rooms, Weighing and Sampling Rooms the following should be considered:

- As a minimum, all surfaces including floors, walls, ceilings, doors and fixtures should be uniform, gap free, sealed, inspectable and easily cleanable around all edges and corners with aggressive cleaning agents.
- The internal room finishes, the benches and any fixtures and fittings should allow for the easy cleaning of all surfaces by high pressure water and cleaning agents between the product runs.
- Work surfaces should be smooth, monolithic, chemical resistant and impervious to moisture.
- Work benches are to be free-standing, preferably mobile, and in stainless steel. They shall be seamless to prevent contamination from spillage. Splashback or coved upturns must be provided when the benchtop abuts a wall.
- There should be no gaps between attached elements, or any such gaps must be sealed.
- Stainless steel trolleys can be provided for minimal storage
- High performance 2-coat epoxy paint, preferably with antibacterial properties, must be applied to the walls to form an impervious, scrubbable, continuous monolithic finish. Alternatively, full height wall vinyl with fully welded joints may be used.
- High performance 2-coat epoxy paint must be applied to gypsum, cement board or similar ceiling materials to form a continuous monolithic finish. Drop-in tiles or materials with joints and gaskets should be avoided.
- For flows, homogeneous vinyl flooring (or similar) with hot-welded joints may be used. High performance 2-coat epoxy paint to the floors is also acceptable.
- The joints between floors and walls, walls to ceilings and internal corners of walls should be rounded for easy cleaning by a minimum of 25mm radius.
- Light fittings within the clean rooms should be mounted flush and sealed but openable via Allen keys for maintenance. Any access hatches required in the ceiling must be hermetically sealed and openable via alan keys.
- Any other finish should be at least equal or better than these products. Nothing in these

guidelines dictate a requirement for panelised metal walls or ceilings. If, however, such finishes are preferred, the jointing system must ensure that the surfaces are impervious, gap free, fully sealed and smooth with no rebates, grooves etc.

- In other areas the following should be considered:
- Wall and door protection should be installed to prevent damage to walls caused by mobile equipment such as trolleys.
- Floor and walls should be anti-static, heat resistant, anti-bacterial, anti-fungal and chemical resistant. All joints in flooring must be sealed and coved at the edges (against walls or fixed joinery) where possible. Water and chemical resistance are also important characteristics of selected flooring. Walls shall be painted with lead free paint, or prefinished for easy cleaning.
- Wall finish treatments must not create ledges or crevices that can harbour dust and dirt.

Refer to Part C – Access, Mobility and OH&S of these Guidelines for more information on wall protection, floor finishes and ceiling finishes.

Fixtures, Fittings and Equipment

- Equipment, furniture, fittings should be selected to ensure that users are not exposed to avoidable risks or injury.
- Specialised equipment will require services and installation according to manufacturers' specifications, in particular:
  - Space requirements may vary according to equipment selected
  - Structural assessment may be required for large equipment items
  - Space requirements for maintenance of equipment must be considered
- A safety shower and eyewash should be provided close to production areas for harmful spills. However, safety showers and eyewash should not be provided directly within the Production Clean Rooms.
- Refer to Part C – Access, Mobility and OH&S of these Guidelines and Standard Components of individual rooms for specific information related to fixtures, fittings, and equipment.

Radiation Protection

- Radiation protection requirements should follow the local authority requirements and guidelines.

Window Treatments

- Window treatment should be installed to external windows to control sunlight and glare to administrative areas and offices.
- The Production Clean Rooms, Sampling and Weighing rooms should avoid windows and natural light.
- In other areas if windows are used, curtains and horizontal blinds should be avoided.

Building Services Requirements

Information and Communication Technology

The Pharmaceutical Factory requires reliable and effective IT / Communications service for efficient operation. The IT design should address:

- Voice/ data cabling and outlets for phones, computers and equipment, where required
- Network data requirements and wireless network requirements in service areas of the facility
- CCTV surveillance
- Intercom system between positively or negatively pressurized rooms and their adjacent spaces
- Data entry including reporting

- Bar coding of supplies within the warehouse and stores
- Optional availability of Wi-Fi for staff

Power

All major equipment within the Production Area should be connected to emergency power. Computerized systems of the production equipment must retain the system set up and/ or run values, therefore they must be connected to uninterrupted power.

HVAC systems serving production of hazardous pharmaceuticals must be operated on uninterrupted power.

Heating Ventilation and Air-conditioning (HVAC)

- All Storage, Warehousing, Sampling, Weighing, Production and Packaging Areas must be fitted with temperature and humidity controls. Temperature and humidity upper and lower limits for the different areas must be selected according to the requirements of the materials and products, in order to maintain their viability. Where identified, the temperature and humidity should be maintained within the defined limits of product viability.
- In the absence of such information, the temperature and humidity should be set at the below values:

Temperature	Humidity
20°C	60%

- Visible alarms are required to monitor the temperature range and humidity levels
- Exhaust should be provided in rooms for storing and recharging of pallet jacks, motorized transporters and other equipment depending on battery type to avoid build-up of noxious gases.
- Special air-conditioning systems that provide either positive pressure or negative pressure will be required. The HVAC system should support the grade / classification of the clean room and all adjacent rooms, as per production requirements and national and international standards.
- Where required, the HVAC system should be set for either positive or negative pressure as indicated in this FPU. The system cannot be switchable between positive and negative pressure.
- The HVAC system must be designed to control parameters such as temperature, relative humidity, airflow and pressure differential and these should be monitored.
- Freestanding humidifiers, dehumidifiers and air conditioners are prohibited within the Production areas
- Audible and visual alarms for pressure, temperature and humidity within the clean rooms and airlocks are required. Such alarms must be capable of remote monitoring.
- Dust removal should be designed into the HVAC system where necessary. As much as possible, dust should be removed as close as possible to the source in order to limit its dispersal. A dust extractor should be dedicated per room to avoid back flow resulting in cross contamination.
- Radioactive gases and vapours should be monitored with alarm systems. Separate air handling units are required for these, and recirculation of air is prohibited.
- HVAC air blowers in the ceiling should be located to precent air currents within laminar airflow cabinets and other such equipment.
- Air return grills should be placed at low levels on the wall and distributed throughout the room.
- All HVAC units and systems are to comply with services identified in the Standard

Components and Part E – Engineering Services.

Hydraulics

- Warm water should be supplied to hand wash basins, eye-wash stations and emergency shower.
- Provision of purified water is required for cleaning of areas including the clean room, weighing area and sampling areas.
- For cold, warm & hot water technical details, refer to Part E – Engineering Services in these Guidelines.
- Drains should be avoided where possible and should not be present within the Clean Rooms or Airlock/ Gowning Rooms.
- There should be no sources of water within the Clean Rooms.
- Sprinklers within the Clean Room should be recessed and covered.

Infection Control

Infection Control measures applicable to the Factory will involve proper handling of products and materials to prevent contamination of staff and material as well as cross contamination of products and materials.

Standard precautions apply to the Factory areas and Personal Protective Equipment (PPE), including protective clothing, gloves, masks, and eye protection, will be available close to all processing areas and clean rooms.

Hand Basins

- Handwashing facilities shall be required in rooms as specified by the Standard Components. Taps to Hand Basins should be either elbow-action taps or automatic taps (sensor/ foot operated).

For further information refer to Part D – Infection Control in these Guidelines.

Emergency Shower and Eye-wash Station

- Weighing, Sampling and Production Clean Rooms must have access to at least one emergency shower and eye-wash station.

Antiseptic Hand Rubs

- Antiseptic hand rubs should be located so they are readily available for use.
- Antiseptic Hand Rubs, although very useful and welcome, cannot fully replace Hand Wash Bays.

Chemical Storage

- Storage for chemicals and reagents should be physically separated from other storage in the Factory with designated cabinets. Chemicals and reagents should not be stored in cabinets if they are fixed above a sink/s.
- The storage of flammable materials must be subject to the requirements of local Civil Defence or fire authorities.

5 Components of the Unit

Standard Components

- Standard Components are typical rooms within a health facility, each represented by a Room Data Sheet (RDS) and a Room Layout Sheet (RLS). Sometimes, there are more than one configuration possible and therefore, more than one room layout sheet can be found in the Standard Components for a room with same function. They may differ in room size and/or the requirement of FF & FE items.
- The Room Data Sheets are presented in a written format, describing the minimum briefing requirements of each room type divided into the following categories:
- Room Primary Information; includes Briefed Area, Occupancy, Room Description and relationships, and special room requirements.
- Building Fabric and Finishes; identifies the fabric and finish required for the room ceiling, floor, walls, doors, and glazing requirements.
- Furniture and Fittings; lists all the fittings and furniture typically located in the room; Furniture and Fittings are identified with a group number indicating who is responsible for providing the item according to a widely accepted description as follows:

Group	Description
1	Provided and installed by the builder
2	Provided by the Client and installed by the builder
3	Provided and installed by the Client

- Fixtures and Equipment; includes all the serviced equipment typically located in the room along with the services required such as power, data and hydraulics; Fixtures and Equipment are also identified with a group number as above indicating who is responsible for provision.
- Building Services; indicates the requirement for communications, power, Heating, Ventilation and Air conditioning (HVAC), medical gases, nurse/ emergency call and lighting along with quantities and types where appropriate. Provision of all services items listed is mandatory.
- The Room Layout Sheets (RLS's) are indicative plan layouts and elevations illustrating an example of good design. The RLS indicated are deemed to satisfy these Guidelines. Alternative layouts and innovative planning shall be deemed to comply with these Guidelines provided that the following criteria are met:
- Compliance with the text of these Guidelines
- Minimum floor areas as shown in the Schedule of Accommodation
- Clearances and accessibility around various objects shown or implied
- Inclusion of all mandatory items identified in the RDS
- Standard Components have considered the required design parameters described in these Guidelines. Each FPU should be designed with compliance to Standard Components – Room Data Sheets and Room Layout Sheets, nominated in the Schedules of Accommodation in Appendices of this FPU.

Non-Standard Components

Entrance Lobby

The Entrance Lobby adjoins the Entry Airlock, Main Reception and Waiting areas. Convenient access to public amenities is required.

Key consideration in the Entrance Lobby are:

- Selection of floor finish to reduce the risk of slips and falls to visitors and staff
- Provision of good internal lighting

- Sufficient signposting and directional signs to identify key areas within the zone including Reception, Enquiries, Public Amenities, Lifts and circulation routes

Sampling Room

The Sampling Room is a Clean Room used to perform a quality check on a small quantity of a batch of the material to be used during production.

Pre-Staging

This area is where the external packaging of the materials is removed and then wiped down in order to be weighed.

Weighing

The Weighing room is a Clean Room where the materials from the Raw Materials Warehouse are weighed and then transferred to the Production Room.

Post-staging

This area adjoins the airlock upon exiting the Weighing area and is used to organise the different materials to be transferred to the different Production Clean Rooms, if there are multiple Production Rooms. This area is optional.

Production Room

A Clean Room where the pharmaceutical product is manufactured.

Secondary Packaging

An area where the secondary packaging is applied to the finished product.

6 Schedule of Accommodation

The Schedule of Accommodation (SOA) identifies the rooms required in the Unit along with the quantity and the recommended room area. The sum of these room areas is the Sub Total and Total Departmental areas with a recommended circulation percentage. The circulation percentage represents the area required for internal corridors and is a target for efficient planning. SOAs and room sizes are developed for typical units and are organised into the functional zones applicable to the Unit. Not all rooms identified are mandatory requirements and optional rooms are indicated. Quantities of rooms may need to be proportionally adjusted to suit the desired unit size and service needs.

The Schedules of Accommodation are developed for particular levels of service known as Role Delineation Level (RDL) and numbered from 2 to 6 (including in-between numbers such as 4-5). Level 2 represents uncomplicated health facilities, ascending to level 6 representing complex specialist services and hospitals. Refer to the full Role Delineation Framework in these guidelines for a full description of the RDL's identified. RDL Levels not listed are not applicable for this service.

Pharmaceutical Factories

ROOM/ SPACE Unit Size	Standard Component Room Codes	2 Production Rooms			NA			Remarks
Entry/ Reception								
Reception/ Clerical	recl-5-d or similar	1	x	5				
Entrance Lobby	NS	1	x	20				
Change - Staff (M/F)	chst-14-i chst-20-i similar	2	x	20				
Toilet - Staff (M/F)	wcst-i	4	x	3				
Raw Materials Warehouse								
Loading Dock	lodk-i	1	x	0				External space
Stork - Bulk	stbk-40-i or similar	1	x	40				Size according to requirements
Store - Refrigerated	stref-5-i stref-10-i or similar	1	x	5				Optional. May be located as refrigerator bay within Store - Bulk, size according to requirements
Store - Flammable Liquid	stfl-i or similar	1	x	9				
Control Office	off-s9-i or similar	1	x	9				
Office - single Person	off-s12-i or similar	1	x	12				For Warehouse Manager
Office - 2 Persons Shared	off-2p-i	1	x	12				For Purchasing Officers or Warehouse Personnel
Property Bay - Staff	prop-2-i prop-6-i	2	x	2				Separate for Male & Female
Toilet - Staff (Male/ Female)	wcst-i	2	x	3				Separate for Male & Female
Sampling								
Material Airlock	airl-6-i similar	2	x	6				second airlock optional
Gowning	gw-up-i	1	x	6				
Sampling Room	NS	1	x	20				Comply with international clean room standards; comply to Part E - Engineering Service
Clean Up	clup-7-i or similar	1	x	7				
Weighing								**Optional. Required if there are multiple Production Rooms within the block**
Pre-Staging	NS	1	x	15				
Material Airlock	airl-6-i similar	2	x	6				
Weighing	NS	1	x	20				Size according to requirements
Clean Up	clup-7-i or similar	1	x	7				
Gowning	gw-up-i	1	x	6				
Post-Staging	NS	1	x	15				
Production								
Gowning (Male/ Female)	gw-up-i	4	x	6				Can be combined with the Airlock
Airlock (Male/ Female)	airl-6-i similar	4	x	6				
Material Airlock	airl-6-i similar	4	x	6				
Production Room	NS	2	x	30				Size according to requirements
Secondary Packaging	NS	2	x	20				Size according to requirements
Warehouse								

ROOM/ SPACE Unit Size	Standard Component Room Codes	2 Production Rooms			NA			Remarks
Loading Dock	lodk-i	1	x	0				External space
Stork - Bulk	stbk-40-i or similar	1	x	40				Size according to requirements
Control Office	off-s9-i or similar	1	x	9				
Office - Single Person	off-s12-i or similar	1	x	12				For Warehouse Manager
Office - 2 Persons Shared	off-2p-i	1	x	12				For Warehouse Personnel
Property Bay - Staff	prop-2-i prop-6-i	2	x	2				Separate for Male & Female
Toilet - Staff (Male/ Female)	wcst-i	2	x	3				Separate for Male & Female
Administration/ Support Areas								
Quality Check Laboratory								
Office - Single Person	off-s12-i or similar	1	x	12				For Production Manager
Office - Single Person	off-s9-i or similar	1	x	9				For Line Manager
Office - 2 Persons Shared	off-2p-i	2	x	12				
Cafeteria	srm-35-i	1	x	35				Located outside of the Production building
Sub Total		**629**						
Circulation %		**30**						
Total Area		**818**						

Please note the following:

- Rooms and areas indicated in the schedule reflect the typical arrangement. Rooms should be designed in order to suit the operations to be carried out and the equipment planned.
- All the areas shown in the SOA follow the No-Gap system described elsewhere in these Guidelines.
- Exact requirements for room quantities and sizes will reflect Key Planning Units (KPU) identified in the Clinical Service Plan and the Operational Policies of the Unit.
- Office areas are to be provided according to the number of endorsed fulltime positions in the unit.

7 Further Reading

Planning and design should consider the following developments in Pharmaceutical Factories:

- https://www.pharmamanufacturing.com/production/automation-control/article/11363373/pharmaceutical-weighing-weighing-and-dispensing-do-it-right-pharmaceutical-manufacturing
- Annex 2, WHO good manufacturing practices for sterile pharmaceutical products
- Annex 2, Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products, Part 2: Interpretation of Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products
- Annex 9 Guidelines on packaging for pharmaceutical products, WHO