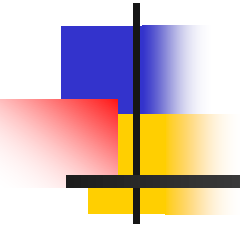


Understanding the Basics of Facility Design



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Understanding the Basics of Facility Design

- **Design Criteria**

- Location and area of physical building
 - ❖ Geographical stability
 - ❖ Cost for property
 - ❖ Water source
 - ❖ Electrical power
 - ❖ Waste management



Understanding the Basics of Facility Design

- **Design Criteria**

- Climate and seasonal changes
- Future expansion in 5 to 10 years
- Size of the physical building
- Footprint of Critical and Controlled areas
- Minimize Critical work area if possible
- Remember the HEPAs and temperature controls will be on line 24/7 which equates to a significant cost



Understanding the Basics of Facility Design

- **Design Criteria**

- Single story building
 - ❖ Minimal adjacencies
 - ❖ Liquid transfer usually pump or pressure
 - ❖ Piping is usually horizontal
 - ❖ Increase difficulties to properly slope piping



Understanding the Basics of Facility Design

- **Design Criteria**

- Multiple story building
 - ❖ Adjacencies are increased
 - ❖ Liquid transfer using gravity
 - ❖ Piping is usually vertical
 - ❖ Decreased slope requirements
 - ❖ Elevators required



Understanding the Basics of Facility Design

- **Design Criteria**

- Type of building

- ❖ Modular

- ✓ Lowered initial costs
- ✓ Speed to market
- ✓ Ease of installation
- ✓ Expandable
- ✓ Needs supports to install items in wall
- ✓ Reduction in seams 20%

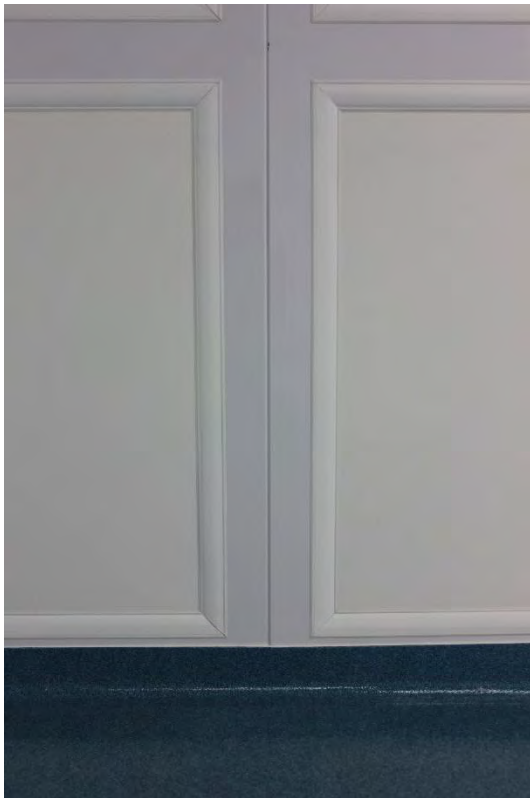
Understanding the Basics of Facility Design

- **Modular Design Criteria**



Understanding the Basics of Facility Design

- **Modular Design Criteria**



Understanding the Basics of Facility Design

- **Modular Design Criteria**





Understanding the Basics of Facility Design

- **Design Criteria**
 - Vendors
 - ❖ Plascore
 - ❖ Pharmaduel
 - ❖ Cleanpak



Understanding the Basics of Facility Design

- **Design Criteria**

- Type of building

- ❖ Traditional

- ✓ Longer to market
- ✓ More options
- ✓ Custom build design
- ✓ Significant impact when expanding
- ✓ More dirty/dusty work



Understanding the Basics of Facility Design

- **Design Criteria**

- Classification of the fill room
 - ❖ Grade-A, full HEPA ceiling
 - ❖ Grade-A/B, partial coverage
- Gowning requirements per area
- Personnel required for processing



Understanding the Basics of Facility Design

- **Clean Room**

- A room in which environmental parameters are highly controlled to provide a predefined level of control
- Most notably used in the Electronics and Pharmaceutical industries



Understanding the Basics of Facility Design

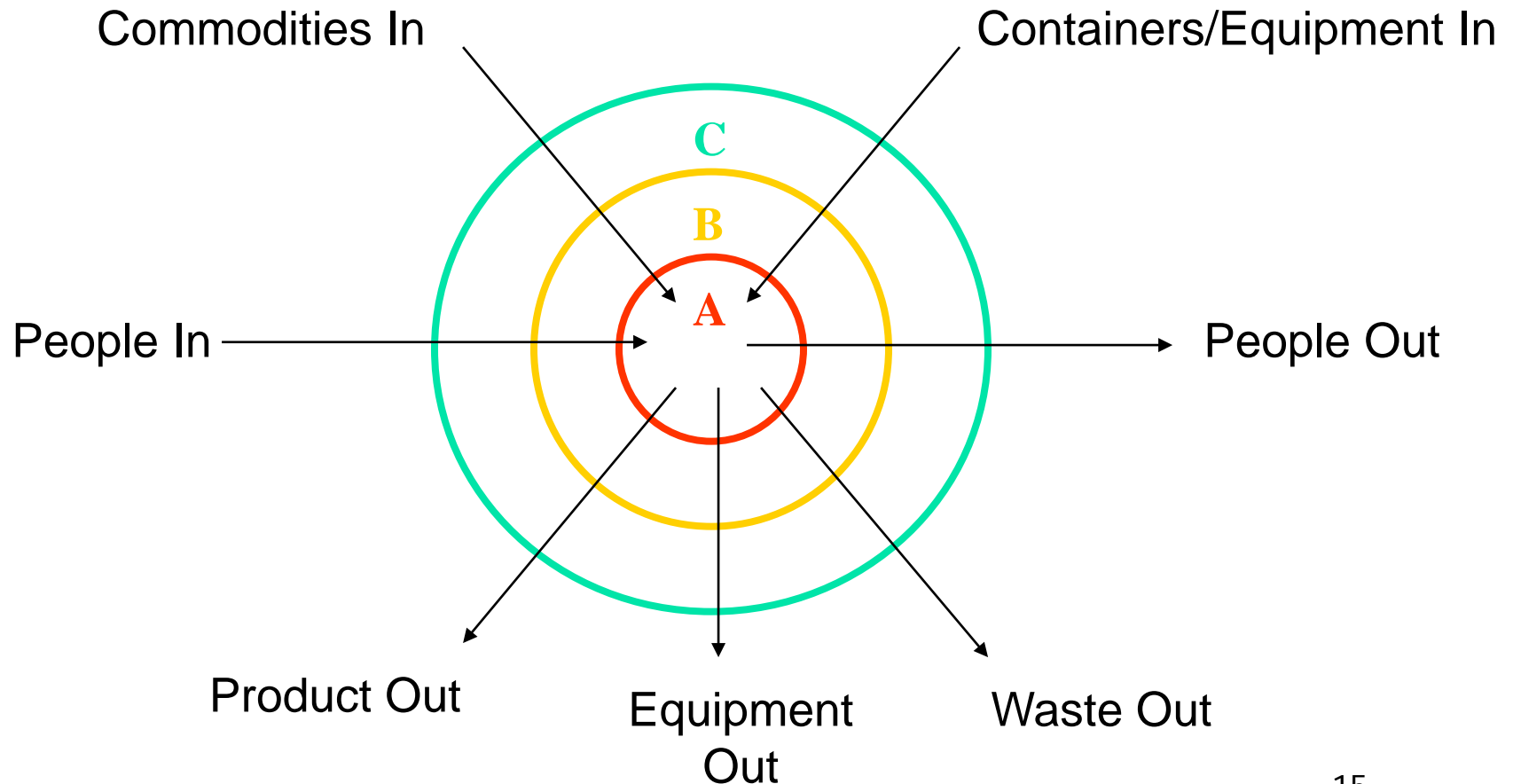
- **Facility Design Criteria**

- Nested Zones

- ❖ Critical zones surrounded by lesser Classified areas
- ❖ Classical pharmaceutical design

Understanding the Basics of Facility Design

Nested Zones/Single Pass Design





Understanding the Basics of Facility Design

- **Facility Design Criteria**
 - Single pass process flow design
 - Defined ingress and egress for the facility
 - ❖ Personnel
 - ✓ Gowning must have a one way flow
 - ✓ What is the number of personnel who can gown at a time
 - ✓ How many rooms and areas are required



Understanding the Basics of Facility Design

- Single pass process flow design
 - ❖ Personnel
 - ✓ Re-gloving area
 - ✓ System for stocking gowning supplies
 - ✓ De-gowning area must be performed in a separate room
 - ✓ Method for removing used gowns



Understanding the Basics of Facility Design

- Single pass process flow design
 - ❖ Commodities
 - ✓ Prep
 - ✓ Storage
 - ✓ Autoclave
 - ✓ Storage
 - ✓ Pass through
 - ✓ Use
 - ✓ Removal
 - ✓ Cleaning



Understanding the Basics of Facility Design

- **Process Flow**

- Single Pass Design

- ❖ Product

- ✓ Liquid, direct to packaging

- ✓ Freeze dried products

- Filling

- Lyo

- Capping

- Packaging



Understanding the Basics of Facility Design

- **Process Flow**
 - Single Pass Design
 - ❖ Waste
 - ✓ Wrapping material
 - ✓ Broken vials
 - ✓ Clean up if spills
 - ✓ Sanitizing wipes



Understanding the Basics of Facility Design

- **Process Flow**

- Single Pass Design

- ❖ Waste

- ✓ When and how is waste removed

- During filling operations

- During breaks

- End of fill

- ✓ Use of sterile trash bags

- ✓ Defined pass through only for waste



Understanding the Basics of Facility Design

- **Process Flow**

- Single Pass Design

- ❖ Equipment

- ✓ Dedicated equipment

- ✓ Single use equipment

- ✓ Procedures for introducing into the clean room

- ✓ Dedicated pass boxes or large pass throughs



Understanding the Basics of Facility Design

- **Design Criteria**

- Filling equipment
 - ❖ Traditional
 - ❖ Modified aseptic processing
 - ❖ Barrier technology
 - ❖ Isolator systems
 - ❖ Blow/Fill/Seal
 - ❖ New Technologies



Understanding the Basics of Facility Design

■ Design Criteria

- Freeze dried and/or liquid product
- Freeze dryer
 - ❖ Size, usually too small
 - ❖ Functionality and operations
 - ❖ Cycle time
 - ❖ Type of door opening
 - ✓ Pizza door
 - ✓ Regular door swing



Understanding the Basics of Facility Design

- **Design Criteria**

- Freeze dryer

- ❖ Automatic loading system
- ❖ Time to validate
- ❖ Distance from filler
- ❖ HEPA cart to transport vials
- ❖ Accessibility to gray spaces



Understanding the Basics of Facility Design

- **Design Criteria**

- Freeze dryer
 - ❖ HEPA coverage
 - ❖ Where to store trays after loading
 - ❖ Environmental locations



Understanding the Basics of Facility Design

- **Design Criteria**

- Liquid products

- ❖ Direct to packaging
 - ❖ Mouse hole required
 - ❖ Classification of fill room to dirty side of mouse hole
 - ❖ Movable conveyor to allow access to the back of filler



Understanding the Basics of Facility Design

- **Design Criteria**

- Autoclave

- ❖ Proximity to clean room/storage room
- ❖ Interior size
- ❖ What ever the size specification is, double it!
- ❖ Single door or double door single pass



Understanding the Basics of Facility Design

- **Design Criteria**

- Autoclave

- ❖ Design of interior rack and cart
- ❖ Storage post sterilization
- ❖ Functionality and/or programs
- ❖ Design of unloading carts
- ❖ HEPA filter for cool down area

Understanding the Methods of Sterilization

- Cool Down Zone





Understanding the Basics of Facility Design

- **Design Criteria**

- Dry heat oven
 - ❖ Area to prep vials and wash dry
 - ❖ How are vials covered/wrapped
 - ❖ HEPA filter for cool down area
 - ❖ Transportation to filling room
 - ❖ HEPA cart required



Understanding the Basics of Facility Design

- **Design Criteria**

- CIP & SIP

- ❖ Location of the skid
 - ❖ Size requirements
 - ❖ Longest distance to point of use
 - ❖ Transfer panels to tanks



Understanding the Basics of Facility Design

- **Design Criteria**

- Integrated vial wash and heat tunnel
- Size and speed of the filling system
- Stainless steel change parts verses Delrin



Understanding the Basics of Facility Design

- **Design Criteria**

- Projected number of vials
- Vial sizes
 - ❖ Volumes of products being filled
 - ❖ Stopper and cap sizes
 - ❖ Change parts including pump sizes



Understanding the Basics of Facility Design

- **Design Criteria**

- Cleanroom support facilities
 - ❖ Formulation area
 - ❖ Gowning rooms
 - ❖ Preparation of disinfectants
 - ❖ Sterile storage areas
 - ❖ Glove change



Understanding the Basics of Facility Design

- **Design Criteria**

- Cleanroom support facilities
 - ❖ Batch record documentation
 - ❖ Pass through into clean room
 - ❖ Dirty parts wash area
 - ❖ Clean parts preparation and storage



Understanding the Basics of Facility Design

- **Design Criteria**

- Facility control system
- Visual and audible alarm systems
- Laboratory & office areas
- Viewing corridors
- Gray spaces for equipment



Understanding the Basics of Facility Design

- **Design Criteria**

- HVAC

- ❖ Heating Ventilation and Air Condition
 - ❖ Temperature
 - ❖ Humidity
 - ✓ Controlled
 - ✓ Monitored
 - ❖ Building management system
 - ✓ Controls all classified areas
 - ✓ Independent of non classified areas



Understanding the Basics of Facility Design

- **Design Criteria**

- HVAC

- ❖ Size of HVAC

- ✓ Cooling capability, from 62 – 66 °C
 - ✓ Individual fans for supply and return
 - ✓ Increases ability to control fill room
 - ✓ Ability to balance the fill room

- ❖ Supply to terminal filters 90 ft/min at 70% of fan speed or less

- ❖ Differential pressures of 0.5 in of water



Understanding the Basics of Facility Design

- **Design Criteria**

- HVAC

- ❖ Segregation of areas by classification or functional areas
 - ✓ Cleanroom
 - ✓ Freeze dryer area
 - ✓ Formulation
 - ✓ Gowning/Entrance to area
 - ✓ Autoclave/Dry heat oven unload and storage area



Understanding the Basics of Facility Design

- **Materials of Construction**

- Use materials that resist chipping, flaking, oxidizing and other deterioration
- Compatible with disinfectants
- Durable and easy to maintain
- Does not discolor over time
- Abrasion/Impact resistant



Understanding the Basics of Facility Design

- **Materials of Construction**

- Floor Material

- ❖ Terrazzo
- ❖ Mipolam
- ❖ Polycarbonate Polymer
- ❖ Epoxy with various grits
- ❖ Perforated Stainless Steel

Understanding the Basics of Facility Design

- **Materials of Construction**
 - Terrazzo



Understanding the Basics of Facility Design

- **Materials of Construction**
 - Epoxy with various grits



Understanding the Basics of Facility Design

- **Materials of Construction**
 - Mipolam





Understanding the Basics of Facility Design

- **Materials of Construction**

- Floor Material

- ❖ Balance cost of materials with longevity
- ❖ Surface finish from a safety standpoint
- ❖ Evaluate time and cost to repair
- ❖ How well does disinfectant sheet on it



Understanding the Basics of Facility Design

- **Materials of Construction**

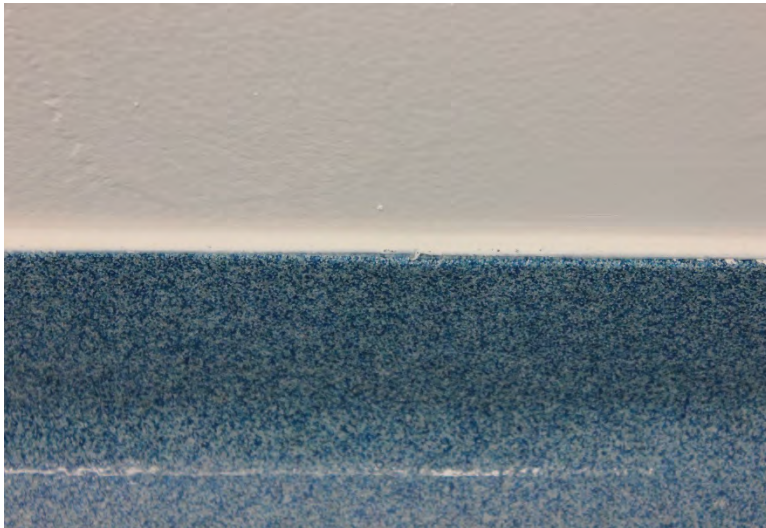
- Floor design

- ❖ Floor to wall interface coved

- ✓ Eliminate difficult to clean areas
- ✓ Radius must be large enough to sanitize with mop
- ✓ Floor to wall interface should be seamless to reduce contamination

Understanding the Basics of Facility Design

- **Materials of Construction**
 - Floor to wall interface covered





Understanding the Basics of Facility Design

- **Materials of Construction**

- Floor design

- ❖ Preparation of floor prior to installing

- ✓ Evaluate the water tables

- ✓ Vapor barrier/sealing floors

- ✓ Primary adhesion layer

- ✓ This is the most important aspect to installing a floor



Understanding the Basics of Facility Design

- **Materials of Construction**

- Floor design

- ❖ Installing floor

- ✓ Floor material

- ✓ Sealing floor

- ❖ Install floor

- ❖ Maintenance of floor



Understanding the Basics of Facility Design

- **Materials of Construction**
 - Ceiling and wall materials
 - ❖ Plastic laminates
 - ❖ Stainless steel
 - ❖ Synthetic panels like Kydex
 - ❖ New PVC material



Understanding the Basics of Facility Design

- **Materials of Construction**
 - Ceiling and wall materials
 - ❖ Plaster with epoxy paint
 - ❖ HEPA filters



Understanding the Basics of Facility Design

- **Materials of Construction**
 - Specific wall material
 - ❖ Flexible curtain
 - ❖ Lexan /Plexiglass
 - ❖ Glass for a viewing corridor
 - ❖ Bumper gards



Understanding the Basics of Facility Design

- **Materials of Construction**

- Specific wall material

- ❖ Modular partitions

- ✓ Cold Rolled/Cold Annealed (CRCA)
- ✓ Powder coated and durable
- ✓ Sandwich polyurethane foam (PUF)
- ✓ Non-flaking, bacterial resistant
- ✓ Non-corrosive



Understanding the Basics of Facility Design

- **Materials of Construction and Design**

- Air returns

- ❖ Location and number within the room
- ❖ Clean and sanitizable
- ❖ Stainless steel construction
- ❖ Size and shape

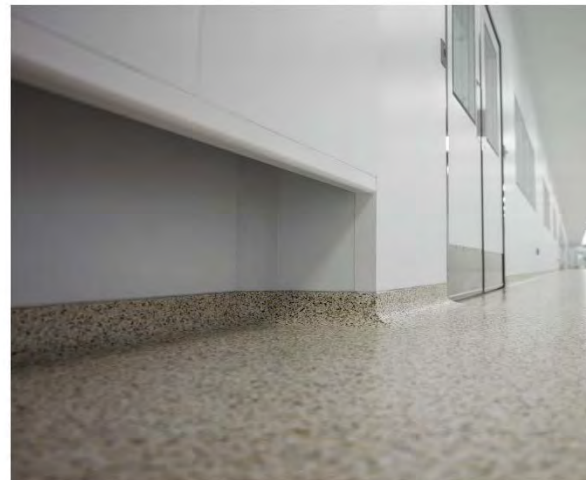


Understanding the Basics of Facility Design

- Air returns
 - ❖ Grills inside room
 - ✓ Type of cover matrix
 - ✓ Louvers or grills
 - ✓ Louver facing up or down
 - ✓ Will this effect the airflow
 - ✓ Removable for periodic cleaning
 - ✓ Wall behind the grill must be finished

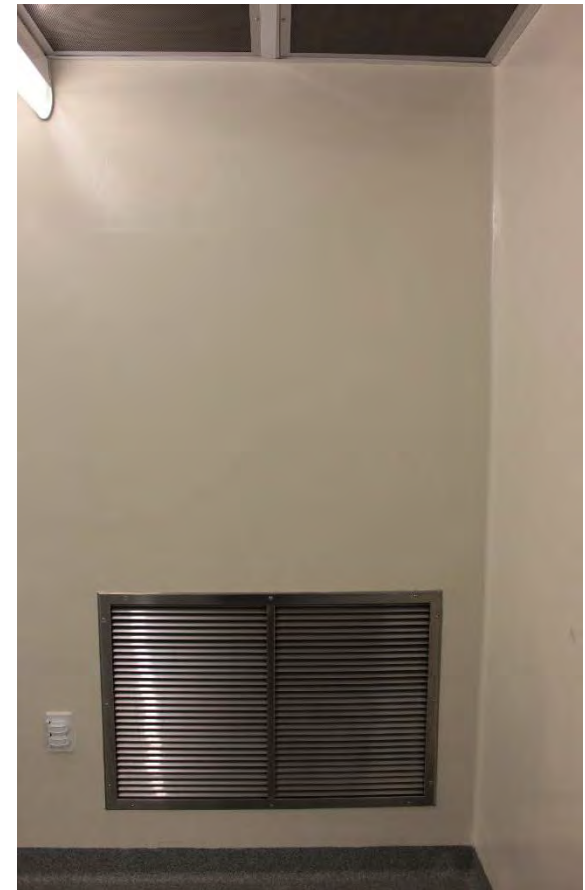
Understanding the Basics of Facility Design

- Air returns
 - ❖ Low wall returns
 - ✓ Less than 18- inches above floor
 - ✓ The lower the better



Understanding the Basics of Facility Design

- Air returns
 - ❖ Mid wall returns
 - ✓ Top is approximately
 - ✓ 36 inches above the
 - ✓ floor
 - ✓ Not recommended





Understanding the Basics of Facility Design

- Air returns
 - ❖ High wall returns
 - ✓ Above 5-feet above the floor
 - ✓ Old facility design
 - ❖ Ceiling returns
 - ✓ Old facility design
 - ✓ Re-design using a false wall to provide low wall returns

Understanding the Basics of Facility Design

- Air returns
 - ❖ Ceiling returns





Understanding the Basics of Facility Design

- Air returns
 - ❖ Grills within the wall
 - ✓ The floor is the bottom of the return
 - ✓ Keep very low on the wall
 - ✓ Grill is not visible and therefore can be blocked.
 - ✓ Check as a line clearance item
 - ✓ Use a stainless steel rod with a polished flat surface
 - ✓ Recommended design feature



Understanding the Basics of Facility Design

- Air returns
 - ❖ Grills within the door
 - ✓ Mid to low wall location
 - ✓ Minimizes depressurization of the room
 - ✓ Grill is not visible and therefore can be blocked.
 - ✓ Check as a line clearance item
 - ✓ Use a stainless steel rod with a polished flat surface
 - ✓ Recommended design feature

Understanding the Basics of Facility Design

- Door air returns





Understanding the Basics of Facility Design

- **Materials of Construction**

- Ceiling

- ❖ Compatible with HEPA and light grid
 - ❖ Panels must seal tight to ceiling grid
 - ✓ Gel track
 - ✓ Silicon
 - ✓ Silicon foam
 - ✓ Adhesive

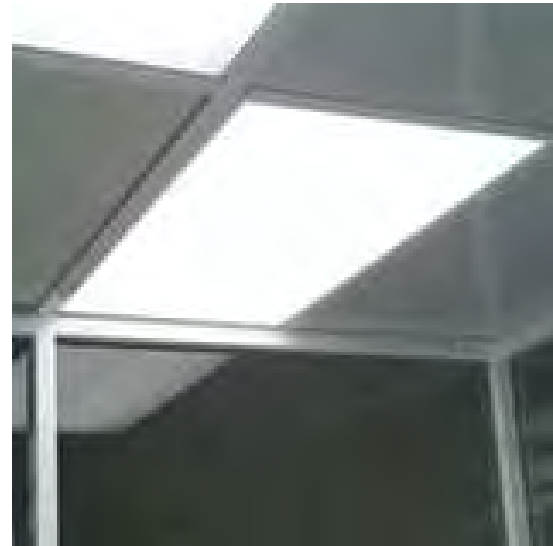


Understanding the Basics of Facility Design

- **Materials of Construction**
 - Ceiling lights
 - ❖ Recessed /flat
 - ❖ Tear drop
 - ❖ Small LED

Understanding the Basics of Facility Design

➤ Lights



Understanding the Basics of Facility Design

➤ LED Lights



Understanding the Basics of Facility Design

➤ Lights



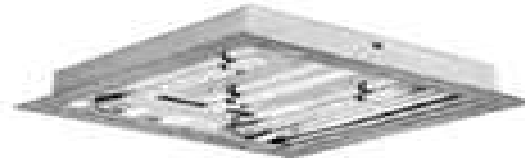
Recessed Bottom Opening
2x36 W TL-D Luminaire



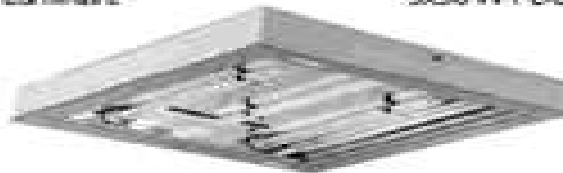
Recessed Top Opening
2x36 W TL-D Luminaire



Recessed Top Opening
3x36 W PL-L Luminaire



Recessed Bottom Opening
3x36 W PL-L Luminaire



Surface mounted Bottom Opening
3x36 W PL-L Luminaire



Understanding the Basics of Facility Design

- **Materials of Construction**

- Ceiling and Wall considerations

- ❖ Cost and durability
- ❖ Does disinfectant sheet well on the surface or form droplets
- ❖ How well does the material seam together



Understanding the Basics of Facility Design

- **Materials of Construction**

- Doors

- ❖ Construction

- ✓ Welded, ground and finished joints
 - ✓ Seamless frame
 - ✓ No seals between door and frame
 - ✓ Vented returns in the door
 - ✓ Clean room stainless hinges



Understanding the Basics of Facility Design

- **Materials of Construction**

- **Doors**

- ❖ Single or double door
- ❖ Sliding or hinged
- ❖ Door swing into, or out of the room
- ❖ Confirm doors do not block returns
- ❖ Differential pressure does not prevent the door from closing



Understanding the Basics of Facility Design

- Doors
 - ❖ Manual opening
 - ✓ Turn handle
 - ✓ Push plate
 - ✓ Pull bar
 - ❖ Automatic
 - ✓ Push plate
 - ✓ Flushed wall mounted sensors
 - ✓ Vertical non exposed sensor

Understanding the Basics of Facility Design

➤ Doors



Understanding the Basics of Facility Design

➤ Doors





Understanding the Basics of Facility Design

- **Materials of Construction**

- Work Surfaces

- ❖ Stainless Steel
 - ❖ Solid not perforated
 - ❖ Clean and sanitizable
 - ❖ Lowest useable shelf must be above the top of air return

Understanding the Basics of Facility Design

- **Materials of Construction**
 - Work Surfaces





Understanding the Basics of Facility Design

- **Materials of Construction**

- Work Surfaces

- ❖ Carts

- ✓ Clean and sanitizable
 - ✓ Finished edges
 - ✓ Non-ball bearing wheels
 - ✓ Wheels must be cleanable and cleaned with room
 - ✓ Lowest useable shelf must be above the top of air return

Understanding the Basics of Facility Design

- **Materials of Construction**
 - **Cart Work Surfaces**





Understanding the Basics of Facility Design

- Work Surfaces

- ❖ Tables

- ✓ Underside must be cleaned and sanitizable
 - ✓ If in the Grade-A areas, must be 6-inches off the wall
 - ✓ Does not block air returns
 - ✓ Consider fixing to wall or floor for consistency

Understanding the Basics of Facility Design

- Work Surfaces
 - ❖ Tables





Understanding the Basics of Facility Design

- Work Surfaces
 - ❖ Storage Racks
 - ✓ Wire racks are extremely difficult to clean/sanitize
 - ✓ Lowest useable shelf above top of return vents
 - ✓ Confirm it does not block returns
 - ✓ Evaluate the number required

Understanding the Basics of Facility Design

- Work Surfaces
 - ❖ Storage Racks





Understanding the Basics of Facility Design

- **Aseptic Processing Areas**

- Pass through

- ❖ Optimize size and locations
 - ❖ Confirm door swing is acceptable
 - ❖ Doors interlocked
 - ❖ Stainless steel material of construction



Understanding the Basics of Facility Design

- Pass through
 - ❖ Glass/Lexan to see inside
 - ❖ HEPA filter above pass box opening to the fill room
 - ❖ Clean room pass through
 - ✓ Hinges
 - ✓ Door handles
 - ✓ Gaskets required or not



Understanding the Basics of Facility Design

- Pass through
 - ❖ Active
 - ✓ Automated system with HEPA's and return ducts
 - ✓ Very expensive and not usually recommended
 - ✓ Can be difficult to validate
 - ✓ Minimal contact time for items sanitized with alcohol due to the air movement within

Understanding the Basics of Facility Design

- Pass through
 - ❖ Active





Understanding the Basics of Facility Design

- Pass through
 - ❖ Passive
 - ✓ Manual system
 - ✓ Inexpensive
 - ✓ Easy to install and validate
 - ✓ Good contact time for items sanitized with alcohol

Understanding the Basics of Facility Design

- Pass through
 - ❖ Passive





Understanding the Basics of Facility Design

- **Aseptic Processing Areas**

- Stacked pass through

- ❖ Entrance

- ✓ Top for equipment and supplies
- ✓ Bottom for large items and carts

- ❖ Exit

- ✓ Top for dirty/used items and equipment
- ✓ Bottom trash



Understanding the Basics of Facility Design

- **Aseptic Processing Areas**

- Grade A

- ❖ The highest standard of air/surface cleanliness
 - ❖ Full aseptic gowning required
 - ❖ Areas where product, sterile components and sanitized equipment are exposed to HEPA filtered air



Understanding the Basics of Facility Design

- **Aseptic Processing Areas**

- **Grade A**

- ❖ Full HEPA coverage over the critical areas
- ❖ Uniform laminar flow air required
- ❖ Design criteria for the velocity of air at the filter face is 90 ft/min \pm 20%
- ❖ Room air changes per hour: 100 - 300



Understanding the Basics of Facility Design

- **Aseptic Processing Areas**

- Grade A

- ❖ Placement and number of return vents is critical
 - ❖ Direction of air flow is extremely important in the critical areas
 - ❖ Minimize turbulent air flow if possible
 - ❖ Use the first air concept



Understanding the Basics of Facility Design

- **Aseptic Processing Areas**

- **Grade B**

- ❖ The second highest standard of air/surface cleanliness
 - ❖ Surrounds or is adjacent to the Grade A aseptic processing areas
 - ❖ Critical airlocks within the aseptic areas
 - ❖ Full aseptic gowning required



Understanding the Basics of Facility Design

- **Aseptic Processing Areas**

- Grade B

- ❖ Full HEPA ceiling not required
- ❖ Laminar air flow not required
- ❖ Design criteria for the velocity of air at the filter face is 90 ft/min \pm 20%



Understanding the Basics of Facility Design

- **Aseptic Processing Areas**

- **Grade B**

- ❖ Room air changes per hour:
Approximately 100 for good air flow
- ❖ This design should meet the at rest Grade A environmental monitoring criteria
- ❖ Clean side of the aseptic gowning room



Understanding the Basics of Facility Design

- **Aseptic Processing Areas**

- **Grade C**

- ❖ Room air changes per hour: Greater than 30, however greater than 75 for good air flow in the gowning room
- ❖ Area used for handling of primary materials and preparation of solutions and/or commodities that will be sterilized



Understanding the Basics of Facility Design

- **Aseptic Processing Areas**

- **Grade C**

- ❖ Used for preparation, washing and cleaning of non-sterile equipment and materials
- ❖ Equipment airlocks leading to Grade B areas
- ❖ Initial aseptic gowning areas



Understanding the Basics of Facility Design

- **Aseptic Processing Areas**
 - Grade D
 - ❖ Initial preparation and washing of components



Understanding the Basics of Facility Design

- **Identify a Facility Design Company**
 - Put together an experienced and knowledgeable design team
 - Team must encompass line operators, senior management and consultants
 - The more information the company provides the design firm, the better the final outcome



Understanding the Basics of Facility Design

- **Identify a Facility Design Company**
 - Identify firm capable of providing all requirements of the facility
 - Reputable company with significant number of various build designs
 - Assess regulatory compliance of previous designs



Understanding the Basics of Facility Design

- **Identify a Facility Design Company**
 - Visit facilities to determine additional information
 - Evaluate ISPE facility design awards
 - Assess and understand what is considered cGMP. The key word is current.
 - Many companies have a template that may be out of date



Understanding the Basics of Facility Design

- **Identify a Facility Design Company**
 - Identify a single individual that understands all aspects of the facility design
 - Not just the design of the facility but the process that will occur
 - The project manager needs to understand how all the pieces to the puzzle fit
 - If the pieces do not fit, the project will be significantly delayed



Understanding the Basics of Facility Design

- **Takeaway Message**

- Get Quality involved with facility design based on sampling requirements
- Ensure qualified personnel review plans. Confirm plans are cGMP and not old designs
- Budget for all the nice to haves because it will make operations easier
- Design for 5 years into the future