1. Proper cGMP Facility Layout

Proper cGMP facility layout separates or segregates critical plant functions. This is especially important for products that pose significant risks of migration of contaminants through the plant. The first step is to separate the receiving and shipping functions to eliminate the possibility of cross contamination. For example, a U shape layout locates dedicated docks on each leg. If it isn't feasible to physically separate shipping and receiving, incorporate a barrier wall in between the two areas.

Ideally, your receiving warehouse should be used exclusively for incoming raw product. A dedicated quality assurance laboratory verifies that the package labeled Product A is indeed Product A. Tests ensure that there are no microbiological contaminants and visual inspection detects foreign material. It is critical to determine that the ingredients are pure before they move over to the processing side. Contaminated material should be destroyed or returned to the supplier.

As an additional precaution, consider using dedicated material handling equipment such as forklifts for each dock area. Forklift traffic and personnel movement throughout the plant are two of the primary sources of potential cross contamination.

2. Access Control

It is important to understand how people enter your cGMP facility and how they move around the plant. Having a separate entrance for employees and visitors is common practice today rather than a unique facility design.

Additionally, you want to keep truckers and other delivery personnel out of the plant. They don't know how you operate; you don't know what kind of plant they were in before yours. There is simply no reason for them to have access to the production area. Keep them outside of receiving and shipping in a dedicated area which allows them access to the receiving or shipping clerk. A waiting room and restroom facilities are nice amenities to provide since truckers have to wait for their rig to unload or be loaded.

Zone your facility to restrict access by job functions. This is easily done with security badges or fingerprint verification scanners and guards against cross contamination between manufacturing steps that could threaten the safety of your product. This also reinforces the overall concept of segregating the processing area and the reasons behind it.

For example, sanitation areas should be located next to the processing area so that clean equipment doesn't have to pass through "dirty" areas on its way back to the line. If possible, provide a "utility" corridor so that clean equipment doesn't pass through other areas of the plant. Operating and maintenance personnel should be able to sanitize equipment and bring it directly back into the production area. Only those personnel whose job functions are involved in this step should have access to both areas.

3. Proper building pressurization

Pressurizing your entire facility relative to the outdoors minimizes the opportunity for airborne contaminants to enter. When a door is opened in a building under positive pressure, the air is more likely to go out rather than come in. Proper pressurization deters insects from being brought into the building as well.

This principal also holds true from room-to-room within the building. Typically, the production area is the cleanest in the plant and should be pressurized positive relative to the other support areas. For example, the production area should be under a higher pressure relative to the packaging area. Air should flow away from clean areas toward less clean areas.

In some cases, separate and isolated air handling systems may be used to further reduce the possibility of cross contamination. This is especially important if your operation generates large amounts of dust or airborne contaminants.

4. Airborne sanitation

Although building codes set guidelines for air intake locations, common sense plays a role as well. Installing them over the loading docks or putting them next to the waste area isn't a good idea. Also consider the quality of the outside air source. Most large plants use economical roof mounted packaged units. It is more difficult to effectively control the intake quality on these units than on a central interior unit.

Using UV lights in the air handling unit minimizes the risk of bringing in airborne contaminants. The lights kill bacteria and insects as well as prevent mold from growing in the damp environment around the cooling coils and other parts of the air handling unit. Keeping the air in the production area cool and dry will further reduce the growth of potential airborne pathogens.

Best practices in ventilation include educating and training your staff about its importance to cGMP safety. A successful ventilation system is designed for static conditions, but day-to-day

operations are dynamic with forklifts, personnel, and materials moving through roll-up doors. For example, during hot summer months, problems often are caused by employees propping open doors, especially during breaks. Plant practices should support the ventilation system and staff should be reminded of this on an ongoing basis.

5. Design for cleanliness

Good design includes avoiding horizontal surfaces that can collect dust and moisture. Since it is nearly impossible to design a plant without horizontal surfaces, they should be slightly tilted to form a sliding ledge. Install equipment and other utilities so that maintenance staff can get hands or cleaning tools behind them to clean. If hangers are used to support piping overhead, they should be either non-threaded or covered with a plastic sleeve to prevent dust from accumulating. Ideally, avoid using threaded rod altogether to achieve an optimum level of cleanliness throughout your plant.

The location of lavatories is another common sense design consideration. They should always be located outside the production area with a hallway or vestibule in between. These aren't meant to be impediments or an inconvenience; they are opportunities to post reminders of the proper personal hygiene steps employees should take before returning to the production floor.

Regardless of whether the area is wet or dry, it's always a good idea to have relatively smooth, impervious surfaces. Wet areas should be resistant to moisture and the cleaning chemicals typically used. Dry areas should minimize the opportunity for dust and stray product to collect on surfaces. It's a good idea to have a sanitation plan in mind when you begin selection of the types of walls and finishes that you'll be using.

6. Install durable wall and ceiling materials.

Time and exposure are the enemies of any facility. As your facility ages, surfaces become scarred and abraded, paint and finishes peel and flake, and it becomes harder to keep clean. Your ceilings have degraded, too, from exposure to heat, moisture, and concentrations of airborne contaminants. As these surfaces break down, the chance of product contamination increases. This is especially true of insulated ceilings. As they age, the ceiling surface breaks down and fine particles of insulating material can fall into your process areas.

Selecting durable wall and ceiling materials is an absolute must for cGMP plant design. Where paints are used, they should form a tight bond with the substrate and resist peeling and flaking. Hard surfaces should resist cracking and flaking, too. Ceiling materials should be resistant to extremes of temperature and moisture, as well as offer good chemical resistance to substances that might become airborne from your process operations. Insulating materials should be

immobilized wherever possible. Solid insulation rather than soft, friable materials should be considered. Even solid insulation needs to have a good system of providing protection against mechanical damage.

7. Separate maintenance from production

Maintenance and production areas should be kept separate from each other. Personnel that may be machining, grinding, welding or any of the normal maintenance functions should follow appropriate cleaning and gowning procedures before entering the production area.

A walkable ceiling or other interstitial spaces help separate pipes and utilities from your processing line. Maintenance personnel can access them without contaminating the production area below. Further, if there is a leak, it collects on the impervious ceiling and doesn't come down into the production area. However, segregating pipes and utilities requires additional discipline from the plant maintenance crew; the old adage, "out of sight, out of mind" often applies. When designing these spaces, determine how they will be routinely cleaned.

8. Plumbing design practices

Install independent plumbing networks for water used in the production process and water that is used for lavatories or for drinking water. This is especially useful when you want to use a hot water process loop to supply sanitation systems. A process water loop can be isolated from a handwashing system, reducing the chance of inadvertent scalding. Treat water used in production to meet sanitation and quality requirements.

Process waste water, or gray water as it is sometimes called, is generated by washdown of equipment, rinsing floors or other maintenance activities. If these are collected in a separate system, employ simple steps like filtration and pH adjustment to help reduce sewage burden.

Black water is sewage from toilets and waste streams that should be kept separate from process water until it leaves the facility. Avoid merging these streams until just before they are introduced into the main sanitary sewer in order to protect the facility against backflow from the black water system.

9. Pest control

Pest control starts outside your plant, where pests live. Evaluate all entry points including doorways, shipping docks, piping and utilities, and air vents. Landscape designs often incorporate an 18" – 36" strip of sharp-edged rock around the perimeter of the building to deter rodents from coming in. This also prohibits planting shrubbery or other landscaping that harbor

pests too close to the building.

Dock doors should be designed, installed and inspected to ensure that they close tightly and are properly sealed. Pipes and utilities should be sufficiently caulked and air vents should be covered with insect screens. Install exterior lighting away from the building as much as possible to minimize insect attraction. It's also important that bug zappers aren't visible from the outside so they don't attract bugs into the plant.

Inside the building, a coved floor edge that extends a short distance up the wall eliminates crevices that encourage infestations. Paint a white strip along the edge of the floor to expose vermin that may have eluded other precautions. Hire a qualified pest control company to develop a regular inspection and prevention program.

10. Employee sanitation practices

Your facility should be designed to make it as convenient as possible for production area personnel to follow your sanitation guidelines. After entering the facility in a dedicated entrance, production personnel should have a locker room where they are able to change from their street clothes into their production clothes.

Handwash stations should be judiciously placed outside of lavatories, break rooms, and smoking areas. They should be equipped with automatic water sensors to regulate water flow without the need to handle a faucet. In addition to an initial orientation regarding sanitary practices, ongoing training is essential to ensure that guidelines are followed.

Training your employees on proper sanitation and methods is just as critical as training them on safe operations and equipment. This course should begin with a basic understanding of what contaminants are and what the consequences of producing contaminated product can be. Next, discuss how to prevent contamination and to make sure the chances are minimized. Finally, stress the importance of a strong QC/QA program in plant operation.

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