General principles of hygienic design

An excerpt from the GMP Series PDF Download Applying the Principles of Hygienic Design to Solid Dosage Forms

8 min. reading time

by Richard Denk

Hygienic design is very important when planning and designing machinery and facilities in the food and drugs industry. It refers to the easy-to-clean design of parts, components and production machinery. Hygienic design results in machines with a closed design that have little dead space and are easy to clean. It is particularly important when handling solids because solids, unlike liquids, can be distributed throughout the entire building by the ventilation system, from surface to surface and from person to person if the solids are not handled properly or are handled open. At the same time, there is a risk of product cross-contamination which in accordance with the EU GMP Guidelines must always be avoided. The design of the machinery to be used is extremely important in this context and should be taken into account at an early stage of planning.

The designer must first of all consider the parts of the machine that will have direct contact with the product. These parts have the highest priority when it comes to hygienic design. The designer must then consider the parts without product contact, as well as the working environment. The requirements affecting these areas are less stringent.

The following points apply in general to hygienic design of machinery:

- **Microscopic fissures, pores and cavities:**
  Microscopic fissures include all irregularities in surfaces and in contact surfaces of component parts. These fissures are practically impossible to clean due to capillary action. The designer must examine the design carefully for the presence of microscopic fissures and remove them, if necessary, using appropriate design measures.

- **Macroscopic fissures and cavities:**
  Visible fissures can occur, for example, where bolts/screws pass through larger drilled holes. Cavities occur, for example, when seals are recessed below surfaces, e.g. when screws are used. When dealing with this type of problematic area, problem awareness and careful examination are required if a constructive solution is to be found.

- **Problematic flow conditions:**
  Sharp edges in transition zones where the cross-section widens or narrows, sudden flow diversions, shadow areas, as well as dead zones have an adverse impact on the flow properties. These areas are particularly critical because the flow rate at these locations is practically zero. This can lead to a build up of deposits, which support bacterial growth. A hygienic design facilitates an optimal flow and prevents deposits.

- **Self-draining/draining:**
  The insides and outsides of machinery must be self-draining or drainable, and easy to clean. Horizontal surfaces must be avoided, i.e. they should always slope to one side. External surfaces should be sloped in such a way that any liquid from the production area runs off.

Product contact surfaces

The internal parts of a machine, i.e. the "product contact surfaces", must be free of dead space and easy to clean. Internal fittings in the machine parts should be avoided because they prevent simple cleaning. This is, however, difficult to realise when working with solids.

When filling an API, for example, it may be necessary to crush agglomerates after drying, which requires the installation of a crusher with a sieve. Representative samples are taken from the product using a sampler. The product is then filled into intermediate or final containers using a precise metering system. All of this requires a considerable number of mechanical parts and many fittings in the product flow.

As a result, it is not always possible to use a CIP system for cleaning. In practice, WIP processes (washing in place) are used, which involves the critical machine parts being dismantled and manually recleaned after automatic pre-washing. The critical parameters must be checked prior to and during the cleaning validation and documented in the cleaning SOP.

Non-product contact surfaces and the area surrounding the machinery

If the machines have to be opened during the production process, hygienic design should not be limited to the product transfer systems and processes. Cleanrooms especially, where specific requirements apply to the cleaning of machinery and surfaces, must have as few additions, cable bushings etc. as possible.

The design of the area where emptying or filling takes place is also important because of the close proximity to the product and the increased risk of contamination. It must also be taken into consideration whether a monofunctional or multifunctional system is being used. The cleanroom class (A, B, C or D) is also important. Each area requires its own individual design which must be defined and documented in the user requirements specification during the early stages of planning. The following aspects are important for a hygienic design of the outside of the machine:

- Outer surfaces polished to a required surface quality
- No open cable routing

The panelling of added components such as e.g. drives, should be moved from the production to the technology area. This also simplifies the servicing and maintenance of the machine.

Weakness in the planning phase

Problems that occur in practice often result from mistakes made during the planning phase. The issue of supply and discharge of solids is often only taken into consideration after planning of the room or building has been completed. The rooms or buildings are already under construction before the supply and discharge of solids is planned for. During API production, for example, the reactors and crystallisers are usually installed on the upper floors, the centrifuges on the middle floors and the dryers on the lower floors. Equipment inlet and outlet heights for the solids feed must be taken into consideration, because the input materials are sometimes delivered in large containers. These aspects must also be considered when designing machines for manufacturing medicinal products.

When the solids feed is not taken into consideration, the solids can sometimes no longer be supplied or emptied using gravity. They must then be supplied to the machines using transport systems (e.g. pneumatic conveyor systems) in order to feed the solid to the reactors or load a tablet press, for example. When emptying dryers and centrifuges in API production and blenders in medicinal product manufacture, a pneumatic conveying system must also be used if the room ceiling is not high enough.

The design of solid transfer systems is often not covered in enough detail during the planning phase. Open pipes, open cable ducts and an inadequate design of the machine surfaces are frequently encountered, so that the machine is often difficult to clean.

The room design is another weak point. Most APIs are filled in a classified room after drying, but the design of the room is often inadequate. There are often weaknesses in the wall design and spatial planning with GMP-compliant transitions in particular.

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