PRO-GUIDE		
Industry	Pharmaceuticals	●●●
	Food	●
	Cosmetics	●
	Chemicals	●●
Funktion	Planner	●●●
	Operator	●●●
	Purchasing	●
	Manager	●●

KEY-FACTS

For Planners and Operators

- Depending on the product-related or process-related requirement, numerous protective measures and containment concepts are possible.
- Efficiency and cost-effectiveness criteria should always be examined to determine whether it is worth investing in system technology or whether it makes more sense to use personal protective equipment.
- In order to identify the best possible solution in terms of safety and cost-effectiveness, the individual requirements are analyzed and a concept is developed in the "Efficient Containment Concept".

Individual Containment Solutions

No Contradiction: Containment and Efficiency

Whether or not personal protective equipment is the most economical solution when handling toxic active ingredients depends on the general conditions of production.

Images: Glatt

If the safety of personnel can be achieved by investing in a high-containment system, then there is no need for a cumbersome protective suit – whether or not the investment pays off has to be analyzed.

High-potency substances require highly effective protective measures for the product and people. Given the growing demand for OSD products containing high-activity and toxic ingredients, the legal requirements for containment are becoming increasingly stringent. A quarter of all pharmaceutical ingredients are highly active. Increasingly more stringent requirements are therefore being placed on system manufacturers. They have to protect operating staff from contact with toxic active ingredients while also ruling out the risks of cross-contamination.

Alongside the familiar FDA and ICH guidelines, the current EMA guideline has been setting new standards since June 1, 2015. It is the first to state that toxicological data should be used to assess the maximum limits of exposure. Earlier assessment criteria such as „visibly clean" or „1/1,000 of the therapeutic dose" need revisiting. This is a challenge for pharmaceuticals manufacturers, as it requires well-founded toxicological knowledge of the active ingredients involved.

Different requirements need different solutions

Depending on the product-related or process-related requirement, numerous protective measures and containment concepts are possible. Notably, the cost-benefit ratio is an important decision-making criterion when selecting the optimum system solution. So ensuring an optimum containment investment solution starts even before the system selection process. A risk assessment and analysis of parameters of relevance to production indicate the right approach. Here the toxicological values, frequency of production cycles, and operator exposure impact on the decision-making process.

A PDE (Permitted Daily Exposure) is defined for operators working with pharmaceutical substances. This is determined using toxicological studies. It is calculated from the maximum dosage that a person can be exposed to without this having a pharmaceutical effect.

Protective equipment or containment-optimized system technology?

Strict containment requirements place particular demands on the system. However, high containment is not always needed for the complete system. Depending on the toxicological assessment and frequency with which the product is changed, the operating staff can be protected from contamination using full protection at individual points which require particular attention.

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At first glance, personal protective equipment (PPE) may seem to be the most economical option. However, under certain circumstances a specially equipped high-containment system is more cost-effective. In principle, all Glatt systems can be equipped for total containment. Efficiency and cost-effectiveness criteria should always be examined to determine whether it is worth investing in system technology or whether it makes more sense to kit out the operator with personal protective equipment. The following questions must therefore be answered:

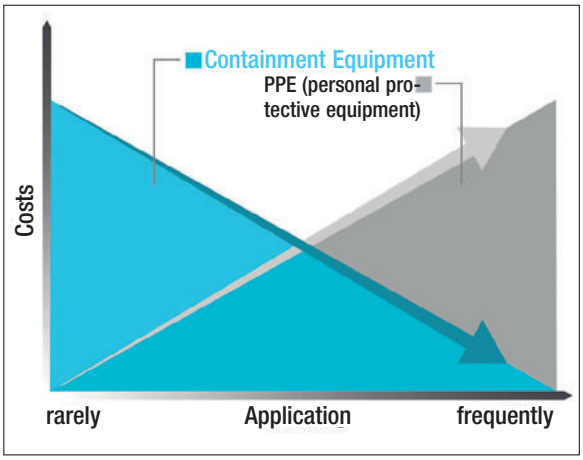
- What is the maximum workplace concentration?
- How concentrated are the toxic active substances?
- How often are the operating staff exposed to the substances?

If not providing your staff with full protective equipment is more profitable in the long term, the system technology must meet special requirements. This concerns the observance of the OEL level as well as the contained cleaning of the system after a process. In order to identify the best possible solution in terms of safety and cost-effectiveness, an analysis is first carried out in the Glatt "Efficient Containment Concept" to determine which containment level is required in which area of the system. The production process is then adapted to these requirements with the appropriate containment technology.

Technology for high containment

This is illustrated using the example of a granulation process in a batch procedure. Certain interfaces must be given special attention and designed to be free of contamination in order to protect against dust exposure. This mainly affects charging, discharging, sampling, maintenance, and repairs. Only hermetically sealed, 12 bar pressure-shock resistant components made from stainless steel in line with the Glatt Pro concept are used along the entire process chain. Seals are designed or optimized for this purpose.

A number of technical solutions are available to achieve containment in the granulation line. This includes, for example, the TKS double-flap system, which is used to dock containers to the system without contamination. Special sampling equipment is used in this process, which prevents product dust from being released in an uncontrolled way as well as preventing cross-contamination. Not only do special metal filter cartridges separate out dust by means of their filter fabric, they are also easy to clean. When it comes to system cleaning, there are semi-automatic devices for WIP cleaning or fully automatic solutions for CIP cleaning.



Which solution is the most economical depends on how frequently the operators are exposed to toxic dusts throughout production. In the "Efficient Containment Concept" approach, this is analyzed for the specific application in question.

Design in line with GMP guidelines is very important

Alongside technical functionality, the fact that the components are designed in line with GMP guidelines is very important. In order to achieve optimal system cleaning, sealing systems, bushings, shaft seals, and interfaces with other systems should be produced to GMP standards. The design of surfaces which come into contact with the product is especially important in this respect. The higher the containment level, the higher the surface quality needs to be. In order to permanently ensure high containment, regular maintenance and repairs must be carried out. This applies in particular to mechanical components such as double-flap systems, but also filter and exhaust air systems, seals, flange systems, tri-clamp connections, and shaft bushings. The optimal maintenance strategy is also developed for the application in question as part of the "Efficient Containment Concept". ●

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