BATCH PROCESSING SOLUTIONS.

Beyond the Granulator.

GEA Engineering for a better world.

GEA.com

GEA combines trusted technology with an ongoing program of innovation and price-performance leadership.

Relationships matter. We believe that by giving you access to the scientists and engineers who created our equipment and developed our technologies, you can invest with confidence, safe in the knowledge that GEA plant is designed to achieve its maximum potential and has been optimized for manufacturing excellence.

When compression problems occur, for example, it's all too easy — and common — to focus on the tablet press. The root cause of the issue, however, is more likely to be a consequence of upstream processing.

Poorly granulated materials will not compress well and most fine pharmaceutical compounds require granulation to improve their flowability and processing properties prior to tableting. Likewise, poor mixing, granulating and drying will lead to issues with tableting that cannot be rectified by adjusting the press.

To cite a Japanese proverb: we learn little from victory and much from defeat. In pharmaceutical terms, this means selecting the most appropriate technology, using the equipment to its maximum capacity and keeping a strong focus on the total cost of ownership.

By delivering everything from technical know-how and process support to product development, cutting-edge equipment, project management and the service you need to bring your plans to fruition, we supply the added value and the deep-rooted knowledge that counts.

Whether it's a single piece of equipment or a long-term strategic collaboration, our focus is on price-performance leadership, safety and quality. How do we do this? By shaping the future with better processes.

Tablet Compression

Our innovations include a unique dual control, PAT-compatible technology that monitors and controls tablet weight, hardness and density with an accuracy that cannot be achieved any other way.

Weight is controlled at pre-compression and hardness is controlled at main compression. As a result, weight and hardness can be controlled simultaneously and continuously on a standard tablet press.

GEA also offers adjustable dwell times at pre-compression (by up to 300%) without slowing the press: this functionality allows an increase in dwell time at pre-compression that's independent of machine speed, resulting in higher outputs and more consistent tablet quality. In addition, constant dwell times while varying the machine speed can be used to match the production capacity of the line without influencing tablet quality.

Other unique features ensure a constant flow and equal distribution of powder that are without equal, as well as integrated data collection and analysis, and advanced process control.

Our MODUL tablet presses provide the fastest product changeover in the market and our PERFORMA tablet presses provide the highest outputs. Plus, with the introduction of the ECM (Exchangeable Compression Module)-based MODUL rotary tablet press in 2002, GEA revolutionized the pharmaceutical industry.

The ECM succeeds in combining productivity, flexibility and safety — all in one — setting a new standard for pharmaceutical tablet production. A WOL (Wash-off-Line)-ECM version is available for the high-containment processing of potent and toxic formulations.

MUPS (Multiple Unit Pellet System) Production

MUPS tablets are a multiparticulate pharmaceutical solid dosage form produced by compressing a mixture of drug-containing pellets and powder excipients. The pellets have a spherical core that contains or is coated with the active ingredient, and have one or more protective layers (cellulosic and acrylic polymers) to control drug release.

Producing MUPS tablets using conventional bin blending to feed a tablet press is reported by many pharmaceutical manufacturers to pose significant challenges regarding productivity and batch content uniformity.

As a result, to increase process yield and ensure tablet quality, an innovative continuous dosing, blending and compression system has been developed by GEA that eliminates these production inefficiencies and product quality risks. Segregation is kept to an absolute minimum and online process monitoring detects out-of-specification (OOS) tablets.

Tablet Coating

Coating is used to add color, protect, mask the taste or create a modified release form in pharmaceutical production. GEA offers a range of standard, innovative batch coater systems for particles, powders, granules, crystals, pellets and tablets.

Coating is used extensively in the solid dosage industry for the application of non-functional or functional coats (aesthetic, protective or rate controlling polymer films) and for the deposition of active pharmaceutical ingredients (APIs) onto nonpareils (multiparticulate dosage forms).

Applications include taste masking, color modification, physical protection and/or to create modified release forms. Beyond efficient API layering techniques for multiparticulate systems, the pharmaceutical industry has an inherent need to accurately coat objects that are 3–30 mm in length (the most common size range for single-unit solid dosage forms) with APIs.

These include tablets for oral administration and other delivery methods (human implantation, for example). Existing coating methods in this size range have coating speed and accuracy/uniformity limitations, particularly for the deposition of low dose APIs onto single unit tablet dosage forms.

The GEA Coater

The GEA Coater is a revolutionary, high performance tablet coating technology that gently and accurately deposits controlled amounts of coating materials on tablet cores — even if they are extremely hygroscopic or friable.

The GEA coater is able to process small quantities of tablets at very high rates, offering improved heat and mass transfer. PAT-compatible, the GEA Coater is easy to clean and offers significant cost savings compared with conventional systems in terms of time, materials, downtime, process revalidation, stability testing, etc.

With a smaller technical space requirement than established technologies, less cleaning and a reduced plant area is needed. And, being a continuous production technology, no scale-up is required and the maximum batch size is almost infinite.

Contained Materials Handling

Taking an individual approach to each customer's needs and applying our extensive experience and know-how, we combine performance excellence with technological innovation to deliver long-term competitive advantages.

With thousands of installations worldwide, GEA has developed an outstanding reputation for quality and service to become the clear leader in contained materials handling technology, including powder handling, intermediate bulk container (IBC) systems, containment valves, container systems, in-container blending, tablet handling and IBC washing.

Our distinctive specialization lies in the integration of BUCK® containment technology into complete solutions for pharmaceutical solid dosage form facilities.

How Much Containment?

Containment issues have become a vitally important aspect of solid dosage form production. Active pharmaceutical ingredients (APIs) are becoming increasingly effective, with more than 50% of all new chemical entities (NCEs) being classified as potent (OEL <10 µg/m3); at the same time, the health and protection of operators, all over the world, is being put under an ever more intense spotlight.

Why is the pharmaceutical industry interested in containment? For two reasons: operator exposure and the prevention or elimination of cross-contamination. But how much containment is required? A key point is that the required level of equipment and containment performance is not simply a matter of measuring the Occupational Exposure Limit (OEL) of the product. This is a common misconception and, as a result, there is a tendency within the industry to over specify.

Selecting an overly complicated solution means that the system is more difficult to operate, difficult to clean and maintain and, of course, more expensive to buy. It can be problematic to show that a particular solution is "good enough," but it can be done. By understanding containment and looking at the product, the operator and the equipment, we can create well engineered and better value solutions.

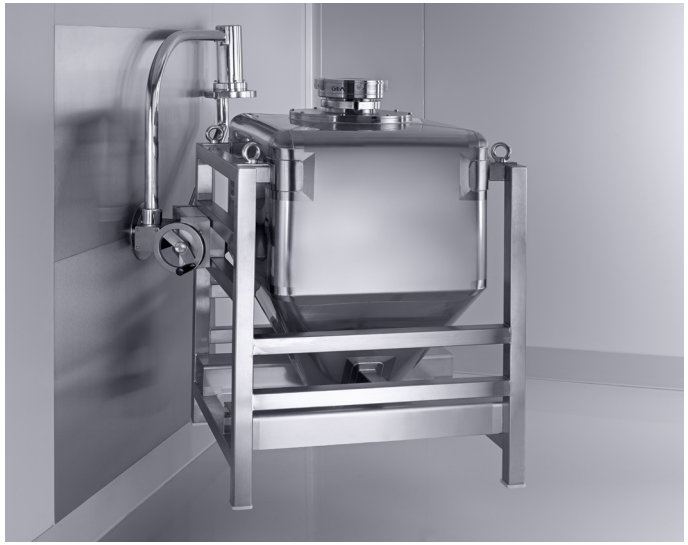
Three main factors dictate how much containment is required and, therefore, which method of containment is best: the nature, especially the potency, of the API handled is of paramount importance; the type of process to be executed; and, lastly, the working regime of the operators.

In Summary

Containment is determined by the characteristics of the product, equipment performance and operator function. Operator exposure depends on the type of equipment being used, product dilution levels and frequency of operation.

As exposure can't be fully prevented, the employer must ensure that the operator's RDI of a hazardous substance doesn't exceed the product-specific ADE by using suitable equipment. The company should only implement additional personal preventive measures when this cannot be guaranteed by appropriate technical options, including

- eliminating the source of risk
- substituting the hazardous material with a less harmful one
- modifying the process
- using engineering controls to reduce exposure (contained handling)
- improving administrative procedures (SOPs).



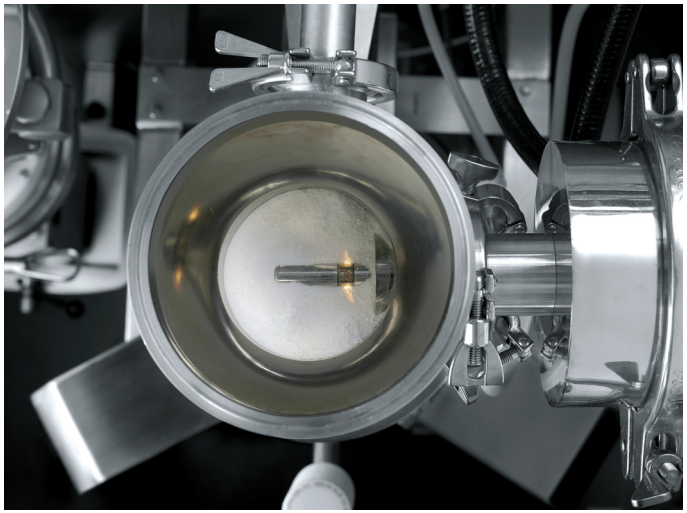
The selection, placement and implementation of suitable containment equipment can be a daunting task; it requires an in-depth understanding of the overall process, primarily to ensure that the chosen equipment performs at the necessary level, but also, from a financial point of view, to prevent any expensive and unnecessary investment in an over-performing solution.

GEA not only offers the largest variety of robust and compliant hardware solutions for contained materials handling, but it also boasts unrivaled expertise in identifying the most appropriate solution and a thorough understanding of containment risk analysis.

GEA can assist and advise you to determine what level of containment is required where and when, optimizing the manufacturing process and making it efficient, safe and cost-effective.

Digitalization

Multivariate monitoring and advanced process control (APC) solutions for batch and continuous pharmaceutical process units.



The US FDA's PAT (Process Analytical Technology) initiative has enabled GEA to combine its equipment design skills and process engineering know-how to integrate online (PAT) analyzers into its systems in a way that can provide real insight into the operation of the process and help customers to achieve key product quality targets.

The goal of the PAT initiative is to ensure that pharmaceutical products are manufactured using processes that are understood and monitored, so that the key quality characteristics of the products can be actively controlled.

Combining process monitoring with solid engineering principles and advanced modeling techniques will enable procedures to be actively controlled to compensate for minor input variations (raw materials), so that the specifications for the final product will be closer to ideal targets.

Plus, the continuous monitoring of product quality can prevent out-of-specification deviations and decrease production costs, as well as reducing final quality inspections by facilitating real-time release testing.

Built into its control systems, GEA has integrated its collective knowledge to help operators monitor and regulate their processes. For several steps, endpoints based on process parameters are available, and guidelines are given depending on the set points entered. In addition, GEA has experience with integrating innovative analytical tools for process monitoring and control.

The Lighthouse Probe

The Lighthouse Probe can be used with a range of spectroscopic techniques, including NIR and UV/Vis, to monitor moisture content and uniformity, determine endpoints during drying and coat growth. It also overcomes the traditional problem of product sticking to the observation window.

Cleaning

Current good manufacturing practices require that product is fully contained during processing to protect both operators and the environment. Integrated process systems not only offer containment, but also provide improved productivity through automation, increased yield and efficient cleaning procedures.

Today's increased demands for customized design, special construction materials, surface treatments, advanced control systems, compliant production and process validation have resulted in continuous improvements in solid dosage plant design for the pharmaceutical industry.

Automating the cleaning process ensures repeatability, allows validation and minimizes downtime. In recognition of the fundamental role played in today's advanced powder processing industry by automated clean-in-place procedures, GEA has developed a unique approach to CIP.

Concealed Services
The integrated design ensures that all lines and hoses for the utilities of the plant (water, electricity, hydraulics, etc.) are concealed. This creates a safe and uncluttered working space.

CIP and WIP Systems
More efficient cleaning is one of the key advantages of system integration. We provide validated cleaning with minimal downtime. GEA offers CIP-by-design features in all of its processes. Every aspect of the integrated plant, from inlet to discharge, has been value-engineered for optimum cleanability. Spray system, tanks cleaners, nozzles and seals are an integral part of our equipment design.

IBC Washing
Although it is important to handle and transfer powders in a contained way to prevent operator exposure, it is equally important to be able to wash the IBC and the containment valves in place — without the need for operator intervention to strip and clean the valve.

Tablet Press Cleaning
Thanks to its inherently closed design, the ECM model significantly reduces the concentration of airborne particles in the tablet compression room and contributes to the protection of equipment operators and supervisors.

Easy and Safe Single-Pot Processor Cleaning
To verify the CIP approach, a cleaning validation study was done on a single-pot processor using both a water-soluble (theophylline) and a water-insoluble (mebendazole) material. The results showed that the CIP system is capable of removing both products to a level well below the generally accepted acceptance criteria.

Using our unique CIP approach, a product changeover can take place in 2–3 hours, reducing the downtime of the equipment (depending on the product characteristics and the cleaning program used). As the whole CIP cycle takes place automatically, it is also possible to start the cleaning in the evening, allowing it to run overnight and prepare the equipment for a new production run in the morning.

For more information
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