KEEPING CONTAINMENT COMPLIANT.

The Flexibility You Want.
The Quality You Need.

GEA Engineering for a better world.

GEA.com

GEA has a long history of expertise in the field of containment.

Driven by the development of more potent active ingredients and a stronger focus on health and safety by the regulatory authorities, the last 20 years have seen a significant increase in the need for contained handling and processing in the pharmaceutical industry.

Containment is the separation of the product from the people — and from the environment — by a barrier. Containment is used to prevent any negative impacts (contamination) being transferred from one area to another and vice versa.

Why is the pharmaceutical industry interested in containment? For two reasons: operator exposure and the prevention or elimination of cross-contamination. Failure to adopt appropriate measures could have disastrous consequences, from non-compliance issues to product recalls, and from legal and financial implications to the negative impact on operator health and wellness.

Established standards and practices in western countries are now being adopted in emerging geographies as mandatory procedures migrate from using PPE (personal protection equipment) to maintain operator safety to practicing containment at the source. The message has never been clearer: it is the first duty of the employer to protect the health of their staff.

In addition, it is becoming increasingly apparent to manufacturers that the implementation of seamless containment solutions offers considerable housekeeping benefits, such as

- faster changeover times owing to reduced (room) cleaning
- significantly decreased cross-contamination risks
- substantial savings (air filters, air suits, contaminated cleaning fluid, for example).

Keeping the real operating conditions of the final installation in mind, GEA can determine what level of containment is required where, optimizing the manufacturing process and making it efficient, safe and cost-effective.

Containment Experts

The company not only offers a comprehensive range of robust and compliant containment products, it also boasts unrivaled experience in identifying the most appropriate solution and a thorough understanding of containment risk analysis. We don’t just know about containment, we live and breathe it!

What level of containment do I need?

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.

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.

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.

The ADE (Acceptable Daily Exposure) describes the absolute amount of a specific drug substance that an operator can absorb without any negative health effects. The OEL defines the maximum concentration of a drug substance that can be tolerated in the air of the production room without imparting any negative effect on the health of the operators. Dust inhalation is recognized as the biggest risk to operator health and safety.

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 into an over-performing solution.

We provide tailor made containment for the pharmaceutical industry — for now and for the future.

Contained Materials Handling Expertise.

GEA specializes in contained materials handling solutions for primary and secondary pharmaceuticals and healthcare companies. With BUCK® high containment split butterfly valves, we offer a wide range of technologies and equipment that improve and enhance the efficiency and performance of solid dosage form plants for the safe transfer of powders. We know what level of containment is needed where.

With a long-established pedigree of expertise and implementation, GEA equipment and technologies meet the very stringent demands of production performance, plant and market flexibility (single and multi-product) and, of course, value. With worldwide experience and market-leading credentials, we have developed an outstanding reputation for quality and service to become the leader in contained materials handling.

Dispensary Handling Expertise and Management
Our modular dispensing solutions ensure simple, ergonomic operation and consistent flow whilst effectively controlling the dispensing process. The control system integrates the process with the recipe management system to provide batch data security and traceability for validation purposes.

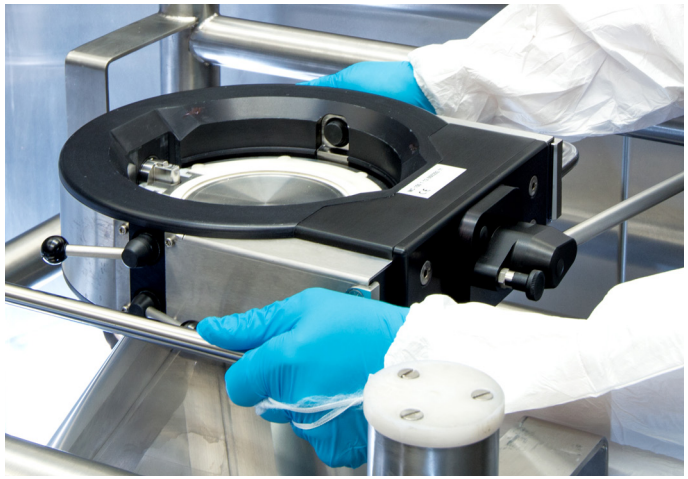
Additional features such as removable hoppers and supplementary extraction provide increased safety for operators and facilitate cleaning. Solutions range from single-level, simple application solutions to multiple-level, integrated dispensary management systems. Bulk ingredient dispensing includes fully automated excipient dosing or interfacing with bulk ingredients for high containment. Active pharmaceutical ingredients (APIs) can be dispensed into a contained charge vessel, which can then be safely transported to the point of use within the plant.

IBC Blending
Flexible blending solutions: Container blending as part of an intermediate bulk container (IBC) system has long been established as the most efficient method of mixing granules and powders in pharmaceutical manufacturing. R&D, small-scale and full-scale pharmaceutical production blenders enable contained process technology transfer during scale-up, minimizing process validation activity.

This is fully supported by GEA's detailed research program and testing facilities. Hoist- and pedestal-mounted versions are available, as well as through-the-wall designs that offer significant room layout benefits.

Vibroflow
Prevents product segregation: Vibroflow technology allows IBCs to discharge poorly flowing product in a reliable and repeatable manner. With product containment and operator safety being of paramount importance, it is no longer acceptable for operators to intervene and open the IBC to remove blockages.

Vibroflow is a proven discharge technology that has been thoroughly tested by leading pharmaceutical manufacturers and installed successfully in a number of primary and secondary API facilities.



How do I optimize the granulation process to ensure both product and operator safety?

Drawing on its world-class expertise and technologies, GEA offers an entire range of state-of-the-art process equipment that has been designed and built with system integration in mind. Safety, containment, product flow and building requirements are in-built for full integration and optimum process efficiency.

Our service includes design, installation assistance, commissioning and process validation, as well as training and technical support. Installation, operation qualification and documentation are done according to FDA/GAMP guidelines. With an emphasis on quality and GMP standards, we are committed to working together with our customers to deliver custom-built, first class solutions for projects of all sizes and complexity.

Safety and the Environment: For full compliance with national, local and in-house regulations, GEA offers a range of emission control options, including solvent recovery systems, outlet filters and full containment plant. Equipment can be supplied to meet explosion-proof and pressure shock standards as required.

Feeding the Granulation Process
The effective and safe transfer of both excipients and active ingredients is essential. A number of options are available:

Gravity feeding/loading through a discharge station from above or via a post hoist are ideal solutions, ensuring containment and simplicity of cleaning. API discharge vessels can be used to deliver more potent formulations directly into the granulator.

Vacuum feeding: When room height is a limiting factor, a contained vacuum station can be used: incorporating containment valves that improve airborne dust levels, they can help to reduce area classification categories. Safety levels can also be enhanced by combining interlocking containment valves with a nitrogen purge system.

Unloading granulation equipment: Inline sieving or milling before the granules are loaded into a container can facilitate the process. A lubricant and/or other materials can then be added (often done using charge containers or Hicoflex® bags) and blended with the granules.

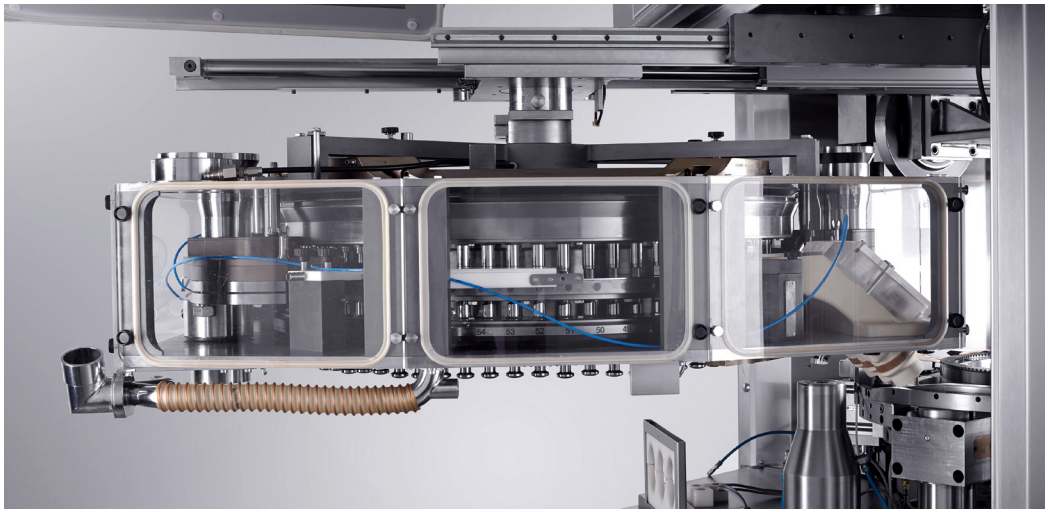
Granulation
GEA specializes in the design and manufacture of fluid bed and high-shear granulation technology and is uniquely qualified to provide integrated, state-of-the-art high shear mixer-granulator and fluid bed drying solutions.

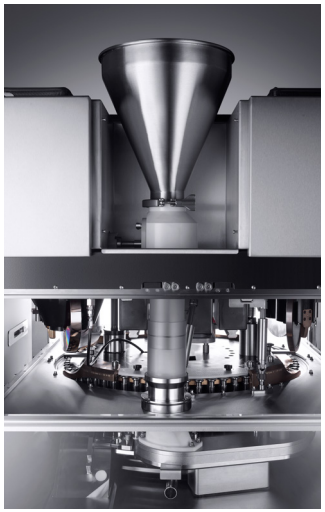
A modular approach means that customers can select standard process modules to suit their project needs. Fluid bed dryers and coaters can be combined with high shear mixer-granulators, wet and dry milling facilities, product handling systems, binder and coating preparation units, and filtration units, all of which have been designed for use in fully contained integrated systems.

Single-Pot Processing: Because of its very nature, a single pot process is contained. No transfers are required between process steps, except to load the raw materials and unload the dry granules. This is not only beneficial for the operators, protecting them from potent products, but also to protect the products from external influences such as heat, light or moisture. Specific solutions are available for product loading and discharging that achieve the desired level of containment for the whole process.

End-Point Detection
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. Technologies such as optimized liquid addition systems are also available that ensure the granulation process runs smoothly, without operator intervention, further promoting operational excellence.

Can I compress dosage forms with highly potent actives?





Owing to the complex geometry of tablet presses, compression is the most challenging stage of the tablet manufacturing process. Fitted with GEA's Exchangeable Compression Module (ECM), MODUL tablet presses are tailor made to handle highly potent substances.
concept.

The MODUL Tablet Press
Much more than a conventional exchangeable die table, the ECM is a sealed unit that's isolated from the remainder of the tablet press and not only contains the turret and compression tooling, but all the product-contact parts as well.

This means that the press itself remains powder-free and requires no cleaning. The Wash-off-Line (WOL) feature allows the ECM to be washed and cleaned away from the machine without any risk to the operator or environment. This is the only concept that combines containment with productivity.

Standard ECM: The standard ECM provides a closed environment that ensures contamination levels outside the machine remain below 10 µg/m3. This is ideally suited for non-potent pharmaceutical applications in which a dust-tight seal provides adequate protection when the doors of the press are opened. The ECM can then be safely removed for cleaning in a designated area, usually with a simple air hose. There is no further need to clean the inside of the press or the room in which it operates.

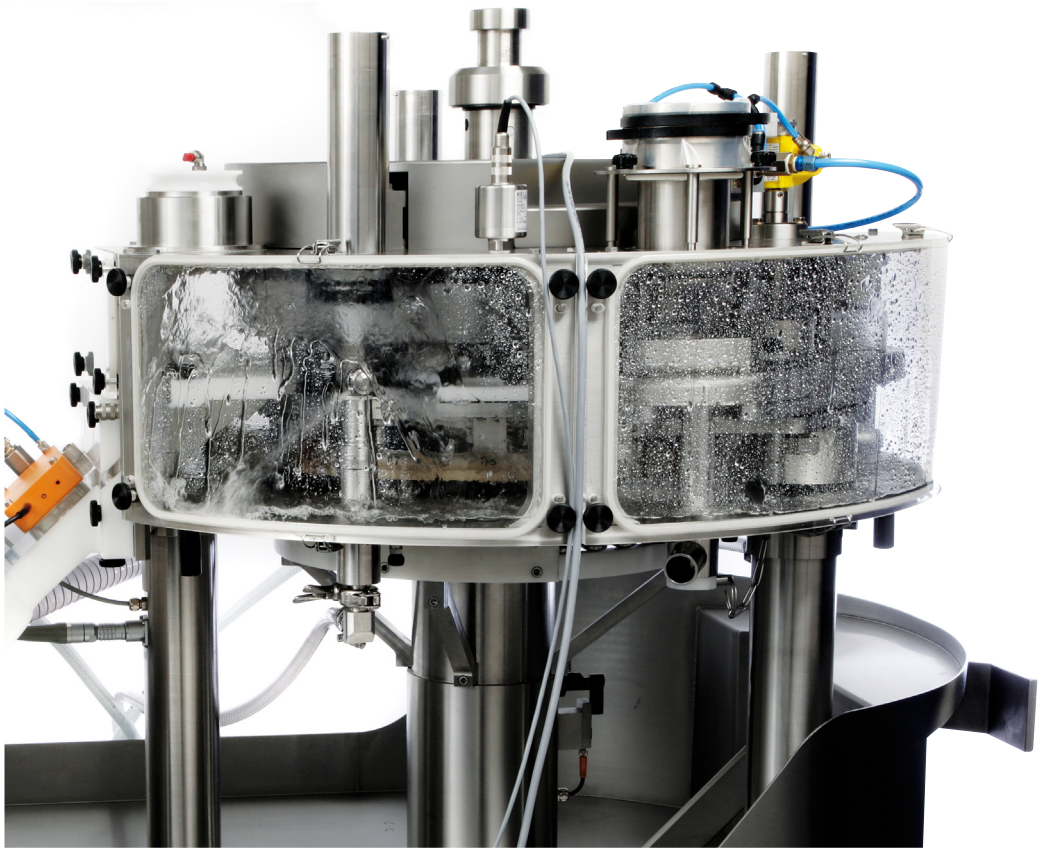
High-Containment ECM: The WOL-ECM has been specifically designed for tableting operations using highly potent APIs to keep operators safe from harmful compounds, without the use of cumbersome air suits, and to prevent cross-contamination. The WOL-ECM maintains the concentration of harmful APIs in the environment around the tablet press below 1 µg/m³.

Made from corrosion-resistant materials, the WOL-ECM can be removed from the press and washed separately, using strong detergents, without any risk of damage. Washing takes place in a sealed environment using a special wash skid that avoids the need to open the ECM or remove any components (such as punches) and uses the minimum amount of water and detergent. The WOL-ECM can be opened for final manual rinsing and drying without any risk of toxic material becoming airborne.

All electrical components, or components that cannot be constructed from suitably corrosion resistant materials, such as cams and bearings, are kept outside the confines of the ECM so do not require cleaning. The fast product changeover time of just 30 minutes is particularly significant for high containment operations as the same operation on a standard isolator-based system can take up to 16 hours.

Benefits
- Fast product changeover
- Reduced downtime
- Dust protection for working environment
- Easy cleaning in safe area
- Wash-off-Line facility for high containment applications
- No need for air suits

How can I limit operator exposure during cleaning and avoid cross-contamination?



The prevention of cross-contamination depends on efficient, effective cleaning, and is a critical aspect of any containment strategy. Automating the cleaning process ensures repeatability, allows validation and minimizes downtime. In recognition of its fundamental role in contained powder processing, GEA has developed a unique approach to automated clean-in-place (CIP) procedures.

Concealed services: An integrated design ensures that all utility lines and hoses (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 easy-to-validate cleaning systems that minimize downtime. GEA offers CIP-by-design (patented) features in all of its processes. Every aspect of the integrated plant, from inlet to discharge, has been value engineered for optimum cleanability, including spray systems, tank cleaners, nozzles and seals.

In addition to providing complete containment plant services, the company also offers multifunctional wash skids that can be moved from one location to another and used to clean different parts of the process. Every plant delivered by GEA has a tailor-made WIP or CIP system that suits your process.

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.

Any system that relies on the operator to remove a contaminated valve for cleaning will directly expose the operator to the product. All BUCK® IBCs fitted with a standard MC passive valve are designed to be fully cleaned-in-place within the BUCK® wash station.

Tablet Press Cleaning: Whereas, in the past, tablet presses were out of operation for 8–12 hours for cleaning (manual or wash-in-place), GEA's ECM technology means that a full product changeover can be achieved in less than 2 hours. All product-contact parts are contained in an isolated dust-tight module, which can be disconnected and removed in minutes.

Another clean and prepared WOL ECM can then be installed and the tablet press is ready for a new product. The off-line cleaning process is done away from the tablet press area, allowing the machine to do what it has to do — make tablets.

How can I implement off-line analysis?

The US Food and Drug Administration'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 process systems in a way that provides real operational insight and can 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 product quality characteristics can be actively controlled.

Combining online analysis/monitoring with solid process engineering principles and advanced modeling techniques will enable processes to be actively controlled to compensate for minor input variations (such as raw materials), so that final product specifications will be close to ideal.

Using process models that identify optimal conditions during specific production steps means that the whole production process can be optimized to improve the performance of the final dose, rather than just focusing on each unit operation individually. GEA's wide scope gives it a unique perspective on the complete process.

Lighthouse Probe

Robust, reliable and available with inline calibration and cleaning capabilities, the Lighthouse Probe is the only device of its kind on the market that can clean its own observation window and recalibrate online. And, combining the online measurement capability of the Lighthouse Probe with the correct process models enables real-time release and eliminates the need for sampling, further enhancing containment.

The Lighthouse platform ranges from manual to fully automatic and is suitable for (and upgradeable from) R&D up to (continuous) production. It stretches from a standalone online LOD sensor to a completely integrated solution capable of using online multivariate models.

ANY MORE QUESTIONS?

GEA has pioneered contained material handling for many years and has been instrumental in developing state-of-the-art solutions. Examples include

- the GEA range of containment interfaces
- the highly flexible BUCK® MC (Modular Containment) split valve
- Hicoflex®, which has become a synonym for disposable containment in solid dosage manufacturing
- Vibroflow for reliable and repeatable powder/product discharging
- The Lighthouse Probe, replacing offline IPCs with inline, operator-free PAT analysis.

Even for experienced manufacturers, however, 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 into an over-performing solution.

GEA was fundamentally involved and worked with an international working group to create a guide to containment testing. Now published by the International Society for Pharmaceutical Engineering (ISPE) and known as SMEPAC (Standardized Measurement of Equipment Particulate Airborne Concentration), this guide defines the test processes and parameters needed to assess the different levels of containment required throughout a plant.

Contact us today to learn more about our extensive containment experience and discuss your specific project.

We have the right solution for you.

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