



Containment Technology

for Solid Dosage Processing



Understanding Containment

Containment is an issue in 9 out of 10 cases of solid dosage form production.

Containment issues have become a vitally important aspect of solid dosage form production. Active pharmaceutical ingredients (APIs) are becoming evermore 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 increasingly intense spotlight.

In addition, navigating the maze of available hardware components and the huge variety of containment solutions has made it more and more difficult to select the most appropriate equipment for the specified task: suppliers of various hardware components have developed a huge variety of containment solutions, making it difficult, even for experienced people, to decide on the optimal solution.

Containment Experts

GEA has a long history of expertise in the field of containment. The company not only offers a comprehensive range of robust and compliant containment products, it also boasts unrivalled 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!

BUCK® Technology and SMEPAC

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.

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.

What level of containment do I need?

GEA Design for Containment

The production of oncology drugs, hormonal products and/or other highly potent compounds requires particular attention: it is essential to avoid exposure of the operators to the drug as well as prevent the cross-contamination of other products manufactured in the same facility.

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 plants.

CASE STUDY: Containment Project Direct Compression of Hormonal Tablets

Wishing to maximize the solid dosage production of a highly potent hormonal product, a leading drug manufacturer tasked GEA with significantly increasing their output, providing a safer and more efficient factory environment and introducing new systems that would replace the existing isolator-based process.



The challenge for GEA was to use their product flow and containment expertise to remove as much isolator-based processing as possible, making the production flow more efficient, whilst maintaining the high levels of containment and operator safety required. Another key factor was maintaining blend homogeneity.

GEA first demonstrated a patented high containment system, the MODUL™ S rotary tablet press with a Wash-off-Line (WOL) Exchangeable Compression Module (ECM). GEA also demonstrated the use of multi-tip tooling: using two tips per punch (station) doubled the tablet press output. A specially designed feeder and dedicated software ensure optimal output.

GEA then demonstrated their ability to successfully blend the low levels of API with poorly flowing excipients. This was achieved using the company's blending Prism™ technology, a very effective aid to the bin-blending process.



The new system was fast tracked; the preliminary details were agreed within 4 months and the equipment was delivered less than one year after contract signing. Removing much of the isolator-based processing and expanding into the new factory space has enabled a significant increase in both batch size and yield, and improved the overall working environment.

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

Feeding the Granulation Process

Process flow interfaces for the granulation area

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

Gravity feeding: Gravity 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 improved 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 or other materials can then be added (often done using charge containers or Hicoflex® bags) and blended with the granules.

Granulation

Designed for integrated containment

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. Safety, product flow and building requirements are built in for full integration and optimal process efficiency.

Integration by Design

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. A modular approach allows customers to select standard process modules to suit project needs: fully integrated turnkey installations can be supplied, including fluid bed process equipment combined with top- and bottom-drive high shear mixer-granulators with integrated contained materials handling, wet and dry milling facilities, product handling systems, binder and coating preparation units, filtration units and tablet compression.

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.

System Integration

Our distinctive specialization lies in the integration of the GEA containment technology into complete solutions for pharmaceutical solid dosage form facilities. 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 plants. Equipment can be supplied to meet explosion-proof and pressure shock standards as required.

End-Point Detection

The 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.

CASE STUDY: Penn Pharma

Fully integrated, high-containment, contract drug development and manufacturing

After conducting extensive market research, Penn Pharma identified an increased need in the solid dose oncology market for the outsourced development and production of highly toxic drugs. Its production site had been manufacturing potent solid dosage products for more than 20 years but needed additional capacity.

Penn Pharma elected to work with GEA because of its proven track record in containment technology and expertise in creating fully integrated production lines. GEA's approach was to eliminate the use of isolation suits in favor of containment interfaces (BUCK® MC valves and Hicoflex®).

The new plant now includes the first commercial PharmaConnect® “through the wall” system in Europe. The contained R&D line for wet granulation also includes the dispensing of excipients and potent powders, GEA's PMA™ 150 and FlexStream™ 1000 for granulation and drying, dry milling, granule collection and blending, tablet compression using a MODUL™ P tablet press with a Wash-off-Line ECM (Exchangeable Compression Module) and pellet coating.

The plant also has a contained R&D line for direct compression and a separate production line that offers containment interfaces for powders, API and excipient dispensing, dry milling and powder collection and blending.

Penn Pharma is now a single source for the development and production of highly toxic drugs at one of the world's most advanced and efficient plants. The project has significantly increased their capacity and the company can now manufacture approximately 500 additional batches during a standard two-shift operation.



How do I eliminate product transfers during granulation?

By definition, a single-pot process is contained, making it the first choice for the granulation of highly potent compounds. No transfers are required between process steps, except to load the raw materials and unload the dry granules (using BUCK® high containment split-valve technology). This not only protects the operators from exposure to potent products, it also protects the products from external factors such as heat, light and moisture. Specific solutions are available for product loading and discharging to achieve the desired level of containment for the whole process.

Single-Pot Processing

Whether the customer's requirement is for mixing, granulating or drying, GEA has a solution for every processing challenge. The UltimaPro™ single pot (or one pot) technology offers a choice of mixing, granulating and drying options that are integrated into a single processing vessel. With our help, this allows the customer to choose the most appropriate technique for the product.

With high-shear granulation technology at its core, single pot processing relies on the application of a vacuum within the bowl to dry the wet mass. This technique allows pharmaceutical compounds to be dried at very low temperatures and, even if organic solvents are used during the granulation process, an efficient solvent recovery systems means that environmental exhaust levels are minimal.

Key Characteristics

Single pot processing is an extremely flexible technology; with its various processing options, it's ideal for many different applications and products. Whether for standard wet granulation, melt granulation, pelletizing or effervescent production, and/or combined with vacuum or microwave drying, a single pot processor can achieve the required result.

The swinging bowl option enhances this flexibility even further by being able to process older formulations to a high quality standard. Quick product changeover is simple and efficient, and the equipment is easy to clean as a result of the clean-in-place (CIP) system.

The UltimaPro™-HC is equipped with containment tools for loading and discharging (Hicoflex®, MC valves, etc.); a full, validatable CIP system; contained sampling options or PAT for end-point determination; and an optimized vacuum system with HEPA filtration. Vacuum drying is the basic drying technology with the option of adding microwaves to increase yields by optimizing the process parameters, reducing wet lumps and sticking.

Using proven standard components, GEA can supply both simplicity and flexibility in plant design. User-selected process options, control systems and liquid recovery units combine in a system that meets your process requirements exactly. This approach ensures that qualification and validation work can be kept to a minimum and ensures successful results. As demonstrated in the case study, for example, we have a leading position and a proven track record as a system integrator for high containment projects with single pot technology for oncology and hormone applications.

Cleaning and Maintenance

Process optimization depends on efficient, effective cleaning. Automation of 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. 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 (patented) features in all of its systems. Every aspect of the integrated plant, from inlet to discharge, has been value-engineered for optimum cleanability. Spray systems, tank cleaners, nozzles and seals are an integral part of our equipment design. Every plant delivered by GEA has a tailor-made WIP or CIP system that suits your process.

CASE STUDY: Ranbaxy Laboratories Ltd

Top-end containment line for anticancer drugs

GEA supplied a complete containment line to Ranbaxy Laboratories Limited (Gurgaon, India) to manufacture highly potent anticancer drugs with an OEL of 1–10 µg/m³. It was essential that the process prevented any cross-contamination in the production area and limited operator Real Daily Intake (RDI) of hazardous substances to well within the Acceptable Daily Intake (ADI).

During the selection process, several key equipment features were specified:

- all units had to provide full containment
- the entire process had to be contained in a single machine to avoid contamination and limit material handling
- the technology had to be flexible enough to adapt to different products and batch sizes
- the process should provide maximum yields with minimum wastage
- there should be a clear and straightforward documentation procedure.

In addition, it was essential that the operators had an in-depth understanding of both the equipment and the relevant containment issues.

To meet their production, containment and whole-life cost requirements, Ranbaxy chose two single pot processors from GEA: the UltimaPro™ 10 and the UltimaPro™ 75 (10 L and 75 L processing bowl, respectively).

The safe, low temperature, vacuum drying technology was augmented with microwaves or Transflo™ (gas-assisted vacuum drying); end-point determination was achieved using a torque sensor (granulation) and NIR (end humidity); a built-in camera allowed operators to view the process without opening the lid; and cleaning was done by a comprehensive fully validatable CIP system.

The new equipment has allowed the company to develop niche oncology products in a contained environment that protects its workforce and the wider environment from toxic compounds. Since installation, predicted levels of production, containment and operational efficiency have been achieved. In addition, factors such as very effective microwave drying for aqueous feeds, more consistent granule sizes and much less operator intervention than had been anticipated have been cited as “areas of exceptional performance.”

Lalit Sood, Projects Director for Ranbaxy, said: *“The unit cost reduction has opened up the market and enabled the company to provide a hard-to-resist proposition worldwide. The GEA technology gives us security of outcome with the guaranteed quality and consistency we need.”*



Can I improve tablet press changeover times, even when compressing potent actives?

When dealing with highly potent substances, owing to the complex geometry of tablet presses, compression is the most challenging stage of the tablet manufacturing process. All GEA MODUL™ tablet presses are based on the company's Exchangeable Compression Module (ECM) concept.

Contained Compression

The Exchangeable Compression Module (ECM) is the unique and distinctive feature that sets the GEA MODUL™ tablet press apart. The patented ECM is a tremendous improvement on the exchangeable turret concept and offers very high containment with incomparable productivity and flexibility for tablet compression.

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. At the end of a production run, the ECM can be removed from the machine in just 15 minutes. No machine cleaning is required, as all product-contact parts and powder residues are contained within and removed with the ECM; the inside and outside of the press are left perfectly clean.

A duplicate, clean and prepared Wash-off-Line ECM can then be installed in the machine in another 15 minutes. Off-line washing

and cleaning is done away from the tablet press area, allowing the machine to do what it has to do — make tablets.

Providing both operator and product safety, the ECM can be easily removed and exchanged with a replacement unit in just 30 minutes for fast product changeover. This is the only concept that combines containment with productivity. 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.

Offering easy cleaning, high throughput and removing any risk of cross-contamination, this extremely short changeover time results in unmatched efficiencies and flexible tablet production.

Standard ECM

The standard ECM provides a closed environment that ensures that 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 Wash-off-Line (WOL-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 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 procedure on a standard isolator-based system can take up to 16 hours.

Benefits

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



Is there a safe way to transfer highly active substances?

Smart Hardware Solutions

System Integration with Containment Interfaces (Loading/Unloading)

Our distinctive specialization lies in the integration of BUCK® containment technology into complete solutions for pharmaceutical solid dosage form facilities. With an emphasis on quality and good manufacturing practice (GMP) standards, we are committed to working together with our customers to deliver first-class tailored solutions for projects of all sizes and complexity. With worldwide experience, GEA has developed an outstanding reputation for quality and service.

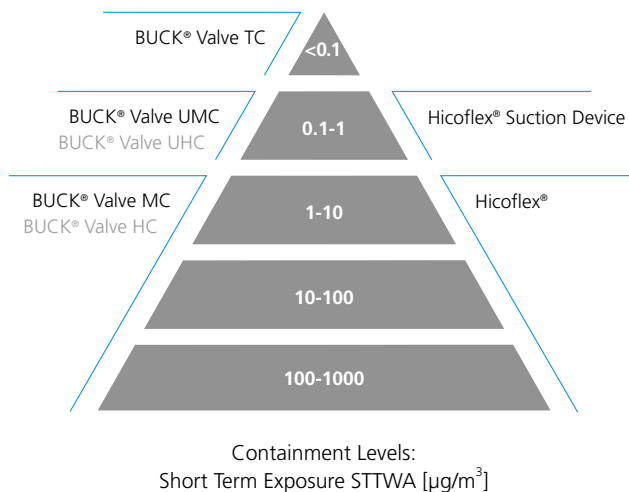
BUCK® Valves

High containment valves for the pharmaceutical industry

GEA is the market-leading supplier of split butterfly valves and contained docking systems for the transfer of powders. The GEA range of containment products includes the BUCK® high-containment valves for solid container use and the unique Hicoflex® disposable containment system.

As pioneers of the split butterfly valve, GEA has been actively involved in many powder containment Communities of Practice, particularly in the development of ISPE's SMEPAC guidelines for evaluating containment equipment and in the risk-based approach to the selection of containment equipment. The BUCK® MC (Modular Containment) split butterfly valve builds on the proven design principles of the first generation of split butterfly valves and offers a number of key additional features and benefits.

Also available, the BUCK® MC Lite DN100/150 is the lightest split butterfly valve for the contained transfer of highly potent solid dosage products and is compatible with existing BUCK® MC half valves. GEA has succeeded in making the actuator ring even more compact and lightweight (just 3.3 kg), which makes the entire unit easier to handle and implement. Offering free orientation during docking, fast product changeovers and simple operation, the MC Lite is designed for rapid disassembly and easy maintenance.



Features of the BUCK® MC Split Butterfly Valve

- Unique passive-to-passive valve design with a centralized actuation ring; the passive valves freely orientate, reducing operator docking error
- Modular containment: with a 1–10 $\mu\text{g}/\text{m}^3$ (STTWA) containment level offered as standard, the system is also available with an advanced air cleaning actuator to further improve containment levels down to $<1 \mu\text{g}/\text{m}^3$ (STTWA)
- Simple maintenance: the passive-to-passive design means fewer component parts and more identical parts, reducing spare part inventory
- WIP, CIP and COP as standard
- Contained quick changeover of the contaminated valve core with working parts remaining on the station, allowing for extremely fast product changeover, fully complements the MODUL™ tablet press ECM containment concept!
- Robust docking: the new central actuation ring design and compensator device overcomes potential misalignment of the container and docking station.

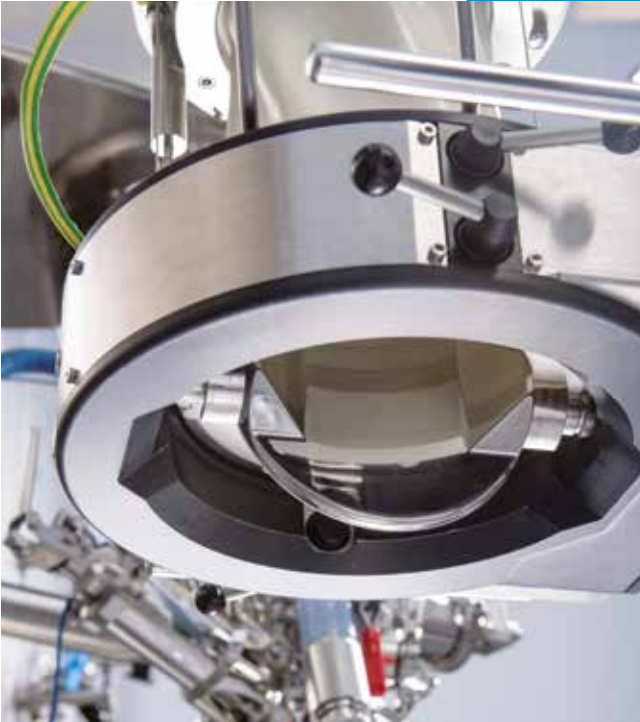
CASE STUDY: Oral Solid Dosage Zydus Cadila

When GEA supplied a complete oncology manufacturing line to a customer in India, they didn't just ensure the health and safety of the operators — complying with internationally recognized standards — the company also increased yields, reduced production cycle times and implemented an ultimate containment solution.

Zydus Cadila intended to improve its solid oral dosage form production processes for highly potent drugs. Planning to use high containment equipment, the company approached GEA, who recommended the use of two single pot processors in a set-up that met all the key requirements: for the development laboratory, an UltimaPro™ 10 equipped with Hicoflex® technology for containment; and for production, an UltimaPro™ 75 equipped with Hicoflex® and MC valves. Both single pot processors were equipped with all the available drying techniques, including microwaves, to ensure flexible processing, higher yields and shorter cycle times.

GEA was able to supply the company with a complete oncology manufacturing line. The entire project was managed in-house, beginning with a risk analysis regarding the amount of containment required, progressing through the overall design of the building and solution to installation and start-up.

By choosing the UltimaPro™ 10 and 75, equipped with all the available options, and with Hicoflex® technology and MC valves, Zydus Cadila has ensured that it will be able to produce their OEB 3 and 4 drugs in a safe, cGMP-compliant environment and guarantee maximum yields with reduced cycle times.



I still use isolators to obtain samples. Is there a better way?

Hicoflex® Disposable Containment

Disposable, low-cost high containment materials handling

The Hicoflex® disposable containment system has been designed to provide a highly contained docking solution between the product handling bag and the process. The system is simple, effective and provides a safe working environment for a minimal investment.

Flexible disposable bags provide a number of benefits compared with solid containers for handling small quantities of material in a production or R&D facility. Benefits include the following:

- lightweight and easy for a single operator to handle
- flexibility to allow poorly flowing materials to be manipulated out of the bag
- disposable, so no cleaning or validation
- low cost compared with solid transfer systems
- full yield discharge
- no cross-contamination
- instant protection for operator and product
- very fast installation
- simple/fast materials handling
- visual product transfer.

The Hicoflex® disposable containment technology consists of two identical couplings that are joined together to seal the external faces, thus enabling closed transfer; it is opened by applying a compression force to both ends to create an opening through which product flows. The Hicoflex® is attached to both a disposable containment bag (from 1–50 L) to transport material and to a disposable containment adapter that fits the inlet or outlet chute of the process to allow product transfer.

With containment performance from 1–10 µg/m³ (STTWA) as standard, and an optional extraction shroud to further improve containment levels down to <1 µg/m³ (STTWA), the system is more than suitable for both API and biotech manufacture, as well as secondary solid dosage production.



Contamination Free Sampling

BUCK® Sampler

Based on split valve technology, the BUCK® Sampler was specifically developed for gravity based process sampling applications in combination with commonly used product sampling equipment in processes such as granulation and drying.

The Sampler offers a fully contained sampling process, even maintaining a process-related pressure resistance during all stages of docking, sampling and undocking.

Disposable Hicoflex® Sampling Technology

The Hicoflex® Sample Bag is a fully contained sampling device that enables a process sample or the bulk material in a Hicoflex® charge bag to be taken through an adaptor.

Compression sampling

Complete tablet production lines for potent/toxic drugs

As powder in-feeding, tablet handling, sampling and tablet collection all have to be done under “high containment” conditions, it became imperative to design complete lines that also integrate the peripheral equipment, such as the powder discharge station, tablet deduster, metal detector, dust extractor and tablet analyzer.

Initially, the most commonly used technique was to build isolators around the equipment and provide wash-in-place capability. However, the latest design trend is toward at-source containment and off-line washing, as these concepts allow equipment to be smaller, easier to install and operate, and lower priced.



CASE STUDY: Servier, Ireland

High-containment tablet compression

Servier, Ireland, invested in three high-containment MODUL™ S tablet presses with WOL-ECM. The raw material is delivered in IBCs, which are lifted above the press with a post hoist. The material is fed into the press through a split butterfly valve.

A custom-designed high-containment Pharma Flex deduster (Pharma Technology Inc.) was installed for dedusting and to check for metal particles, including a buffer system that releases the tablets into an IBC after every Combi-Test tablet check.

Accepted tablets are collected in an IBC, which is connected via an SBV, whereas rejected tablets are taken to a closed bin.

A separate Kraemer-Elektronik washable high-containment Combi-Test tablet weight, hardness and thickness tester performs automatic tablet sampling and measuring for batch reporting and process control.



Do you have an automated cleaning system?

Integrated Cleaning

Process optimization depends on efficient, effective cleaning. Automation of the cleaning process ensures repeatability, allows validation and minimizes downtime. In recognition of the fundamental role played in today's contained powder processing by automated clean-in-place (CIP) 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 (patented) features in all of its processes. Every aspect of the integrated plant, from inlet to discharge, has been value engineered for optimum cleanability. Spray systems, tank cleaners, nozzles and seals are an integral part of our equipment design.

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.

Easy and Safe Single-Pot Processor Cleaning

To verify the CIP approach, a cleaning validation study was done on a single pot processor in GEA's Process Development Centre 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 the 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 can take 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.

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.

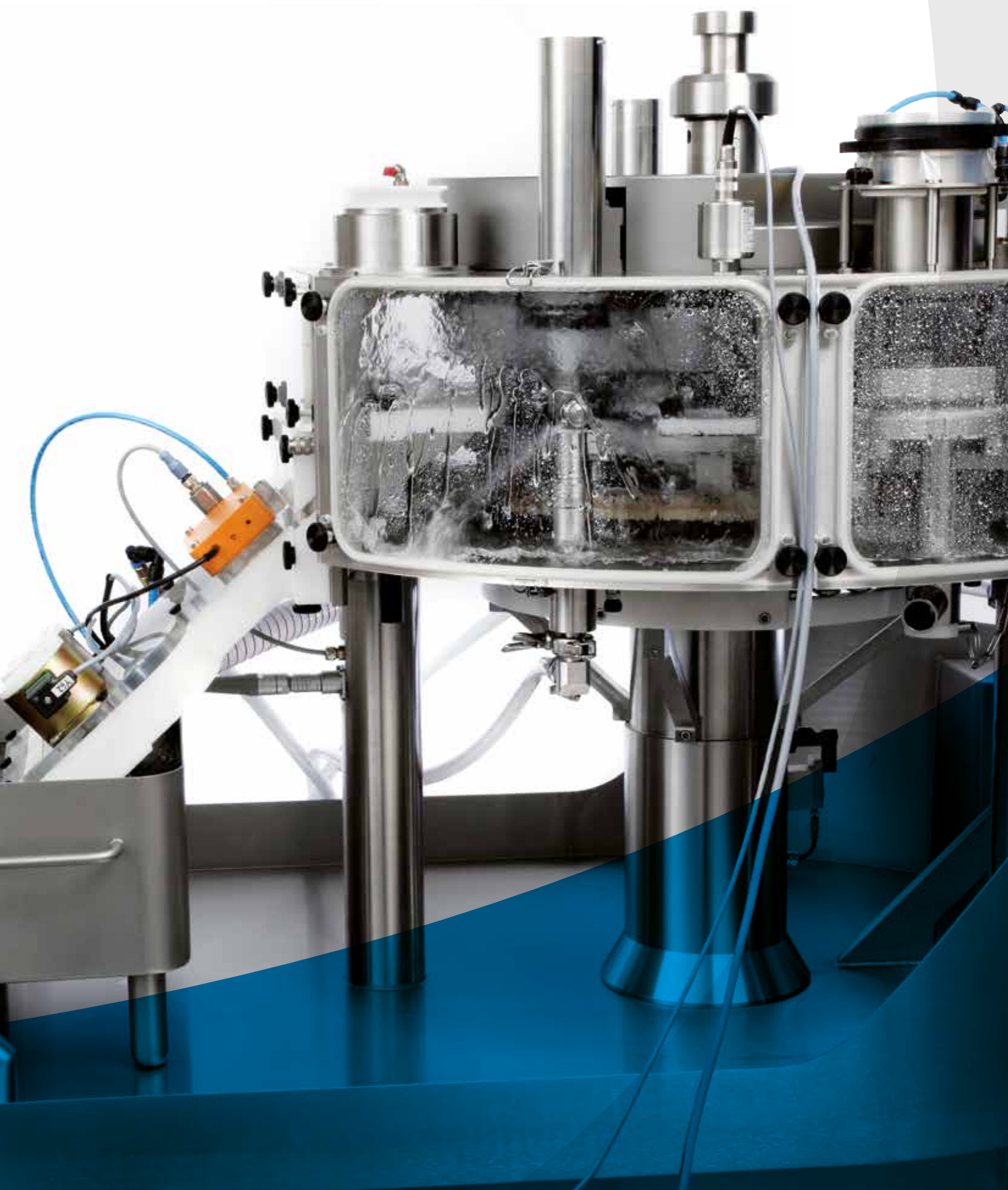
Tablet Press Cleaning

The patented Wash-off-Line (WOL) concept improves on existing WIP/CIP solutions for tablet presses

With the MODUL™ tablet press Wash-off-Line (WOL) concept, GEA introduces a high-containment solution for compression that has a low operational cost, is practical in use and offers the highest productivity. 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.

After the WOL-ECM has been removed from the machine, it can be connected to a washing station in the cleaning area. The WOL-ECM features an ECM constructed from corrosion-free materials and offers automatic, low water consumption washing using specially designed water jets. "Off-line" automatic washing offers considerable advantages compared with "in-place" washing, such as:

- higher productivity
- low-cost, flexible implementation
- no risk of seal damage, protecting the electromechanical section of the press.



Off-line analysis is too slow. How can I optimize end-point detection?

Process Intelligence

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.

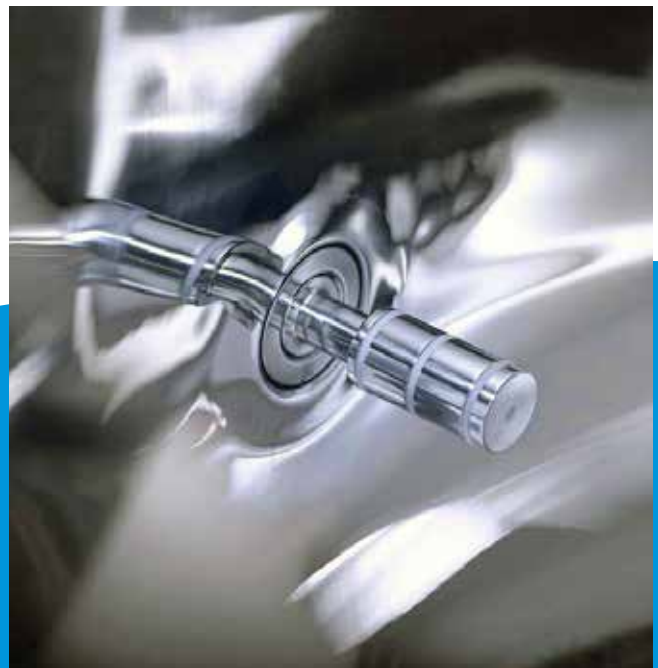
Combining online analysis/monitoring with solid process engineering principles and advanced modeling techniques will enable processes to be actively controlled to compensate for minor input variations (such as raw materials), so that final product specifications will be close to ideal.

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™

After multiple tests with various customers and suppliers of optical measurement techniques in its labs, GEA has developed the Lighthouse Probe™ in co-operation with J&M Analytik AG. The combination of GEA's expertise in containment, automation and pharmaceutical processing and J&M's expertise in optics has resulted in a robust and reliable probe with inline calibration and cleaning capabilities.

The Lighthouse Probe™ is the only probe 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.



Talk to us.

We're here to answer your questions.

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

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. And PPE has been found to be inadequate during modern pharmaceutical drug production.

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).



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 BUCK® TC (Total Containment) high performance split valve
 - 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 not only offers the largest variety of robust and compliant hardware solutions for contained materials handling, it also boasts unrivalled 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. We provide tailor-made containment for the pharmaceutical industry — for now and for the future.

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

We have the right solution for you.



We live our values.

Excellence • Passion • Integrity • Responsibility • GEA-versity

GEA Group is a global engineering company with multi-billion euro sales and operations in more than 50 countries. Founded in 1881, the company is one of the largest providers of innovative equipment and process technology. GEA Group is listed in the STOXX® Europe 600 Index.

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