

Expertise in plant engineering.

High tech for biotechnology and the pharmaceutical industry.



Quality for life. Linde plants
facilitate the future.



Pharmaceutical biotechnology

Human blood plasma fractionation

Chemical synthesis of APIs

Finished dosage forms

Many renowned companies rely on the comprehensive expertise and long experience of Linde-KCA-Dresden GmbH. We have earned their trust through economical, on-time, top-quality execution of global engineering projects. Our references make us one of the world's leading sources for the design, delivery and construction of biotechnological and pharmaceutical facilities.

The larger the project, the more important it is that all gears mesh for a desirable outcome. Our long-time project implementation experience has resulted in planning and controlling tools that can be specifically tailored to your project and streamline its success. Linde-KCA-Dresden GmbH bundles Linde's process engineering expertise in the field of biotechnology.



We design and construct

- New greenfield plants or retrofittings during ongoing production
- Entire plants or fully assembled plant sections
- Research, pilot or large-scale plants

Our services include

- Front-end engineering for reliable, initial-phase project assessment
- Comprehensive planning, from basic design to certified facility delivery
- EPCM services
- Turnkey plant construction



Pharmaceutical biotechnology for high-tech products.



A view of a modern production facility



Facilities for pharmaceutical biotechnology are process facilities based on the application of extremely specific and innovative high-tech solutions. Technologies must fulfil stringent process reproducibility standards to promote validation and ensure consistent, uniform product quality.

In designing highly complex process stages, we draw on our vast experience, for example in the purification of delicate biotechnology products. Our experts grasp the special features of your biotechnology processes, analyse your project's technological challenges, oversee equipment specification and selection and are familiar with the vendor market.



Our core competence includes

- Microbial fermentation
- Cell culture fermentation
- Harvesting techniques
- Purification methods (chromatography, UF/DF)
- Buffer and media formulation systems
- Formulation and filling techniques
- Disposable systems
- Cryotechnology and storage

Product quality and protection of people and the environment stand side by side as principal guides of our effort in every project phase. As necessary, we therefore observe requirements of biosafety levels 1-4 in the design and construction of your facility.

Antibiotics

Vaccines

Hormones

Animal insulin

Recombinant
human insulin

Therapeutic enzymes

Erythropoietin

Monoclonal antibodies



Facilities for human blood plasma fractionation.

Cohn fractions

Factor VIII
vWF
Fibrinogen

Factor IX
PPSB
Protein C
Factor VII

Factor XIII

AT III
Factor XI

Immunoglobulines

a-1 inhibitor

Albumin

Fractionating human blood plasma yields purified and concentrated proteins from which drugs or vaccines can be made. The main steps in blood plasma fractionation are largely standardised and considered common knowledge in the field. Here, product-specific know-how lies with the operator and presents itself primarily in the variation of process parameters. Our extensive experience in plant-specific process implementation stems from numerous projects for many customers. Our expertise guarantees purity of isolated proteins and gap-free traceability along the entire process chain.

We design and install facilities for Cohn fractionation of donated plasma and downstream processing of the concentrated fractions (pastes) as well as equipment for direct product recovery via chromatographic processes.

Our specific know-how in these fields includes

- Cutting and pooling of donated plasma
- Controlled-temperature thawing
- Concentration and temperature gradient minimisation
- Low-shear homogenisation
- Paste precipitation with optimal flake structure
- Paste separation non-destructive to flake structure
- Equipment selection and design for optimal process control in fine fractionation (thermal and chemical inactivation, ultrafiltration, diafiltration, nanofiltration, chromatography)

The scope of our worldwide projects keeps us in close contact with proprietors of various processes for human blood plasma fractionation. Through this network, we can also match your projects with appropriate licensing partners.



Chemical synthesis of active pharmaceutical ingredients on every scale.

In multi-purpose plants for the production of active pharmaceutical ingredients, flexibility has highest priority. Combinations of processing steps, wide variations in raw material and product qualities, and the need for contamination-free handling of powders continually pose new challenges to plant designers and builders.

The basis for successful realisation of your facility lies in the multilateral expertise of our specialists. Our project experience include the design and construction of facilities for the production of active pharmaceutical ingredients, from kilogramme to multi-tonne scales. The spectrum extends from upgrading and expansion of single-product systems in existing buildings during ongoing production to new, multi-product, greenfield plants.

Specialty know-how

- Scale-up from laboratory and/or pilot scale
- Critical reaction stages such as low-temperature design of all reaction types and ranges for essential parameters (pressure, temperature, pH etc.)
- Parameter-governed metering of reactants via closed systems
- Use of optimal processes for crystallisation and/or precipitation
- Separation (filtration, isolation, centrifugation) in combination with dryers of varying design (including packaging)

Linde observes strict occupational health and safety requirements as well as environmental safety standards in engineering plants to produce active ingredients. We target the highest level of reliability and quality in every facility. Containment requirements are incorporated in the design and construction, where necessary up to OEL 5 or Protection Level 4 under the German Hazardous Materials Regulation.

Peptides

Hormones

Antibiotics

Chemotherapeutics

Glycosides

Sulphonamides



Sterile vaccine filling

The best pharmaceutical dosage forms.

Pills
Dragées
Effervescent tablets
Capsules

Ointments
Gels

Juices
Tinctures

Infusions
Injections
Single-use syringes

Patches

Dosage form fabrication – achieving a product form suitable for use in health-care practice – is the last step of production of pharmaceuticals. We focus on sterile systems due to the large number of products available for intravenous administration. Our spectrum of references also includes other critical dosage forms such as effervescent tablets and patches.

We master the high demands placed on product, person and environmental protection in plant design, from closed-system manufacturing to high-purity facilities. Our experts can advise you on the full range of automation options, cleaning issues such as CIP/SIP, and prevention of cross-contamination through targeted flows of personnel and materials. In plants constructed for hormone and cytostatic drug processing, we have designed injection lines, qualified isolators and commissioned freeze dryers with automatic charging and unloading for these products.

Our specialist know-how encompasses

- Integrated plant designs in laminar flow realisation, RABS, CRABS, isolators
- Isolators for handling and filling
- Enclosed stopper handling
- Final sterilisation and aseptic production, with or without freeze-drying
- Production of sterile gels and hormone tablets
- Organic film coating and solvent recovery
- Equipment selection and control systems for plants manufacturing solid, semi-solid and liquid dosage forms and for warehouses (including high-bay warehouses)
- Capacity calculations for existing and projected production facilities

Proven expertise. In all areas of the pharmaceutical industry.

Our references and customer lists underline our technical expertise and the broad international recognition Linde-KCA-Dresden GmbH has gained through numerous successfully realised projects.



Biotechnological synthesis of APIs, proteins



Glassware installation for producing steroids



Sterile filling in cleanroom



Skid-mounted modular installation



High-activity substances in a product isolator

Selected customers

ALTANA PHARMA AG · AVENTIS BEHRING GmbH · BASF AG · BAYER AG · BAYER BIOLOGICALS Srl. · BIOMED (UA) · BIOTEST PHARMA GmbH · BOEHRINGER INGELHEIM · BRISTOL-MYERS SQUIBB Comp. · CITRICO DEUTSCHLAND GmbH · DEGUSSA AG · NOVARTIS · FDS PHARMA ASS · F. HOFFMANN-LA ROCHE AG/Roche Diagnostics GmbH · GALENICA HOLDING AG · GEDEON RICHTER Ltd. · GLAXOSMITHKLINE BIOLOGICALS · HEXAL AG · INFRALEUNA INFRASTRUKTUR UND SERVICE GmbH · JENAPHARM GmbH · MERCK KGaA · MERCKLE GmbH · NOVO NORDISK A/S · OCTAPHARMA PHARMAZEUTIKA PRODUKTIONS-GESELLSCHAFT m.b.H. · RHEIN BIOTECH · RÜTGERS ORGANICS GmbH · SANOFI-AVENTIS · SCHERING AG · SOLVAY PHARMACEUTICALS B.V. · W. C. HERAEUS GmbH · WYETH MEDICA

Plant engineering specialists. Our key success factors.

LKCA's in-house specialists master the following trades

Process technology

Process infrastructure

Site master/layout planning

Logistics

Instrumentation (process control technology, plant control technology)

Buildings

HVAC (heating, ventilation and air conditioning) and sanitary systems

HSE (health, safety, environment)

Cleanroom technology

GMP
Qualification
Validation

Procurement

A major investment needs a solid basis. Selecting the optimal partner depends on several crucial factors. We offer key advantages:

Our staff

The large-scale commitment of our staff generates the energy to surmount great challenges. Excellently trained and motivated specialists with proven design and engineering experience contribute to every project. Alongside engineers of all disciplines are biotechnologists and pharmaceutical experts, mediating between research and technology.

Our knowledge

Our core competence lies in engineering and construction as well as overall execution of high-tech chemical and biotechnological facility projects. We develop high-quality, reliable, cost-optimised solutions for you based on this expertise. Our tools guarantee the integrated design and efficient handling of your project. We deliver projects according to plan, on schedule and on target, even despite circumstances such as confined space or ongoing production.

Our in-house crafts

Our responsibility extends far beyond process engineering since we master all trades and specialties required for the erection of your plant. We emphasise expertise in trades closely associated with process engineering: site master and layout planning, instrumentation and control, process automation, logistics, cleanroom technology, GMP planning, qualification and validation.

Our HSE philosophy

We are committed to observing health, safety and environmental requirements in all activities. People and the environment remain free of exposure to harm. The outstanding HSE parameters of all our plants and operations are thus an indispensable condition for our company's long-term sustainability.

Our performance

In choosing Linde, you partner with a globally-present, large-scale production facility engineering corporation. Your project is completed with guaranteed outstanding quality, on time and on budget – to the very last detail.

An eye for the big picture. Building design reflects the requirements of process and infrastructure.



Architects: Herzog & de Meuron

Modern production building for the manufacture of monoclonal antibodies



Plant for the production of APIs, infrastructure planning

Simultaneous process and building design

Process is the heart of any plant, so the form of a building depends on process and infrastructure requirements. Layout plays a key role here, since process and building are part of an integrated concept. Our iterative layout technique mirrors the interplay of process and structure. Aspects of a building's presence are kept in view through our collaboration with renowned architects to generate appealing and functional designs for industrial construction.

Specific media supply

Plant infrastructure is precisely matched to the demands of the total process. In complex facilities, the need for extra-pure media is simulated with special programs, so that peak demands can be identified and layouts adapted accordingly. We use CIP/SIP systems as mobile, stand-alone cleaning units or CIP satellites that are continuously supplied with cleaning media from a central unit. Our scope of services also includes the central media supply with its pipeline routes and bridges.

Leading projects to success. Efficient, integrated project management.

The quality, costs and deadlines in complex construction projects can only be kept on target through transparent processes and networked management. Our substantial experience enables us to ensure that your project is realised within the specified time and budget and meets the required precision.

Quality through integrated project management

Our methodology features an integrated management system in which activities and documents of all disciplines – including interactions – can be tracked at every project stage. The system generates operational schedules and procedures. Furthermore, the appropriate planning depth is described at every point in time, facilitating efficient quality and risk management.

Our project management team applies the integrated management system to your project. Controlling takes on a key role here.

Project schedules and budgets established at the inception of the project are periodically reviewed to prevent deviations and initiate appropriate measures upon earliest detection.

Interdisciplinary coordination

Interfaces between your project team, vendors and participant trades receive particular attention. Engineering managers oversee and monitor the efficiency of internal and external coordination.

Our staff manages and coordinates all trades as well as procurement, construction site management, commissioning and qualification. We can also readily integrate your staff or established partners into the team. Identifying your requirements and incorporating them early to minimise deviations during project execution is important to us. We therefore bring together your specialists and ours during the initial phase to establish a common modus operandi.



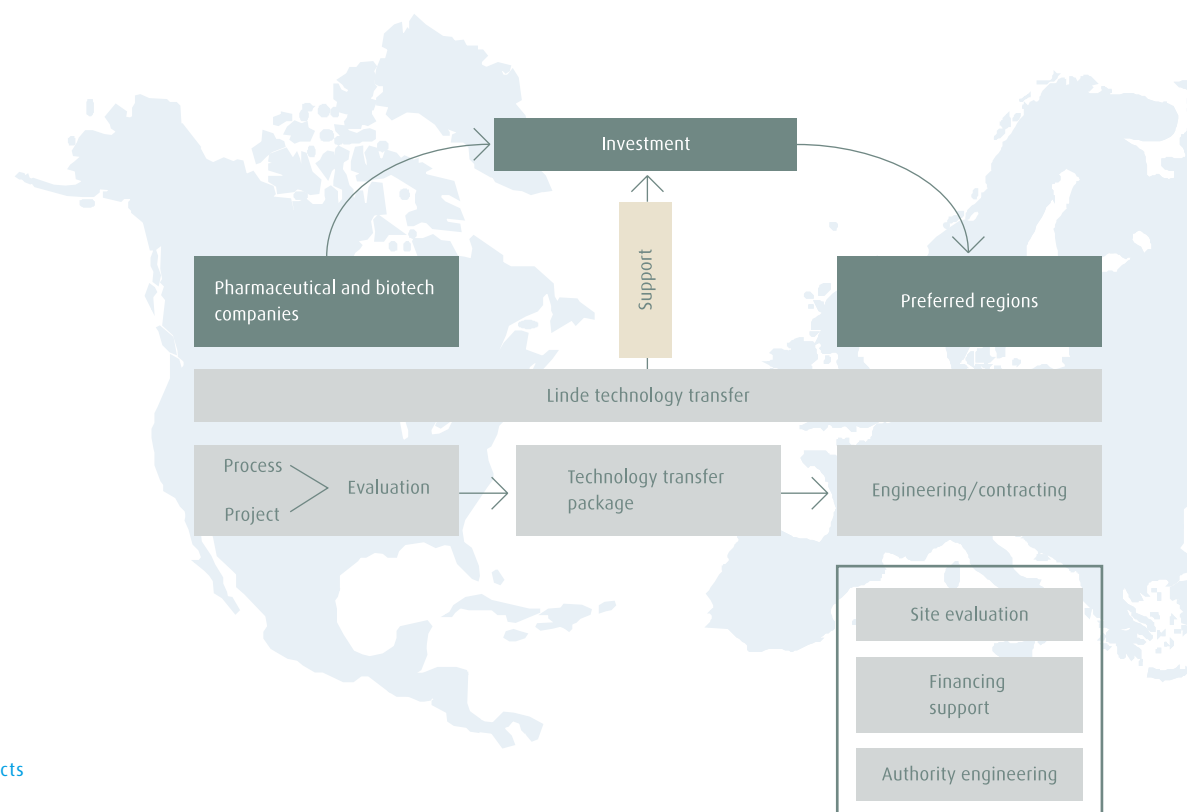
A solid foundation. Investing effectively with our front-end engineering.

Advancing new developments and delivering innovative products to market entails large investments today. To minimise risks and put long-term decisions on secure footing, Linde-KCA-Dresden GmbH has devised an efficient front-end engineering concept that supports you at every step along the path from research to finished product.

This concept allows substantial reduction of total project duration up to commissioning. Our front-end engineering offers you several advantages:

- Evaluation of status and progress with regard to scale-ups
- Use of benchmarks, factors from similar projects and our experience for cost estimation
- Scenario creation enables you to assess development regarding various economic and technical possibilities and select the best option.

- Technology transfer and international investment support in case, e.g., the later production site is not identical with your research and development. Even at a very early stage, we carry out feasibility studies in a wide range of countries. Using our know-how means that your company makes significant savings in management and engineering resources. Moreover, we seek out financing opportunities and prepare an early on-site analysis of the potential workforce, the regional infrastructure as well as the flexibility and support which the local authorities will provide for the establishment of your new plant.
- Management support for strategic project decisions



Custom-made is standard. With individual planning tools.

Every biotechnology or pharmaceutical plant is unique.
Our tools support efficient, high-quality planning.

Library of functional typicals

for efficient flow-sheet preparation:

- Typical solutions for basic functions in process engineering
- Improvement of repeatability in comparable functions
- Standardised presentation, error reduction

Library of layout typicals

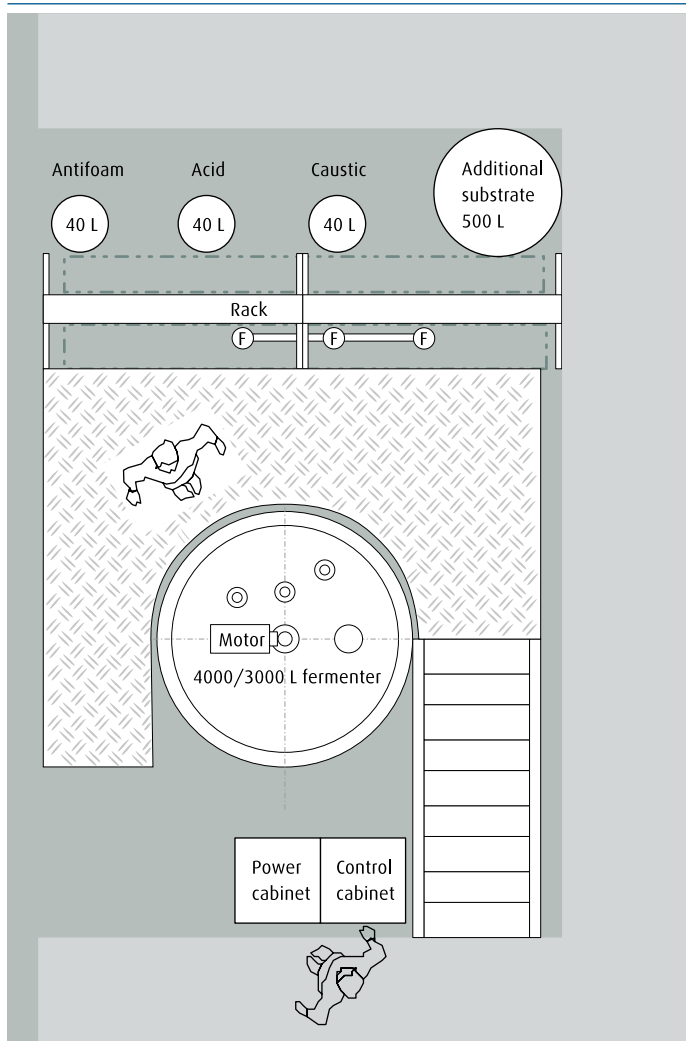
for efficient layout preparation:

- Typical setups for process equipment and auxiliary areas
- Efficient and timely evaluation of footprints

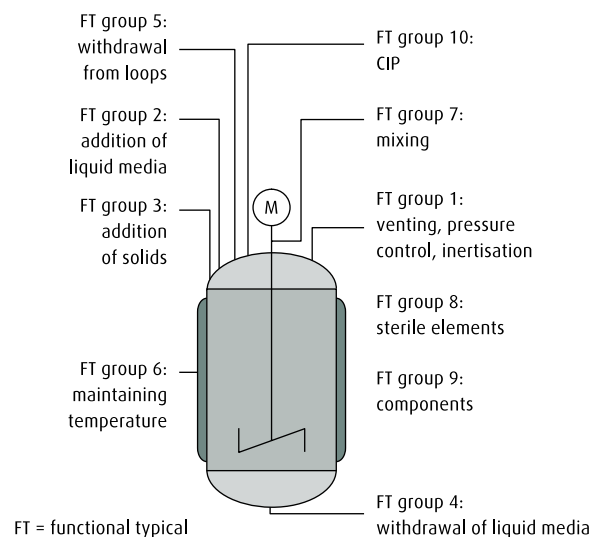
GMP algorithms and Linde qualification system

- Conversion of the requirements of international GMP regulations into Linde guidelines
- Consistent application of GMP philosophy from the initial concept right through to commissioning
- Assurance of GMP-compliant facilities
- Guarantee of efficient qualification procedures

Layout typical



Functional typical



Faster from plan to build. Project management tools shorten construction time.

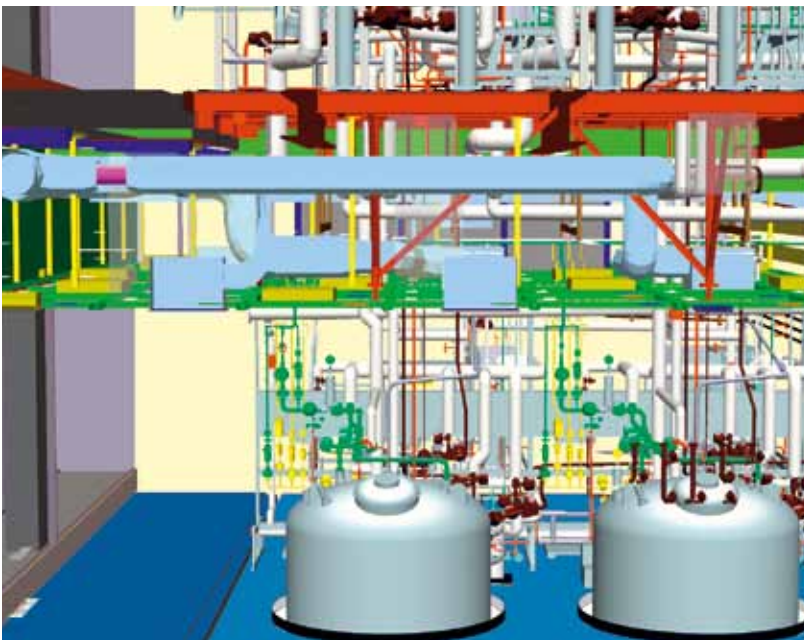
Your plant is designed in 3D CAD for optimal control of all work. With over a hundred internal CAD workstations, even large projects can be dealt with quickly. When the plant model has been thoroughly reviewed in detail, a press of a button creates isometric drawings for spool fabrication as well as parts lists for bulk materials ordering. The accuracy of the 3D model permits significant prefabrication – on-site work focuses on installation of pre-made parts and resolving deviations.

Monitoring with the Linde Project Management System

The Linde Project Management System is the central control tool of project realisation. All data converge here: from calculation, personnel planning and time scheduling, specification and ordering of equipment through to materials handling, generation of parts lists and on-site management. This proven system permits not only efficient controlling, but supports timely reporting of milestones, physical progress and costs as well.

Linde-KCA-Dresden GmbH has built numerous large-scale facilities worldwide over the past years. Let reliable, high-quality Linde systems secure your future too. Our experts are looking forward to discussing the implementation of your project.

3D CAD illustration of a plant under construction



A large Linde construction site



Planting seeds for the future.

Our customers' success is our success. With innovative technologies and our employees' extensive know-how, we are consistently turning our customers' goals into our own – in a fair, transparent and cost-conscious manner. Therefore, every plant we build is a reference for the next one – creative in its concept, efficient in its implementation.

As one of the leading companies in the planning and construction of chemical, gas, biotechnological and pharmaceutical plants, we offer our customers the security of consistently high quality standards. In cooperation with reliable business partners, we combine capacity and expertise in order to realise projects of any dimension.

We regard every assignment as a chance to define a new market standard and to expand our strong international position. Driven by our own performance capability, it is our goal to make the name Linde a globally recognised seal of quality, with plants that speak for themselves – and for us.

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