

We take you further.

Unique competence in biopharmaceuticals



Unique competence in biopharmaceuticals

UNIQUE.

Rentschler Biotechnologie
is a company like no other:
Established expertise – simply unique.

This range of comprehensive services offered by Rentschler Biotechnologie, based on 30 years of experience, will turn your vision of a successful biopharmaceutical product into reality - rapidly and reliably.

Your investment in a partnership with Rentschler Biotechnologie will ensure the success of your project.

You can trust the know-how of this pioneer of biotechnology, from development all the way to the finished product.

Place your project in our capable hands; **A.C.T.** now:

Advanced Service | Competence | Time-to-market

From cell line to development and production of the active ingredient, from marketing authorization to fill and finish, Rentschler offers everything you need whenever you need it. Flexible in our services, capacity and products.

For process development, production of clinical trial and market supplies - from low-dose cytokine to higher-dose antibodies including biosimilars.

Rentschler is your solution.



Management
Rentschler Biotechnologie:

Right: Dr. Nikolaus F. Rentschler
Left: Reiner Winkelbauer

Unique competence in biopharmaceuticals

TRUST.

Rentschler Biotechnologie:
For over 30 years in the market,
a pioneer of biopharmaceuticals.

The development and production of biopharmaceuticals requires experience, creativity, visionary thinking and innovation. Rentschler Biotechnologie is a company driven by competence, persistence and endurance.

In 1947, Rentschler began developing vaccines for bacterial diseases and since 1974, with the establishment of our own biotechnology division, we have launched a number of pathbreaking biopharmaceutical products, including the first interferon compound worldwide.

Knowledge and values are the cornerstones of Rentschler Biotechnologie: Employees at Rentschler take pride in their work and possess a great sense of responsibility, virtues which have led to our traditional family-owned company achieving a leading position in the international marketplace today. This will continue to be the case into the future.

Rentschler now places its entire expertise exclusively at the disposal of its clients. As an independent service provider without the constraints of being part of a larger group or having our own pharmaceutical product range, we are an absolutely loyal partner who deserves your trust.

We take you further.



Milestones of the Rentschler group:

- 1927** Dr. Rentschler & Co. founded for the development, manufacture, and marketing of pharmaceuticals
- 1947** Bacteriological and virological institute established for the development, manufacture, and marketing of vaccines
- 1974** Biotechnology division established for the development of interferon compounds
- 1983** First worldwide marketing authorization of an interferon compound
- 1993** Rentschler Biotechnologie GmbH formed to consolidate all biotechnology activities
- 2010** Since completion of the capacity expansion project, nine separate GMP production lines and three GMP filling lines are operated by more than 570 well-trained employees

Unique competence in biopharmaceuticals

KNOWLEDGE.

Rentschler is a pioneer in biotechnology: As a long-standing developer and manufacturer of biopharmaceutical products, Rentschler Biotechnologie has a wealth of experience at its disposal.

At Rentschler, numerous biopharmaceuticals have been and are being developed for the market to treat diseases that are still difficult to control. Our developments include the first β - and γ -interferons, indispensable today in the treatment of multiple sclerosis, hepatitis and various forms of cancer.

In 1983, we received the first marketing authorization worldwide for an interferon compound.

This wealth of knowledge acquired over decades of research and development work is utilized in the development and production of your new drug.

The outstanding features of Rentschler Biotechnologie are knowledge, experience, reliability and continuity:

Most employees have been with the company for many years; the processes are all GMP certified; quality and safety have been optimized. These facts ensure that your project is in capable hands.

Our knowledge is your gain.



Milestones of Rentschler Biotechnologie:

- 1974 Rentschler Biotechnologie founded; start of development and manufacture of interferon β
- 1979 Introduction of recombinant cell technologies
- 1983 First worldwide marketing authorization of a natural IFN- β compound (Fiblaferon®)
- 1989 Market approval for recombinant IFN- γ and topical IFN- β gel
- 1997 Focus on integrated services for the contract development and manufacture of biopharmaceuticals
- 2003 Commissioning of new facilities to increase manufacturing capacities
- 2005 Start of expansion program for API Production (2 x 500 L und 2 x 2,500 L fermentation lines)
- 2006 US presence with the incorporation of Rentschler Inc. and opening of a sales office in New Jersey
- 2007 Commissioning of two 500 L GMP production lines
- 2008 Commissioning of the first of two 2,500 L GMP production lines
- 2010 Commissioning of the first 1,000 L single-use bioreactor production unit

Unique competence in biopharmaceuticals

ADVANTAGE.

From one qualified source:
all the services leading up to
the launch of your new drug.

We support you in every phase of product development -
from cell line to marketing authorization, including process development,
manufacture and fill and finish of the active pharmaceutical ingredient,
and consultation on regulatory affairs.

Your advantage is to have a responsible partner to implement your
project goals, coordinate activities and provide you with regular progress
updates. Rentschler Biotechnologie saves you valuable time on the path
of your product to the market. Our experience with international
regulatory affairs and authorities speeds up the time to market and
ensures the market success of your product.

Rentschler Biotechnologie has the capacity to handle up to fourteen
individual customer projects. We will continue to expand and improve
our facilities to the advantage of your new and challenging projects.

Your success is our goal.



GMP certified services:

- Development of cell lines
- Process development for clinical and commercial production
- Manufacture of active pharmaceutical ingredients
- Aseptic filling in vials and pre-filled syringes, lyophilization
- Analytics and quality control
- Consultation on regulatory affairs, application for marketing authorization of biopharmaceutical substances
- Quality assurance
- Corporate project management

A.C.T.

Let us A.C.T. together ...

Advanced Service

Rentschler provides customized, integrated biopharmaceutical services, from cell line to marketing authorization, from production to fill and finish.

Competence

Rentschler has over 30 years of experience in the development and production of biopharmaceuticals.

Time-to-market

Rentschler is committed to turn your vision of a successful product into reality - rapidly and reliably.

... for your success!



Our services in detail:

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Advanced Service

CELL LINE DEVELOPMENT.

Cell lines developed by Rentschler Biotechnologie meet all the requirements for optimum process development.

The selection of the appropriate expression system for the production of a recombinant protein is critical. One important factor, starting with the selection and establishment of a cell line, is compliance with FDA and EMA guidelines. The recombinant cell lines developed by Rentschler Biotechnologie meet these requirements.

Cell lines developed by Rentschler Biotechnologie meet all the requirements for the development of an optimum production process.

Cell lines developed by Rentschler Biotechnologie ensure:

- **High-yield production** – this parameter has a significant impact on the implementation of the manufacturing process and on production costs.
- **Genetic stability** – stable cell lines with consistent expression levels throughout the development and production process and without genetic variation are an important regulatory prerequisite.
- **Cells suitable for fermentation** – robust cell lines, well suited for fermentation, guarantee fast scale-up to biopharmaceutical production levels.

Our S1 laboratories offer comprehensive methods for establishing and characterizing recombinant cell lines and are equipped to handle a wide range of molecular biology methods.



Our core competencies in Cell Line Development:

- Development of serum and protein-free cell lines
- Production and storage of Master and Working Cell Banks (MCB/WCB)
- Characterization of Master and Working Cell Banks (MCB/WCB)

Advanced Service

PROCESS DEVELOPMENT.

Rentschler Biotechnologie has comprehensive expertise and modern facilities for the development of cost-effective, robust upstream and downstream processes.

Establishing stable processes with high yields is decisive for the successful production of recombinant proteins.

Rentschler Biotechnologie offers technologies for adherent cell culture and suspension cell culture for the development of robust and reproducible Upstream Processes (USP).

The quality of the active pharmaceutical ingredient depends largely on the processing and purification methods used. In the development of Downstream Processes (DSP), it is essential not to change the structural and functional properties of the recombinant protein while removing any potential contaminants.

Our core competencies in USP and DSP Development:

- USP development and optimization of fermenter processes in stirred tank bioreactors at lab scale and scale-up to production levels
- Development and scale-up of multitray fermenter processes
- DSP development at lab scale and scale-up to pilot and production levels
- Process validation according to GMP guidelines
- Validation for virological safety



Advanced Service

API PRODUCTION UNDER GMP.

All aspects of biotechnological production of active pharmaceutical ingredients (APIs) derived from mammalian cells are available at Rentschler Biotechnologie, from basic services for development and production, to process development in cooperation with clients, and validated routine GMP production.

The GMP certified production of APIs at Rentschler Biotechnologie is done in state-of-the-art facilities. Nine separate GMP suites for Upstream Processing (USP) and Downstream Processing (DSP) currently covering a total area of over 4,500 m² (48,000 sq. ft.) are available for client projects.

Cell fermentation in stainless steel and single-use bioreactors and cell separation using different methods is done in the USP area. We have been working successfully with cell cultures in the production of biopharmaceuticals for over 30 years.

Downstream processing takes place in a separate area with state-of-the-art equipment, including pre- and post virus segregation concepts using centrifugal extraction, membrane technologies and chromatographic separation (from g to kg). The expertise of our experienced personnel covers the entire range from protein production methods to validation.

Our spectrum of methods is state-of-the-art and can be adjusted to meet individual needs.



Our core competencies in GMP certified API Production:

- Production for Phases I-III clinical trials in accordance with GMP guidelines
- GMP production for the market
- Stainless steel bioreactors:
 - 30 to 2,500 L
- Single-use bioreactors:
 - 250 to 1,000 L
- Cultivation methods:
 - Batch, repeated batch, fed batch
 - Continuous processes (e.g. perfusion)

Advanced Service

FILL AND FINISH.

Fill and finish at Rentschler Biotechnologie includes several services:
From formulations development to aseptic filling and lyophilization in vials and pre-filled syringes, to packaging of clinical trial supplies.

Our formulations group has years of experience in the development and optimization of formulations and can also offer, among other services, the formulation of proteins for parenteral dosage forms. Rentschler can also manage the development of special dosage forms through cooperation with other European service providers.

The fill and finish unit of Rentschler Biotechnologie provides formulations, automated aseptic filling and lyophilization or terminal sterilization under FDA and EMA standards. Vials up to 30 ml and syringes up to 20 ml can be filled.

For products intended for clinical trials, in addition to fill/finish, we can handle packaging and shipping to clinics throughout Europe, in addition to the documentation (pharmaceutical development and manufacture) needed for marketing authorization.



Our core competencies in Fill and Finish:

- Proteins as formulated pharmaceutical medicines
- Aseptic filling with or without lyophilization
- Batch size: 100 to 70,000 vials
- Filling line for small batch sizes & development work
- Aseptic filling of pre-filled syringes
- Batch size: 100 to 15,000 syringes
- Labeling, packaging, and shipping of clinical trial supplies
- Our methods all meet the requirements of FDA and EMA

Advanced Service

ANALYTICS AND QUALITY CONTROL.

With over 30 years of experience in the field of biotechnological analytics and method development, Rentschler Biotechnologie can offer effective, competitive and fast solutions to meet your individual needs.

Our units for chemical, biological, pharmaceutical and microbiological analytics and quality control have been certified in accordance with EU-GMP, US-CFR and ICH-guidelines.

Rentschler Biotechnologie can handle the complete development and validation of analytical methods to comply with international guidelines as well as method transfer.



Our core competencies in Analytics and Quality Control:

- Chemical, biological, pharmaceutical, and microbiological analysis
- Protein structure analysis, identity and purity testing
- Glycoprotein characterization, oligosaccharide mapping
- Identification of posttranslational modifications (PTMs)
- Bioassays, SDS-PAGE, Western blots, and ELISA for the quantitative determination of proteins
- Residual analysis for DNA, host cell proteins and process chemicals
- BIAcore analytics
- Stability testing on API, intermediates and drug product

Advanced Service

REGULATORY AFFAIRS.

The Regulatory Affairs team at Rentschler Biotechnologie has years of experience in national and international market authorization procedures.

Through our established contacts with licensing authorities and our expertise in pharmaceutical development and market authorization issues, we can guarantee that the product development and corresponding documentation will meet regulatory requirements.

In addition, through our longstanding cooperation with external institutes we are particularly competent in the field of virological safety of pharmaceutical products derived from mammalian cell cultures.



Our core competencies in Regulatory Affairs:

- Consultation on regulatory affairs and implementation of approval procedures in the course of product development
- Assurance of regulatory compliance from lab scale to commercial scale
- Compilation of submission dossier for marketing authorization
- Contact with regulatory authorities
- Organization and implementation of marketing authorization
- Consultation on biological/virological safety issues

Advanced Service

**QUALITY
ASSURANCE.**

The Quality Assurance department at Rentschler Biotechnologie monitors in-house quality standards and adjusts them to comply with the current requirements of national and international regulatory authorities.

Our quality assurance system and the GMP compliant monitoring of regulations and procedures meet current regulatory requirements.

Individual adjustment is possible to reflect the requirements of our clients and to meet project goals efficiently.



**Our core competencies
in Quality Assurance:**

- Assurance of quality standards during development
- Assurance of EU and cGMP compliance
- Preparation, support and follow-up of process and method transfers
- GMP audits on behalf of our clients
- Qualification of suppliers and subcontractors
- Consultation on the development and implementation of quality systems
- Evaluation of documentation of earlier project phases for GMP compliance

Advanced Service

CORPORATE PROJECT MANAGEMENT.

At Rentschler Biotechnologie you will have a dedicated project leader who is responsible to take your project to its successful completion.

Our corporate project management team is an independent department with overall responsibility for the management of client projects.

Your dedicated project leader plans and coordinates activities across departments and specialist groups and leads the interdisciplinary project team. The project leader is responsible for timelines, budget, and project implementation.

All project leaders at Rentschler Biotechnologie are scientists with years of experience in project management.



Our Project Management services:

- Corporate project management including planning and control
- Proactive communication (transparency of the project status)
- Monitoring of project goals as well as timelines and budget

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