CARBOGEN AMCIS

A Dishman Group Company

BRINGING YOUR SCIENCE TO LIFE

Company Profile

Welcome to CARBOGEN AMCIS

CARBOGEN AMCIS HQ, Bubendorf, Switzerland

Our Vision

Helping our customers create a better world as the partner of choice for development and manufacture of complex and challenging substances, highly potent active ingredients and drug products.

Our Mission

Our products and services contribute to a safe food and medicine supply. We differentiate through the deployment of experienced, creative, disciplined and motivated staff who have an absolute passion for communication, transparency and focus on every task we perform for the Dishman Carbogen Amcis Group, our partners, regulators and, of course, our customers.

Our Focus: Client Satisfaction

- Deploy highly experienced and trained staff committed to projects and to fulfil customers' expectations
- Highest quality standards
- Exclusive custom synthesis
- All compound IP belongs to the customer
- Impressive in-house technologies to support different types of chemistry
- Product lifecycle management through the Dishman Carbogen Amcis Group
- High level of return customers
- Project Managers and Key Account Managers
- Implementation of new technologies

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Company Profile

CARBOGEN AMCIS is a leading service provider, offering a portfolio of drug development and commercialization services to the pharmaceutical and biopharmaceutical industries at all stages of drug development. Our integrated services for Drug Substances (DS) and Drug Products (DP) provide innovative solutions to support timely and safe drug development.

Besides being a service provider we also offer high quality Cholesterol and Vitamin D analog products produced at our facility in The Netherlands. These products are used in a variety of markets around the globe.

BUBENDORF: (SWITZERLAND)	**Late Phase/Commercial** Process development API manufacture commercial supply
NEULAND/AARAU: (SWITZERLAND)	**Early to Commercial Phase** Process research API & commercial supply
SHANGHAI: (CHINA)	**Early to Late Phase** Non-GMP intermediates & cGMP manufacturing
BAVLA: (INDIA)	**Late Phase/Commercial** Highly potent API supply
MANCHESTER: (UNITED KINGDOM)	**Early/Late Phase** Process optimization non-GMP intermediates
VIONNAZ: (SWITZERLAND)	**Clinical Phase** Highly Potent API supply
RIOM: (FRANCE)	**Drug Products Clinical Phase** Development & manufacturing of clinical batches
VEENENDAAL: (NETHERLANDS)	**Large Scale & Niche Manufacturing** Cholesterol & vitamin D analogs

Services for Active Pharmaceutical Ingredients (APIs) & Drug Products (DP)

DP Early Phase
Development and cGMP production of aseptic parenterals

Research → Preclinical → Phase I → Phase II → Phase III → Market

Early Phase API
Process research and rapid supply of APIs prepared according to non/cGMP

Late Phase API
Process development and cGMP manufacture
Process validation based on QbD

Commercial API
Process optimization
FDA audited

We have been part of Dishman Carbogen Amcis Limited since 2006. Custom synthesis operations within the Group include facilities in India, as well as the eight facilities under the CARBOGEN AMCIS brand: four in Switzerland, one in the UK, one in China, one in France, and one in the Netherlands.

We employ more than 800 highly experienced people in the world, including many chemists 40% of whom hold a PhD in Chemistry. Our staff regularly attend internal and external training sessions to keep abreast of the latest safety requirements and technology enhancements.

Quality is central to the CARBOGEN AMCIS business. State-of-the-art facilities operate to the highest standards of current Good Manufacturing Practice (cGMP). We are routinely inspected by SwissMedic, the US Food and Drug Administration (FDA) and the French Health Authority (ANSM).

Process Research & Rapid Supply of APIs

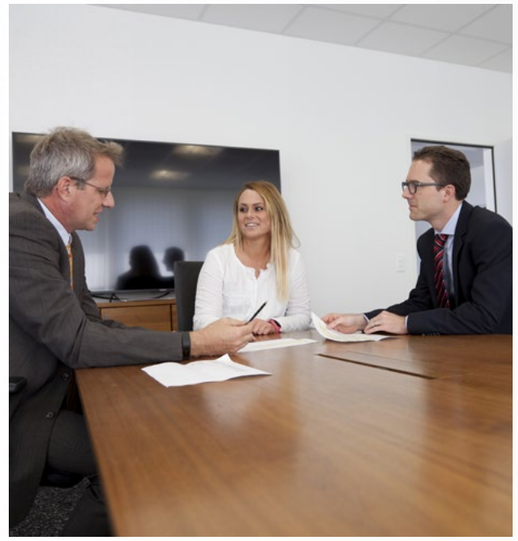
Early phase Active Pharmaceutical Ingredient (API) manufacture centers on the rapid synthesis of supplies necessary to perform both toxicology and early phase clinical trials. Typical batch sizes here range from 1 gram to 50 kg scale and are prepared in the highest standard of cGMP.

We also have an extensive toolbox including microreactor technology, spray drying, lyophilization, milling and wet-milling and a range of chromatography techniques (SMB, HPLC, MPLC, TFF, Biotage). The combination of tools and experienced personnel allows CARBOGEN AMCIS to solve complex chemistry issues and to provide rapid supply of initial quantities of APIs.

Process Optimization & cGMP Manufacturing

Process optimization skills are critical in ensuring a safe and efficient scale-up from development scale to routine cGMP and eventual commercial API manufacture.

We offer experience with a broad range of organic chemistry reactions. This consists of a diverse selection of routine chemistries as well as a wide variety of sophisticated modern technologies, including low temperature and high pressure reactions, metallo-organic reactions, peptide synthesis, and chiral synthesis etc.



"I really enjoy being the interface between customers and internal teams at CARBOGEN AMCIS: internal and external communication is crucial for project success. Our highly experienced co-workers and management implication make us a reliable and sustainable partner."

Rabiaâ – Senior Key Account Manager

Company Profile

Our flexible approach enables customers to benefit from tailored packages of work which balance their needs in terms of speed, cost and quality. We also adapt our communication and reporting to match customer-specific requirements and documentation.

"CARBOGEN AMCIS is full of people passionate about process chemistry, inter-project collaboration is actively encouraged and the availability of highly skilled people to help problem solve is very reassuring. There is continued investment in facilities and resources to offer the best service to customers."

John – Project Chemist

Pharmaceutical Intermediates Supply

The CARBOGEN AMCIS Manchester and Shanghai facilities focus on process research and the synthesis of pharmaceutical intermediates. The large-scale production capacities (up to 8,000 L) allow the efficient production of non-GMP intermediates that can be further processed at the CARBOGEN AMCIS Swiss facilities.

Manufacturing of Drug Products

Our site in Riom (France) offers aseptic cGMP manufacturing for liquid or freeze-dried product including for complex process or products such as drug delivery, highly potent and antibody drug conjugates (ADC). A wide range of filling volumes and packaging components (vials or syringes) could be applied to support pre-clinical and clinical studies all over the world. Formulation, process development and upscaling services for liquid and freeze-dried products are also part of our service offering.

Analytical Services

Analytics provides the foundation for process research and manufacturing activities. A thorough understanding of reactions is critical in process development and validation work. With our ratio development chemists to analysts of 1:2, our team of experts always strive to provide a comprehensive range of tools and techniques to facilitate this work. Analytical chemistry services support both process control and material characterization for laboratory and production chemistry, from initial raw material release to the release of the final APIs and the Drug Products.

Our Laboratory Information Management System (LIMS) accessible on SharePoint 24/7 and efficient integrated data processing ensure that data is recorded and analyzed in a controlled and timely manner and that data integrity is assured.

Moving Toward Full-Scale API Manufacturing

The Shanghai facility can offer large scale production for API Manufacturing. As part of the Dishman Carbogen Amcis Group, CARBOGEN AMCIS can also provide solutions for internal technology transfer to FDA-approved large-scale production facilities in India.

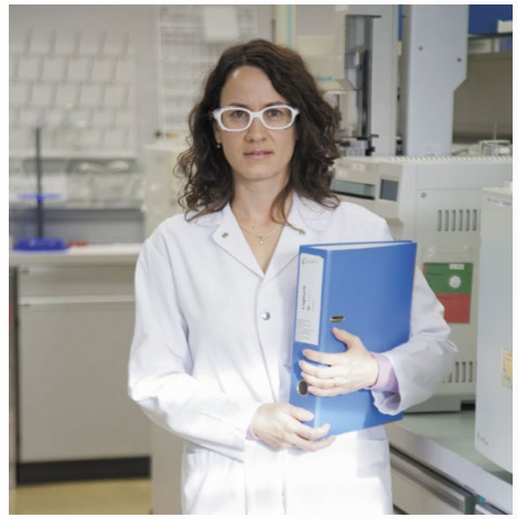
Products Sales Cholesterol & Vitamin D Analogs

CARBOGEN AMCIS is active in the manufacturing, marketing/sales and distribution of Vitamin D analogs, Vitamin D2, Cholesterol and Lanolin derivatives.

These products are used in pharmaceuticals, cosmetics, feed, food, shrimp farming and industrial applications.

We have more than 70 years of experience in the development, production, and worldwide sales of these ingredients. Our production site in Veenendaal is operated under cGMP regime, is certified as EU GMP, and classified as acceptable by US FDA for API manufacturing.

We have all the necessary qualifications and our own testing laboratory. We also provide full regulatory support and complete documentation for export. We control the complete supply chain by manufacturing our own raw material for these vitamin D ingredients. We ship products worldwide.



Highly Potent API Supply

CARBOGEN AMCIS provides services for the development and manufacture of highly potent drug substances (APIs) and drug products applying state-of-the-art containment technologies. All facilities operate to current Good Manufacturing Practices (cGMP) and can produce material for preclinical testing, clinical trials and commercial use. Our manufacturing sites are regularly inspected by the US Food and Drug Administration (FDA) and local regulatory authorities.

Our containment facilities are designed based on a containment concept utilizing barrier isolation technology and Rapid Transfer Ports (RTPs) as well as a strict zone concept with pressure cascades, airlocks and access controls. This allows the safe handling of highly potent compounds including cytotoxics. We offer services starting from laboratory scale for process research and development purposes up to large scale manufacturing in 1'600 L vessels. To support the API development process through all stages, a variety of high containment analytical and purification capabilities complements the chemistry service portfolio.

In addition to our process research and manufacturing services for the fast supply of highly potent APIs, we offer conjugation services for Antibody Drug Conjugates (ADCs) as well as fill-and-finish and freeze-drying services for drug products.

Highly Potent API Supply

The highest category in CARBOGEN AMCIS' categorization system is category 4 with an Occupational Exposure Limit (OEL) range of 1 - 0.05 $\mu g/m^3$. However, recent containment testing performed according to *ISPE's *SMEPAC-guideline, has shown that CARBOGEN AMCIS can safely handle ultra-potent toxins with an OEL as low as 0.01 $\mu g/m^3$ (10 ng/m^3) 8hr-TWA. Very highly potent toxins with an OEL of 10 ng/m^3 are often used as warheads for new generation targeted cancer treatments such as ADCs.

*ISPE = International Society for Pharmaceutical Engineering
*SMEPAC = Standardized Measurement of Equipment Particulate Airborne Concentration

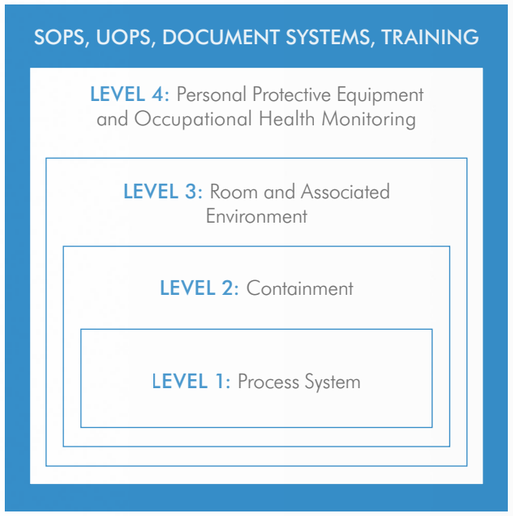
Highly Potent API for (Pre)Clinical Trials & Commercial Use

Switzerland	Up to Category 4 OEL down to 0.05 $\mu g/m^3$	Laboratories Up to 30 L
Switzerland	Up to Category 4 OEL down to 0.05 $\mu g/m^3$	Conjugation Laboratories Up to 20 L
Switzerland	Up to Category 4 OEL down to 0.05 $\mu g/m^3$	Large-Scale Manufacturing Facility Up to 250 L
Switzerland	Up to Category 3 OEL down to 1 $\mu g/m^3$	Pilot Plant Manufacturing Facility Up to 1,600 L
Bavla India	Up to Category 4 OEL down to 0.05 $\mu g/m^3$	Large-Scale Manufacturing Facility Up to 1,600 L
Shanghai China	Up to Category 3 OEL down to 1 $\mu g/m^3$	Large-Scale Manufacturing Facility Up to 6,300 L
Riom France	Up to Category 4 OEL down to 0.05 $\mu g/m^3$	Aseptic Filling Up to 5,000 vials

NB: Containment is ensured through rigid barrier isolation systems and flexible segregation of key equipment. Results are validated by containment testing performed according to ISPE's SMEPAC-guideline.
* Result of surrogate containment testing: 0.01 $\mu g/m^3$

Safety & Product Quality

We are fully committed to managing the risks associated with handling and producing highly potent and/or toxic materials. Safety and quality considerations encompass our personnel, our customers and patients using the materials we produce, as well as the environment and our neighbors. We are dedicated to maintaining and improving safety, environmental and health standards above and beyond the standard legal requirements. This remains the responsibility of both our management and individual employees. All processes follow our "protection cascade" of four increasing levels of containment technology systems and procedures, ensuring that worker safety and product quality are never compromised.



Protection Cascade

In addition, our rigorous system of Standard Operating Procedures (SOPs) and Unit Operation Procedures (UOPs), supplemented by extensive worker training, enhance safe working processes and awareness of potent compound safety at all CARBOGEN AMCIS' production sites.

"My work has a daily impact on many people, as we continually strive to increase the company level of health and safety whilst minimising our environmental impact."

Gavin – Head of ESH

Scientific Specialities

CARBOGEN AMCIS exists to provide innovative solutions for drug development and supply to the pharmaceutical and biopharmaceutical industries that enable customers to bring new generation medicines to market.

Successful drug development is a balance between speed, quality and costs. We aim to offer our customers a choice of state-of-the art tools combined with qualified and experienced staff in order to best meet these often changing priorities. CARBOGEN AMCIS has built up a portfolio of specialist services to give customers the highest degree of flexibility possible.

"We advise our customers on the best conjugation strategy to successfully manage projects from drug-linker synthesis to final drug product manufacturer."

Luca – Manager ADC

Chromatography

Chromatography often forms part of a fast route to producing initial quantities of material. We offer customized chromatography solutions for the separation and purification of APIs and intermediates, including highly active APIs and impurity isolation. Our dedicated group of chemists have more than 50 years' of cumulated experience in method development and scale-up in a variety of different chromatographic techniques, all in accordance with current Good Manufacturing Practice (cGMP) environment.

Cost-effective large-scale chromatography is also possible given the correct infrastructure. CARBOGEN AMCIS offers Flash Chromatography (Biotage), SMB and HPLC to effectively produce clinical trial quantities of APIs and commercial products.

Crystallization Services

Defining the best crystalline form of an Active Pharmaceutical Ingredient (API) is crucial in drug development, since it has a significant impact on its bioavailability and formulation properties. CARBOGEN AMCIS has established a service supporting our customers with crystallization investigations including solubility tests, salt screening, and optimization of the crystallization process and the solid/liquid separation in the API isolation process. Polymorphism screening complements the service portfolio. We offer online monitoring of critical parameters such as particle size, turbidity, temperature, and pH value, as well as analytical services dedicated to solid phase characterization including hot stage microscopy, differential scanning calorimetry, Dynamic Vapor Sorption (DVS) and x-ray powder diffraction.

Ultrafiltration & Nanofiltration

This technique allows concentration of large chromatographic fractions under very mild conditions. In combination with lyophilization, this technique gives access to isolation of highly instable compounds.

Micro-reactors & Flow Chemistry

Micro-reactors and flow chemistry technology are currently used on a number of projects in parallel with conventional chemistry. Micro-reactors offer solutions where classical methods reach their limits. Examples are highly energetic reactions or unstable intermediates. Whilst the size of the vessels is small, the continuous processing allows this technique to produce material also at an intermediate scale.

Small scale flow chemistry may help to overcome technical limitations on conventional large scale production and makes syntheses more controllable with regards to temperature, pressure or concentration. It will help to optimize the production process by widening the possible range of parameters (process intensification) and opens the doors for new chemical prospects.

Bioconjugation & Antibody Drug Conjugates

We have successfully managed numerous drug-linker projects. Since the first ADC project in 2005, many customers, ranging from small biotech to large pharmaceutical companies, expressed a growing interest in our ADC and bioconjugation abilities. We have handled projects from payload/warhead manufacture to drug-linker, then to conjugation and final drug product all in house.

Our clean room suites are fully qualified for cGMP manufacturing dedicated to bioconjugation. In conjunction with our state of the art purification technologies, exceptional analytical/fill-and-finish capabilities, our customers are also provided with regulatory and CMC support.

Chromatography Services Gram to Kilogram

- 2 Asahi/Kasei HPLC/MPLC systems to enable purification of Highly Potent molecules
  0.1 to 2.5 kg/day
- 3x HPLC systems (2x Labomatic, 1x Knauer) for 5-15 cm ID (inner diameter) columns Multi-component separations
  0.02 to 0.8 kg/day
- 3x Biotage 400L Skids
  1 to 5 kg/day
- Preparative HPLC Novasep 20cm (ID) column Multi-component separations
  0.1 to 1.5 kg/day
- 2x Preparative HPLC Skids 30cm & 45cm (ID) columns
  Multi-component separations
  0.4 to 4 kg/day
- 2x SMB Skids, 8x 5cm columns
  Binary separations of racemates
  0.2 to 5 kg/day
- 2x Preparative MPLC 45 & 60cm ID Columns
  Large-Scale Normal-Phase
  2 to 20 kg/day
- 2x Buchi HPLC
  0.005-0.05kg/day

Technology Transfer – Case Studies

As part of a multi-site, transcontinental organization, we offer our customers the opportunity to obtain a comprehensive range of chemical and manufacturing solutions from a single supplier. This extends from rapid supply of intermediates and Active Pharmaceutical Ingredients (APIs) for preclinical use, to large-scale commercial manufacturing. An efficient and effective technology transfer process is the key to the successful transfer of processes either from the customer to CARBOGEN AMCIS or between two CARBOGEN AMCIS sites.

Our technology transfer expertise is a key element in our ability to take advantage of the economies of scale and lower cost base associated with the CARBOGEN AMCIS high potency plants in India and China.

Technology Transfer Process

Complex, multi-step processes under both current Good Manufacturing Practice (cGMP) and non-GMP have been successfully transferred. For transfer outside of Switzerland, a specialist team follows an established three-stage procedure:

1 Initiation: the scope and goals are agreed upon by all parties – preparation of technology transfer master plan, definition of responsibilities, as well as preparation and transfer of technical information package;

2 Piloting: the process is trialled in the lab, analytical method transfer is completed, along with the key change review and pre-manufacturing review processes to ensure compliance with regulatory and quality standards. Finally trial batches are produced;

3 Sign-off: the trial campaign is reviewed in detail, any further learning implemented, and the transfer signed off. Routine production follows against established batch instructions.

A crucial element in successfully transferring technology across linguistic and cultural barriers is the quality of the communication between our experienced personnel, alongside clear definition of roles and responsibilities.

Where it provides benefits, team members from the transferring site are present at the receiving site, for example for project kick-off, and during production start-up.

Case Study 1:

Reduced lead time and cost with continuous local project management

The first 4 steps of an eight stage registered process, previously run in Switzerland on 1,600 L scale, were successfully transferred to operations in India within a timeframe of 5 months. The transfer was mainly driven by growth in product volume coupled to the need to reduce overall lead times. The process is now executed in India at 4 times the previous scale, allowing us to make significant reductions in both cost and lead time. The intermediate is sent to Switzerland for conversion to the final API with no measurable difference in quality. This approach offers the customer flexibility in managing cost and quality demands without draining their own resources.

Case Study 2:

Product lifecycle management

A 3-stage process to manufacture a launched API for a US customer had been successfully running in Switzerland for over 10 years. To support the customer in the generic market with lower costs, the exact process was transferred to India. Following regulatory approval of the change of site, the customer will benefit from a more economic source of the API with identical quality, while the supply chain is maintained with ongoing manufacture in Switzerland.

Case Study 3:

Cost and feasibility aspects

A multistage production process for a non-GMP intermediate was performed at CARBOGEN AMCIS' Manchester site for a Japanese customer. Subsequent transfer to India was successfully accomplished, and the process was subsequently scaled up to 300 kg batches in a multi-ton campaign within 6 months. A chemist from Manchester supported the transfer on-site. In this case the transfer was driven mainly by the scale of production, but the customer also obtained a cost advantage from the increased scale at the new site.

Production Equipment

CARBOGEN AMCIS delivers leading process research services that support the drug development process. Early Active Pharmaceutical Ingredient (API) manufacture centers on the rapid synthesis of supplies necessary to perform both toxicology and early phase clinical trials. Typical batch sizes here range from 1 gram to 50 kg scale and are prepared in the highest standard of current Good Manufacturing Practices (cGMP).

We have over 20 years' of experience in the supply of APIs for clinical trials and commercial production and are specialized in the multi-step cGMP manufacture of APIs (20 kg to 2000 kg). The goal is to supply our clients with market-ready quantities of APIs including drug master files and regulatory documentation. Our services are tailored to the individual needs of each client from initial route finding through to cGMP production.

Process Research & Development

We currently have more than 100 hoods available for PR&D and production support activities. The state-of-the-art infrastructure including double jacket reactors, lab automation and micro-reactor capabilities ensures an efficient and comfortable working atmosphere.

Our chromatography and crystallization services provide an invaluable resource in producing and isolating material without recourse to excessive development time or costs.

Production & cGMP Manufacturing

We are highly experienced and equipped for handling a broad range of organic reactions embracing sophisticated modern technologies including low temperature reactions, organometallic reactions, chiral synthesis and hydrogenation at elevated temperatures.

Our purification capabilities applying chromatography or distillation allow an efficient synthesis of your compounds.

Our equipment includes:

- More than 80 multi-purpose reactors from 6 L to 8'000 L, glass-lined, Hastelloy, and stainless steel in a temperature range from -100°C to +160°C
- More than 10 filter dryers (0.15 m^2 to 1 m^2 Hastelloy)
- 400 L temperature-controlled pressure filter dryer (Hastelloy)
- High temperature reactor (200 L) in a temperature range from -120°C to +350°C
- High-Pressure autoclaves, pressure range up to 20 bar
- High vacuum distillation, 200 L to 900 L, 40 theoretical plates
- 6 cryogenic reactors 10 L to 3'000 L (< -70°C)
- Horizontal Pharma-Peeler Centrifuge, Diameter 630mm
- Lab automation system
- Milling and wet-milling
- Micronization
- Freeze dryers up to 30 kg ice per run

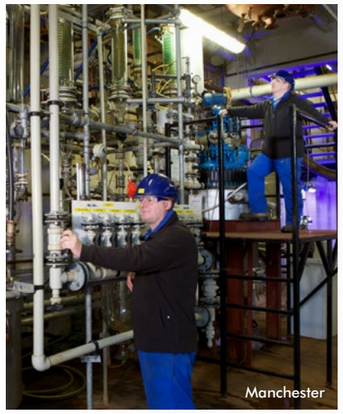

Bubendorf


Vionnaz


Shanghai


Neuland


Aarau


Manchester

Analytical Equipment

We internally optimize each site with all the equipment necessary to help your project to become a success. We provide unparalleled analytical support for research, development and commercial production of late-stage intermediates and APIs, including pre-formulation studies to support drug product development.

"We support our customers during and beyond the project by advising them on how to improve the process and the quality of the drug."

Darja – Chemist QC&A

Analytical Services

Analytics provides the foundation for process research and manufacturing activities. A thorough understanding of reactions is critical in process development and validation work.

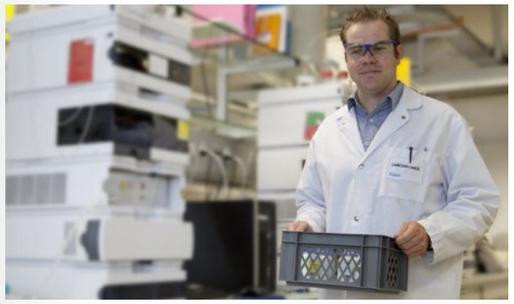
CARBOGEN AMCIS has always strived to provide a comprehensive range of tools and techniques to facilitate this work. Analytical chemistry services support both process control and material characterization for laboratory and production chemistry from initial raw material release to the release of the final APIs.

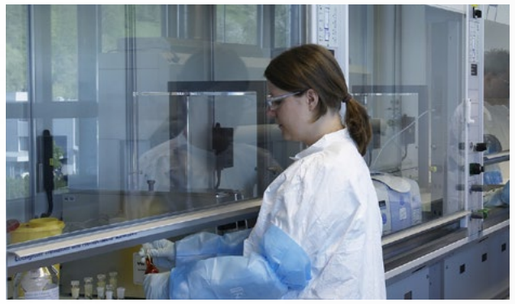
Our equipment includes:

- 3 NMR (400 MHz; H, C, P, F, N)
- 79 HPLC (DAD, ECD, ELSD, RI, MALLS, VWD, CAD
- 14 UHPLC
- 6 HPLC-MS (single Quad)
- 1 HPLC-MS/MS (Ion trap) AAPI, APCI, ESI
- 26 GC (ECD, FID, NPD, TCD, Head Space)
- 1 GC-MS (single Quad)
- 1 GC-MS (triple Quad)
- 6 DSC
- 2 RC1
- 5 FTIR (ATR, KBR, DRIFT)
- 6 UV-Spectrophotometers
- 3 TGA
- 4 Polarimeters
- 2 Particle Sizer
- 6 Ion Chromatographs (conductivity) - 3 anionic and 3 cationic
- 7 Automated Titrators
- 2 Densitymeter
- 3 Refractometers
- 2 XRPD
- 1 Capillary Electrophoresis
- 1 ICP/OES for metal analyses
- 1 Small scale jet mill
- 1 Water activity and moisture analyzing instrument
- 1 Dynamic vapour sorption analyzer
- 2 Microscopes

ICH Stability studies:

- 25°C / 60% r. H.
- 30°C / 65% r. H.
- 40°C / 75% r. H.
- 5°C
- - 20°C
- - 80°C





Highly Potent API Supply Equipment

CARBOGEN AMCIS
A Dishman Group Company

Our state-of-the-art infrastructure includes process research and development (PR&D) laboratories and, one laboratory dedicated to conjugation of small and large molecules and manufacturing capabilities.

The specialized laboratories and kilo-scale manufacturing equipment for small batch sizes of up to 15 kg are designed to operate safely at 0.05 µg/m³ OEL*. This performance allows safe handling of highly potent compounds, including cytotoxic warheads applied in antibody drug conjugates (ADC). Our intermediate and large scale manufacturing equipment currently operates down to 1 µg/m³ OEL (Switzerland) or down to 0.05 µg/m³ OEL (India) on a scale up to 1'600 L producing batches in the 200 kg range.

Our facilities & equipment include:

Bubendorf, Switzerland

- 4 PR&D laboratories proven to operate below below 0.05 µg/m³ OEL; (grade D) * The facilities enable process development for up to 8 projects in parallel and/or up to 3 lab scale cGMP projects in parallel.
- Conjugation laboratory with Grade C and D areas designed to operate below 0.05 µg/m³ OEL
- Kilo-scale manufacturing facility designed to operate below 0.05 µg/m³ OEL Air Cleanliness Class ISO 7 (Class 10'000) *
  - 4 Reactors from 100 L to 250 L (hastelloy and glass-lined), temperature range from -100°C to +160°C, pressure up to 12 bar
  - Hastelloy Filter Dryer with glove box (0.125 m²)
  - Hastelloy Filter Dryer with glove box (0.22 m²)
- Intermediate-scale production facility designed to operate down to 1 µg/m³ OEL by utilizing Rapid Transfer Ports (RTPs), barrier isolation technology and flexible containment of technology

Key equipment:

- Reactors from 250 L to 1'000 L, temperature range from -100°C to +160°C, pressure up to 20 bar
- Hastelloy Filter Dryers (0.25 and 0.4 m²)

Vionnaz, Switzerland

- PR&D labs designed to operate down to 0.05 µg/m³ OEL. The facilities enable process development for up to 3 PR&D projects in parallel
- Pilot plant unit (10, 15 and 30 L) designed to operate down to 0.05 µg/m³ OEL (up to about 1 kg). The facilities enable process development for up to 2 cGMP projects in parallel.
- Chromatography suite equipped with Asahi/Kasei System to enable running MPLC and HPLC up to 15 cm
- Lyophilization capability with up to 30 kg ice designed to operate down to 0.05 µg/m³ OEL

Hunzenschwil (Neuland), Switzerland

- PR&D laboratory designed to operate down to 1 µg/m³ OEL
- Intermediate-scale production facility designed to operate down to 1 µg/m³ OEL
  - 4 Glass-lined reactors of 630 L (2x) and to 160 L (2x), pressure up to 6 bar
  - 2 Filters (0.28 m² and 0.16 m²)

* Performance of the equipment and trained operators was demonstrated down to levels of 0.01 µg/m³

Dishman, India

- 2 PR&D laboratory designed to operate below 0.05 µg/m³ OEL
- Large-scale production facility designed to operate at 0.05 µg/m³ OEL utilizing barrier isolation technology:
  - 6 Reactors from 630 L to 1'600 L
  - Hastelloy Filter Dryer (1.0 m²) fitted with a discharging isolator
  - Hastelloy Filter Dryer (0.6 m²) fitted with a discharging isolator
  - 6 Isolators dedicated to charging and one to dispensing
  - Isolator for milling/micronization (Nara Pin Mill, Quadro)
- Under construction: Kilo-scale manufacturing facility designed to operate below 0.1 µg/m³, Air Cleanliness Class ISO 8 (Class 100'000) including:
  - 3 Reactors from 80 L to 50 L (Hastelloy and glass-lined), temperature range from -80°C to +160°C, pressure up to 10 bar
  - Hastelloy Filter Dryer (0.1 m²)

Analytics of Highly Potent APIs

- NMR • HPLC (SEC-UV, GPC-MALLS, HPLC-MS) • GC (FID, Headspace) • pH meter • UV/VIS • IR (KBr pellet) • KF-determination • DSC (closed pan only) • Heavy metals • Residue on ignition • Optical rotation • RC1 •
- Access to crystallization development and screening for metastable zones in closed vials
- Access to powder X-ray diffraction and particle size determination
- Malvern particle size distribution (PSD)

Purification of Highly Potent APIs (Bubendorf)

- Chromatography suite dedicated to highly potent APIs
  - 3 Multipurpose Walk-in-Barrier Hoods
  - Preparative Chromatography (up and prep. HPLC up to 15cm)
- Tangential Flow Filtration for macromolecules from 10's to 100's of kilo Dalton
- Gel Permeation Chromatography for the removal of aggregates and higher molecular impurities

Formulation Equipment

In addition to pre-formulation services, solid state and crystallization services, and analytical support for physicochemical characterization and method validation, CARBOGEN AMCIS offers a complete range of drug product development and manufacturing services at our Riom site in France. Our specialty is the injectables and the handling of complex compounds such as highly potent APIs, biological products and drug delivery. This site is exclusively dedicated to the development and the cGMP manufacturing to the fast supply of batches for clinical studies.

"It's rewarding to be able to help manage projects and to watch them develop into the production stage successfully. Each project is unique so you're faced with new challenges to overcome each day which breaks up the daily routine."

Emmanuelle – Pharmaceutical Development Project Manager

CARBOGEN AMCIS offers a comprehensive range of development and manufacturing services for the formulation of New Molecular Entities (NMEs) and the reformulation of existing drugs. We are specialized in developing sterile and pyrogen free parenteral formulations for preclinical and clinical trials (phases I, II and III).

With over 15 years of experience, we have gained the necessary expertise to safely develop injectables and liquid pharmaceutical forms for a wide range of drugs including drug delivery, highly potent and antibody drug conjugates (ADC).

Our trained and experienced personnel operate in state-of-the-art containment facilities and can handle materials of the highest occupational exposure band, including cytotoxics.

Our development & production equipment includes:

cGMP equipment list:

- 2 aseptic filling isolators (running under class A)
- 5 isolators (running under class C)
- 3 laminar flow hoods
- Terruzzi freeze dryer (1.2 square meters) with CIP and SIP for GMP production
- Nitrogen loop system
- Autoclave
- Dry heat oven
- Water activity and moisture analyzing instrument
- HPLC chains
- Biological safety cabinet
- Incubators

Development devices:

- Semi-automated dosing Xcelolab
- Dynamic vapour sorption system
- Dissolution testing equipment
- Disintegration testing equipment
- Powder, closed-loop weight dispenser
- Glovebox (2.4 square meters) for the formulation of new highly-potent compounds
- Segregated (0.6 square meters) Telstar lyophilizer

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CARBOGEN AMCIS is a leading service provider, offering a portfolio of drug-development and commercialization services to the pharmaceutical and biopharmaceutical industry at all stages of drug development. The integrated services provide innovative chemistry solutions to support timely and safe drug development allowing customers to make the best use of available resources. CARBOGEN AMCIS is also active in the marketing/sales and manufacture of Vitamin D analogues, Vitamin D, Cholesterol and lanolin related products for key markets as pharmaceutical, cosmetic, food, feed as well as industry applications.

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