CARBOGEN AMCIS

A Dishman Group Company

BRINGING YOUR SCIENCE TO LIFE

Highly Potent Active Pharmaceutical Ingredient Manufacturing

Highly Potent API Supply

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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.

> ***"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

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

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 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
	Up to Category 4 OEL down to 0.05 $\mu g/m^3$	Conjugation Laboratories Up to 20 L
	Up to Category 4 OEL down to 0.05 $\mu g/m^3$	Large-Scale Manufacturing Facility up to 850 L
	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
Saint-Beauzire 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.

Highly Potent API Supply Equipment

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•• 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

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)

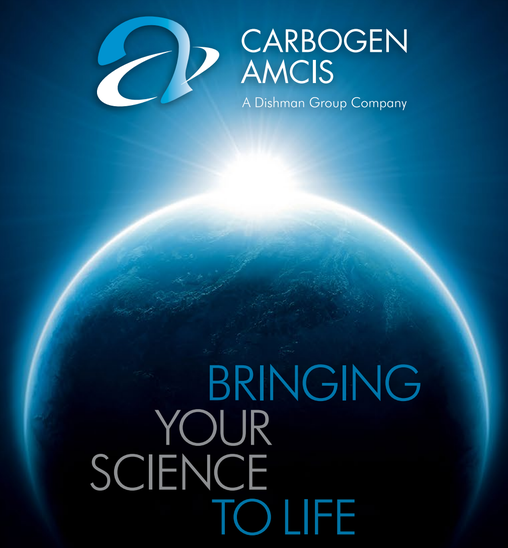
Purification of Highly Potent APIs (Bubendorf)

•• 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



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