CARBOGEN AMCIS

A Dishman Group Company

BRINGING YOUR SCIENCE TO LIFE

Development and Aseptic Production of Drug Products

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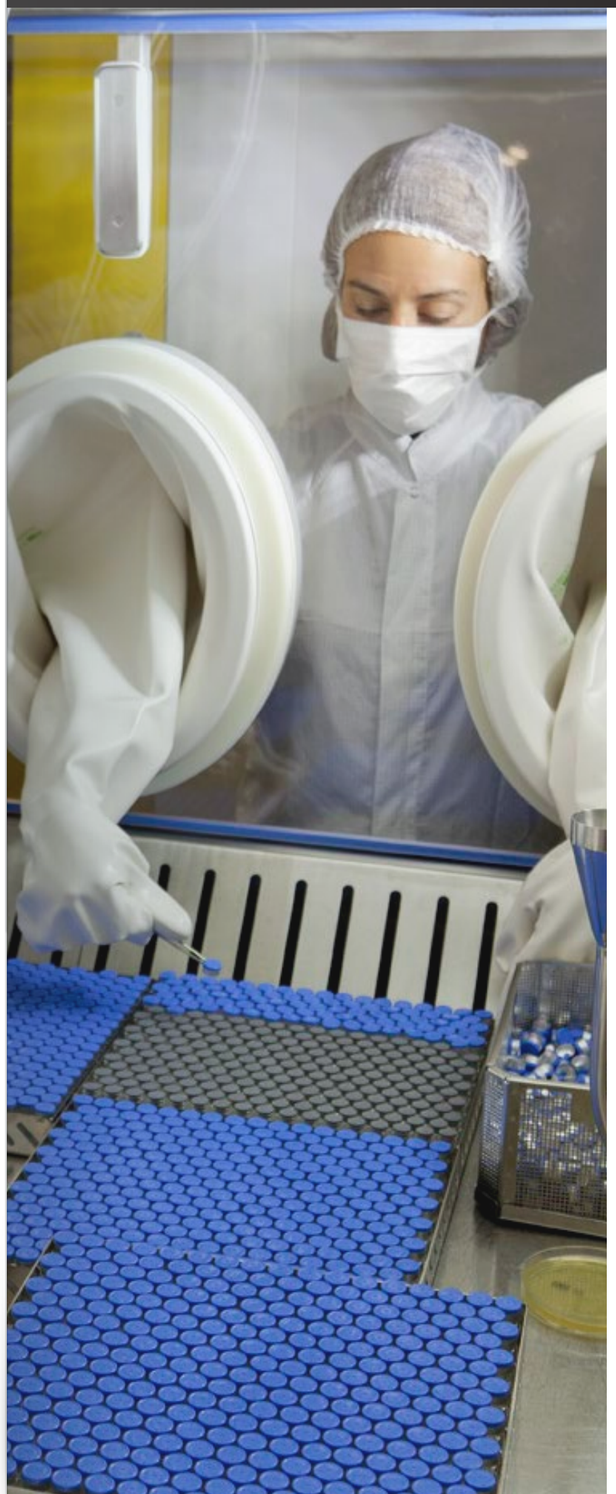

CARBOGEN AMCIS offers a comprehensive range of development and manufacturing services for the formulation of New Molecular Entities (NMEs) and the reformulation of existing drugs. We are specialized in developing sterile and pyrogen-free parenteral formulations for preclinical and clinical trials (phases 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 service offerings for drug products span from pre-formulation and formulation services to aseptic production of clinical batches for parenteral drugs. Formulation services are fully integrated with CARBOGEN AMCIS' API process research and manufacturing services for the fast supply of the product for clinical trials.

Pre-Formulation Services

Pre-formulation services in Switzerland encompass several activities, such as the **physicochemical characterization** of the API, the selection of the best crystalline forms and the **stability profile** of the material. We offer comprehensive pre-formulation services and **integrated analytical and solid state services** designed to provide key information for the formulation of drug substances in both solution and solid states.

Key Services:
- Feasibility and pilot studies for dispensing microdosing and particle size distribution
- Bioavailability studies: dissolution, disintegration testing and solubility testing (simulation in physiological conditions)

Designed for: solutions and solids, including drug in capsule (DIC) and drug in bottle (DIB)

Formulation & Process Development Services

CARBOGEN AMCIS offers a complete range of formulation and process development services for parenteral forms. We have extensive experience with a broad range of substrates, such as small molecules, cytotoxics, proteins, peptides, enzyme inhibitors, antibiotics (nonbeta-lactam), vaccines (non-live), mAbs and antibody drug conjugates (ADC).

Key Services:
- Formulation of new products and optimization of existing formulations
- Development and optimization of lyophilization cycles
- Process development and Scale-up

Designed for: liquid or freeze-dried injectables

Aseptic Production

We offer current Good Manufacturing Practices (cGMP) services for the fast supply of preclinical and clinical batches of liquid or lyophilized parenterals. We provide aseptic filling in a wide range of volumes in vials, syringes and cartridges, from one millilitre to several hundred millilitres.

Key Services:
- Preclinical batches and clinical batches (phases I, II and III)
- Validation of aseptic process (media fill testing)
- Process development and scale-up
- Class A (ISO 4.8) sterility
- Maximum batch size: up to 4000 vials

Designed for: liquid or freeze-dried injectables

Our Service Offerings:

Preclinical and Clinical Studies
- Complex products
- Highly potents
- Biological products

Track Records Since 2000:

> 320 Batches produced under cGMP environment
> 180 Clinical batches
> 129 Media fill tests

Drug Products

PRE-FORMULATION
- Particle size distribution
- Feasibility / pilot studies
- Dispensing / microdosing

FORMULATION
- New formulation
- Reformulations
- Lyophilization cycles
- Parenteral drugs

STERILE PRODUCTION
- Clinical batches (I, II & III)
- Preclinical batches
- Media Fill Testing
- Parenteral drugs

Drug Substances

HIGH POTENCY
- FDA-approved
- Recognized experts
- State-of-the-art facility
- In-house categorization

CHROMATOGRAPHY
- Fast purification of APIs
- Feasibility studies
- Dedicated experts
- Vast range of solutions

CUSTOM MANUFACTURING
- Supply of intermediates
- Process development
- Process research
- Supply of APIs

Drug Products & Substances

ANALYTICAL
- Method validation
- Physical-chemical
- Moisture analysis
- Microbiological controls

ICH STABILITY STUDIES
- ICH studies
- Forced / Stress tests
- Stability indicating method
- Customized studies

SOLID STATE & CRYSTALLIZATION
- Polymorphism screening
- Stereochemical stability
- Structure elucidation
- Salt screening

Our Benefits:

- Chemistry and manufacturing controls (CMC) support from development to market
- State-of-the-art infrastructure
- Highly skilled, cross-functional teams of scientists with decades of experience
- Dedicated project and product managers
- Breadth of equipment and personnel ensuring flexibility and capability to tailor projects to specific needs
- Flawless track record
- Recognized leader in high-potency manufacturing

Case Study

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Client:

Immune Targeting Systems (ITS) Limited is a London-based Biotech Company developing synthetic vaccines for mutating viruses. Their proprietary vaccine technology relies on highly selected long peptides containing protective T cell epitopes modified with a fluorocarbon vector. Designed as a stable freeze-dried formulation, the vaccine delivers the antigens into the body to promote robust T-cell immunity without requiring potentially toxic adjuvants. ITS' lead candidate is a universal influenza-A vaccine containing multiple fluoropeptides.

Needs:

ITS was looking for a CMO that could meet challenging timelines and provide a high level of technical expertise to convert a lab process into a scalable cGMP manufacturing process. The overall project encompassed the transfer of the formulation process and analytical methods, the optimization of manufacturing steps including formulation and freeze-drying and the successful manufacturing of technical and cGMP batches.

Realization

In close partnership with ITS, CARBOGEN AMCIS SAS was able to successfully manufacture several batches to specification, including two engineering batches, one cGMP toxicology batch and a cGMP clinical batch in less than 6 months. Technical challenges were successfully overcome such as:

1 Ensuring the physico-chemical integrity of the product during formulation: Based on a formulation process designed by ITS, CARBOGEN AMCIS SAS successfully scaled-up the process. Technical solutions were implemented to achieve a perfect solubilization of all APIs and prevent aggregation while ensuring good filtration recovery. All specifications were met through an efficient control of key formulation parameters such as process time and temperature around a dedicated and specialized organization in the cGMP suite.

2 Optimization of freeze-dried cycle: CARBOGEN AMCIS SAS reactivity and flexibility permitted the production of an additional engineering batch at full scale to optimize the lyophilization cycle in order to improve the quality of the cake. CARBOGEN AMCIS SAS provided ITS with a strategy that engaged a limited amount of their valuable APIs while ensuring the pertinence and robustness of results generated.

3 Technical and Regulatory support: CARBOGEN AMCIS SAS guided ITS through the product development phase in order to compile a regulatory data package regarding key aspects of the process including filter and microbiology method validation.

Outcomes

CARBOGEN AMCIS SAS successfully met all the project timelines and released a product that met specification for first-in-man studies. This will allow ITS to progress this innovative product through clinical development and keep momentum for their fund raising.

Customer Testimonial

"CARBOGEN AMCIS SAS has not only successfully provided a service, but our project has benefited a great deal from their technical expertise. It has been a pleasure to work with a highly professional and proactive team responsive to customer needs."

Bertrand Georges, PhD.
Head of Vaccine Technology and Innovation.
Immune Targeting Systems, Ltd. London.

Equipment for Drug Product

In addition to pre-formulation services, solid state and crystallization services, and analytical support for physico-chemical characterization and method validation, CARBOGEN AMCIS offers a complete range of formulation services for parenteral and highly-potent products. Our formulation and aseptic drug products services are performed at Riom, France site, which is exclusively dedicated to the development of parenteral products and to the fast supply of batches for clinical trials.

Our cGMP equipment includes:

- 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 cGMP 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
- 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
- Cytotoxic safety cabinet

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CARBOGEN AMCIS AG 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.