CARBOGEN AMCIS

A Dishman Group Company

FORMULATION 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 specialize in developing sterile and pyrogen-free parenteral formulations for preclinical and clinical trials (phases I, II and III). In over **15 years of experience**, we have gained the necessary expertise to safely develop injectables, liquid and semi-solid pharmaceutical forms for a wide range of drugs including oncology and metabolic disorders therapeutics. Our trained and experienced personnel operates 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 badges for parenteral drugs. Formulation services are fully integrated with CARBOGEN AMCIS' API process research and manufacturing services for the fast supply of API drug substances for clinical trials.

Pre-Formulation Services

Pre-formulation services 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. CARBOGEN AMCIS offers 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 Services

CARBOGEN AMCIS offers a complete range of formulation services for parenteral APIs. We have extensive experience with a broad range of substrates, such as small molecules, cytotoxics, proteins, mAbs, peptides, enzyme inhibitors and antibiotics (non-beta-lactam) and vaccines (non-live).

Key Services:
- Formulation of new products and optimization of existing formulations
- Development and optimization of lyophilization cycles

Designed for: Liquid forms, semisolids and injectables

Aseptic Production

CARBOGEN AMCIS offers Good Manufacturing Practice (GMP) services for the fast supply of **preclinical and clinical batches** of parenterals. We provide **aseptic filling** in a wide range of fill volumes in vials, syringes, cartridges and infusion bags from one millilitre to several hundred millilitres.

Key Services:
- Preclinical batches and clinical batches (phases I, II & III)
- Validation of aseptic process (Media Fill Testing)
- Class A (ISO 4.8) sterility
- Maximum batch size: 5000 x 2 mL vials

Designed for: Liquid forms, semisolids and injectables

CARBOGEN AMCIS' Service Offerings

Preclinical and Clinical Studies

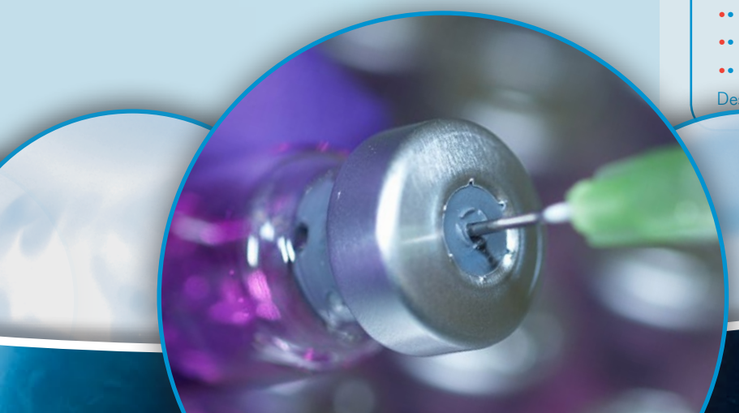
- Complex Small Molecules
- Highly Potents
- Biologics

Track Records Since 2000

> 400 GMP batches
> 220 clinical batches
> 100 Media Fill Tests

CARBOGEN AMCIS Benefits

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



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DRUG PRODUCT - CASE STUDY

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 solubilisation 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 Optimisation 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's Testimony

"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.

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 formulation services for parenteral APIs and highly-potent APIs. Our formulation and aseptic drug products services are performed at our Riom, France site, which is exclusively dedicated to the development of parenteral products and to the fast supply of batches for clinical trials.

Our pre-formulation and formulation equipment includes:

- 2 aseptic filling isolators (running under class A)
- Semi-automated dosing Xcelolab from Capsugel
- Non-GMP jet mill and GMP jet mill (up to 50 grams)
- Water activity and moisture analysing instrument
- 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 and Telstar LyoBeta 20
- Terruzzi freeze dryer (1.2 square meters) with CIP and SIP for GMP production
- Autoclave for sterilization
- Dry heat oven
- Biological safety cabinet
- Incubators

Aseptic filling isolators for the safe handling of highly-potent compounds

GMP lyophilizer for sterile drugs

GMP lyophilizer for sterile drugs

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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.