Coriolis Pharma

Biopharmaceutical Research and Development Service

Lyophilization cycle development, optimization and scale-up

www.coriolis-pharma.com

Corporate overview

Coriolis Pharma is an independent service provider for formulation research and development of biopharmaceutical drugs such as proteins, peptides, monoclonal antibodies, nucleic acids and vaccines. As a fully privately owned company we serve a global client base consisting of both small and large biopharmaceutical companies with molecules in early and late stage development.

An interdisciplinary team of highly qualified scientists with many years of experience in formulation development of biopharmaceuticals is supported by an expert scientific advisory board of leading academic researchers in the field. This structure allows Coriolis Pharma to deliver cutting edge service and know-how related to the formulation development of liquid and lyophilized products to the biopharmaceutical industries.

In addition to the core formulation capabilities, Coriolis Pharma is also specialized in the field of subvisible particle analysis and characterization of protein aggregates. This includes utilization of the latest innovative technologies such as resonant mass measurements (Archimedes), Nanoparticle Tracking Analysis (Nanosight), Micro-Flow Imaging (MFI), asymmetric and hollow fiber flow field flow fractionation (AF4/HF5), as well as provision of cGMP compliant analytics for selected particle measurement and aggregation characterization methods.

Lyophilization cycle development, optimization and scale-up

Process understanding and formulation expertise, in combination with analytical know-how is our strategy for a successful and target orientated lyophilization development. Coriolis Pharma has a strong background in the development, optimization, scale-up and transfer of lyophilization processes for biopharmaceutical drugs.

The company is equipped with several freeze-driers from lab scale to pilot scale, placed within a GMP-like environment with controlled particle levels. State-of-the-art analytical methods for the physico-chemical characterization of the liquid and dried formulations support the lyophilization development work.

For the development of economical freeze-drying cycles suitable process parameters for freezing, primary and secondary drying are selected based on phyisco-chemical characterization of the freezing behavior of the formulations, e.g. by DSC and freeze-drying micro-scopy. When selecting process parameters the suitability for the later transfer to the client and scale up will already be considered. Freeze-drying processes are monitored by modern process analytical tools and it is possible to extract samples from the running processes by a sample thief or generate lyophilisates of different residual moisture by individual shelf closure within a single freeze-drying run.

Lyophilization development service of Coriolis Pharma at a glance

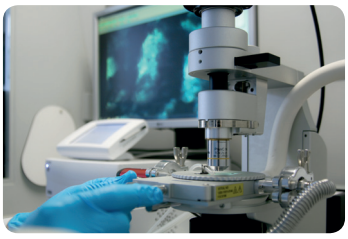
- Facilities
  - Dedicated 200 m² lyophilization development center
  - Dedicated 100 m² clean room fill and finish R&D center
- Freeze Driers

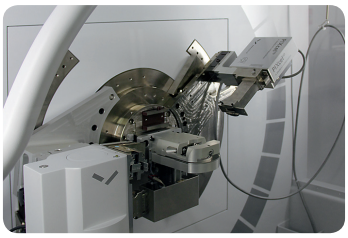
  Lab scale
  - Epsilon 1-6 CC (M.Christ), freezing unit, liquid nitrogen
  - Epsilon 2-6D (M.Christ), shelf area 0.3 m²

  Pilot scale
  - Epsilon 2-12D (M.Christ), shelf area 0.8 m²
  - Epsilon 2-12D (M.Christ), shelf area 1.0 m², liquid nitrogen
  - LyoStar III (SP Scientific), shelf area 0.8 m²
  - Magnum Series 85 (Millrock Technology), shelf area 1.8 m²
  - Epsilon 2-12D special (M.Christ), shelf area 0.6 m², clean room
- Features – process analytical tools (PAT)
  - Various pressure sensors
  - Liquid nitrogen fast freezing
  - Control nucleation (all systems)
  - Individual shelf closure
  - Sample thief
  - Wireless temperature sensors
  - Heatflux monitoring
  - Manometric temperature measurements
  - Visualization sublimation front
  - Microbalance sublimation rate
  - Optical fiber sensors (incl. crystallization events)
- Services
  - Lyophilization process and formulation development
  - Primary packaging investigation
  - Optimization of existing lyophilization cycles, e.g. reduction of cycle time, improving product stability or appearance
  - Quality by design (QbD) incl. design space and process robustness
  - Scale-up and transfer of lyophilization cycles
  - Filling and lyophilization under aseptic conditions stability and tox studies
  - Manufacturability investigation incl. filtration studies
  - Analytical service to determine critical parameters for formulations that should be lyophilized (e.g. collapse temperature Tc, glass transition temperatures of the maximally freeze-concentrated solution Tg')
  - Production of lyophilized formulations with different residual moisture levels in one cycle by individual shelf closure

Analytical methods to support lyophilization development

- Differential scanning calorimetry (DSC) for the frozen (Tg') and dried state (Tg)
- Freeze-drying microscopy (FDM)
- X-ray powder diffraction (XRD)
- Porosity measurement (BET)
- Scanning electron microscopy (SEM)
- Karl Fischer titration (residual moisture)





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Lyophilization needs protein science