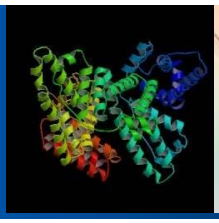
Lyophilization



Custom Lyophilization Services

We are a contract laboratory in the San Francisco Bay area that provides custom lyophilization services to our clients. At HTD, we design a lyophilization process that meets the appropriate criteria for a stable lyophilized drug and that can be scaled up for manufacturing.

Our complete lyophilization services include :

- **Formulation Development**
  - Proteins, antibodies, enzymes, peptides
  - Nucleic acids, DNA, siRNA, mRNA, oligonucleotides
  - Antibody-drug conjugates
  - Vaccines
  - Liposomes and lipid nanoparticles
  - Small molecules
  - Diagnostics
  - Combination products

- **Lyophilization Cycle Development**

Information such as freezing point, glass transition temperature, and eutectic crystallization temperatures is obtained by Differential Scanning Calorimetry (DSC) of pre-lyo formulations. This information is utilized in designing a robust lyophilization cycle in a Vertis lyophillizer that is specifically designed to mimic large production lyophilizers.

- **Characterization of Lyophilized Product & Stability Studies:**
  - Solid state structure (DSC)
  - Residual Moisture (Karl Fischer)
  - Reconstitution
  - Appearance
  - Characterization of reconstituted solution by DLS, nDSF, Protein chip bioanalyzer, IEF, UV spectroscopy, and other methods.

- **Tech Transfer to GMP Manufacturing site**

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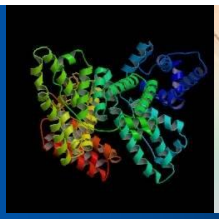
Lyophilization



Lyophilization Process Development

Lyophilization comprises of a series of process steps that include

- **Freezing** at a controlled rate to ensure minimal perturbation of protein structure,
- **Annealing** of the frozen matrix to ensure a consistent frozen matrix across the vials.
- **Primary drying** to sublime the bulk water from the frozen matrix.
- **Secondary drying** to remove more tightly bound water molecules, ensure low moisture content in the product, and have the right solid-state properties in the final lyophile to obtain a stable product.

Certain criteria for development of a stable lyophilized protein are

- A glass transition temperature above the storage temperature.
- Moisture content below 1-2 %.
- Maintain as much native structure of the protein in the solid state.
- No phase separation of the protein from the amorphous phase.

HTD has successfully lyophilized numerous drug products and transferred the process into large-scale manufacturing. We provide a rationale approach to the lyophilization cycle that becomes a critical component of the CMC section for submission to the regulatory agencies and manufacturing groups.

Figure 1. Vertis lyophilizer.

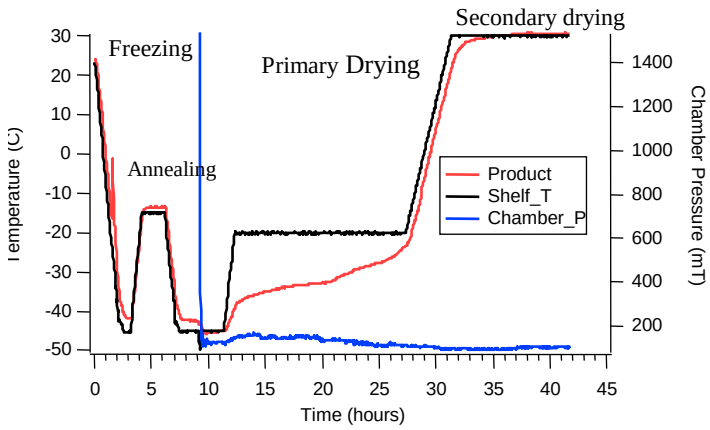


Figure 2. Steps in a freeze-drying cycle.

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