Inhalation Product Development
Cirrus Pharmaceuticals, Inc. offers proven expertise in providing regulatory-compliant inhalation product development services for the following dosage forms:

- Metered Dose Inhalers (MDIs)
- Dry Powder Inhalers (DPIs)
- Nebulizers
- Nasal Sprays

**Chemical and Physical Characterization**

A variety of services are offered to characterize and select the drug candidate, such as:

- Solubility Profile in HFA Propellants and Co-solvents
- Salt Selection
- Excipient Compatibility
- Chemical Stability Evaluation and Degradation Pathway Identification

**Fine Particle Generation and Characterization**

Cirrus has the capability to generate fine particles using conventional methods, such as jet milling and spray drying, as well as more novel approaches. State-of-the-art methods are available to characterize fine particles:

- Particle Size Analysis (e.g. Laser Diffraction and Microscopy)
- Polymorphism Evaluation
- Micronization Optimization
- Amorphous Content Determination

**Formulation Development**

Our inhalation development team has extensive experience formulating:

- Suspensions
- Solutions
- Dry Powder Blends

Services include dosage form selection and product performance testing of candidate formulations. Formulation selection and optimization are aided by statistical experimental design. Studies are facilitated by on-site filling equipment and stability chambers.

**Device Evaluation**

Cirrus can select a suitable delivery device as part of the product development program. Alternatively, devices selected or developed by the sponsor can be evaluated – for example, for comparison to a marketed product. Devices and components commonly evaluated include:

- MDIs (Valves, Cans, and Actuators)
- DPIs (Blisters, Device Durability, and Reliability)
- Nebulizers (Nebulizer, Compressor, or Other Means of Mist Generation)
- Nasal Sprays (Pump and Container)

Moisture protective overwraps, spacers, valved holding chambers, dose counters and other auxiliary components can be incorporated as requested.

**Analytical Testing**

Cirrus provides analytical method development, validation, and testing services to support all phases of product development, from feasibility through regulatory submission and post-approval support. Full product release and stability testing services are available. Key tests include:

- Cascade Impaction (Andersen, Next Generation, Marple-Miller, etc.), Including Evaluations of Single Doses (e.g. two actuations) via LC/MSD
- Dose Content Uniformity
- Drug-related Impurities
- Moisture Content
- Simulated Patient Use

Submission-ready documents will be generated.

**Process Development, Scale-Up and Technical Transfer**

Upon selection of a lead candidate formulation, our process scientists and engineers can develop and optimize an appropriate manufacturing process. For MDIs, equipment is available to execute a variety of cold filling and one- and two-step pressure filling techniques. Blending equipment is available for dry powder formulations.

If requested, Cirrus can select a manufacturing site for clinical or full-scale batch production, transfer and validate the manufacturing process, and oversee batch manufacture.

**A Culture of Innovation**

Cirrus excels in the use of innovative approaches to solving difficult problems:

**Case History 1**

A development program for an MDI was initiated for a sponsor in 1999, and a New Drug Application (NDA) was submitted for the product in 2004. The product, Xopenex HFA®, received regulatory approval in 2005 in the shortest FDA review cycle for an HFA MDI to date. Cirrus’ contributions to that program included development of the HFA formulation, selection of components, and development, scale-up and technical transfer of the manufacturing process.

**Case History 2**

A challenging formulation problem led Cirrus to develop a novel MDI manufacturing process, which resulted in a patent filing for the client. Intellectual property matters are facilitated by an in-house patent agent.