Formulation Considerations for Inhaled Products

Lei Mao, PhD
Group Leader of Inhaled Products and Technologies
April 06 2011
Formulation Considerations of Inhaled Products

Inhalation Therapy

Metered Dose Inhalers (MDI) and Formulations

Dry Powder Inhalers and Formulations

Nebulizers and Formulations

Emerging Technology in Particle Engineering

Conclusions
Inhalation Therapy

- **Inhalation Therapy Refers to Direct Delivery of the Medications to/via the Lungs by Inhalation**
  - **Regional Therapeutic Effect**
    - Respiratory Disease
      - Asthma and Chronic obstructive pulmonary disease (COPD)
    - Pulmonary Hypertension
  - **Systemic Therapeutic Effect**
    - Migraine
      - Ergotamine Tartrate
    - Parkinson’s Disease
      - Apomorphine Hydrochloride
    - Diabete Mellitus
      - Inhaled Insulin

- **Advantages of Inhalation Therapy**
  - Delivery of the Medications Directly to the Action Site
  - Rapid Onset
  - Enhanced Bioavailability by Avoiding First Pass Effect
Challenges in Inhalation Drug Delivery

Dealing with small particles
- Less than 5 µm, majority 2-3 µm in order to reach bronchial regions

- Impaction $\propto D^2, U$
- Turbulent $\propto D^2, F^{2/3}, V^{-1/4}$
- Extra-Thoracic Deposition
- Sedimentation $\propto D^2, T$
- Bronchial Deposition
- Diffusion $\propto (T/D)^{1/2}$
- Alveolar Deposition
Aerodynamic Diameter vs Geometric Size

\[ D_a = D_v \cdot \sqrt{\frac{d_p \cdot C_{(Dv)}}{S \cdot d_0 \cdot C_{(Da)}}} \]

- \( D_a \)  Aerodynamic diameter
- \( D_v \)  Volume diameter
- \( S \)  Shape factor
- \( d_p \)  Particle density
- \( d_0 \)  Unit density
- \( C_{(Dv)} \) & \( C_{(Da)} \)  Slip correction factors

Aerodynamic shape
eg Asbestos Fibres

\( 10.0 \mu m \)

\( 5.0 \mu m \)

\( 2.3 \mu m \)

\( 2.0 \mu m \)

\( 1.9 \mu m \)

1.5 1.3 1.0 0.21 0.05 g/ml

Different density spheres with the same mass and aerodynamic diameter (2.3\( \mu m \))
Measurement of Aerodynamic Particle Size Distribution

- Aerodynamic particle size distribution is measured by cascade impaction method

Andersen Cascade Impactor

- Simulated Oropharynx (Small Volume Throat)
- Cascade Impactor
- Air Flow Diverted
- 3-Way Electric Valve
- Pump
- Timer

- Preseparator
  - 10 micrometers and above

- Stage 0
  - 9.0μ-10.0μ microns

- Stage 1
  - 6.8μ-9.0μ microns

- Stage 2
  - 4.7μ-5.8μ microns

- Stage 3
  - 3.3μ-4.7μ microns

- Stage 4
  - 2.1μ-3.3μ microns

- Stage 5
  - 1.1μ-2.1μ microns

- Stage 6
  - 0.65μ-1.1μ microns

- Stage 7
  - 0.43μ-0.65μ microns

- Filter
  - 0.43 microns

*effective cut off diameter

Inhalation Volume = 3.8 L
Inhalation Flow Rate = 28.3 L/min
Inhalation Time = 8 sec
Flow started prior to actuation
Principles of Particle Size Analysis By Cascade Impaction

- Schematic cross section of the impaction stages.
- Progressively smaller orifices increase the orifice velocity,
- In eight successive stages.
- Causing impaction of smaller particles onto the collection discs of each succeeding stage.
Issues in Dealing with Small Particles

**Ideal Particles**
- Uniform particles with monodispersion
- Uniform density
- None-cohesive
- No agglomeration
- No compaction
- Excellent flowability
- Readily dispersed when delivered as an aerosol

**Real Particles**
- Micronization is a conventional approach for size reduction
- Polydispersity
- Particle size range 0.5 – 10 μm
- High energy input
- Less integral crystalline surface
- Amorphous regions
- Particle shape
- Particle density/porosity
- Cohesive
- Hygroscopicity
- Chemical instability
- Electrostatic
- Poor flow properties
- Age/history
- Batch-batch variability

Small Particles, Big Issues
Impact of Small Particles on Inhalation Formulations

Formulation Challenges

- Formulation uniformity, e.g. dry powder inhaler, suspension MDI and nebulizer formulations
- Cohesive forces
  - Re-dispersion and aerosolization of drug particles
  - Powder flow
- Physical stability and impact on product performance, e.g.
  - Aggregation
  - Bridging
  - Östwald ripening
- Batch-batch variability (drug & excipients)
  - Size
  - Shape
  - Morphology
  - Amorphous content
  - Etc
Impact of Formulations on Inhaler Performance

Consistent Delivered Dose Through Inhaler Life

Consistent Aerodynamic Particle Size Distribution (Fine Particle Dose / Fraction)

Chemical and Performance Stability
Formulation Considerations of Inhaled Products

Inhalation Therapy

**Metered Dose Inhalers (MDI) and Formulations**

Dry Powder Inhalers and Formulations

Nebulizers and Formulations

Emerging Technology in Particle Engineering

Conclusions
Metered Dose Inhalers (MDI)

Formulation
- Drug
- HFA Propellant
- Surfactant
- Co-solvent &/or excipient

Container closure system
- Can
- Metering valve

Actuator

Dose compliance device
How MDIs Deliver Aerosols

**Metering Valve Function**
Reproducibly deliver a fixed volume charge throughout the labelled number of actuations

**Retention valves**

**Uniform drug distribution within the metering chamber and container**

**Smooth movement of the valve stem during actuation**

**Good sealing to provide an accurate volume/dose**

**No drug/liquid retained after dose delivery**
MDI Formulations – Suspension and Solution

**Suspension Formulation**
- Micronized drug particles suspended in the liquefied propellant (HFA134a or 227)
- May contain surfactant and co-solvent to aid suspension.
  - Irregular particles
  - Polydispersed (0.5-10μm)
  - Amorphous/crystalline
- Chemically stable
- Physical stability
  - Sedimentation/creamning
  - Drug deposition
    - Coated packaging materials
  - Particle growth
    - Östwald ripening
    - Aggregation

**Solution Formulation**
- Drug dissolved in the liquefied propellant
- May contain surfactant and co-solvent to dissolve the drug.
  - Solubility
- Excellent dose reproducibility
- ‘Fine’ spray/high throat deposition
- Limited to high potency (ie. low dose products) or highly soluble drugs
- Prone to chemical degradation
Example formulations

- 2-component suspension, ie. Drug/HFA
  - Ventolin™, Flixotide™/Flovent™
- 3-component suspension, ie. Drug/EtOH/HFA
  - Pro Air®
- 3-component solution, ie. Drug/EtOH/HFA
  - Qvar®
- 4-component solution, ie. Drug/EtOH/low volatility additive/HFA
  - Modullite™
- 5-component solution, ie. Drug/EtOH/citric acid/H2O/HFA
  - Atrovent™

Many products with varying degrees of complexity
Formulation = suspension or solution
Patent landscape is complicated & limits formulation options
Key Formulation Considerations

Consistent product performance on stability and through the labeled number of doses

Uniform formulation upon shaking to ensure metering and delivery of accurate and consistent doses

Drug suspension stabilized by forming loose agglomerates and readily re-dispersed upon shaking after storage

No particle growth due to aggregation or crystal growth to ensure aerosolization performance (Fine Particle Dose/Fine Particle Fraction)

No drug loss due to deposition on can to ensure consistent doses through inhaler life

Protection from moisture ingestion to ensure long term stability
Drug Properties

- Size reduced
- Polydispersity
- Particle size range 0.5 – 10 μm
- High energy input
- Less integral crystalline surface
- Amorphous regions
- Particle shape
- Particle density/porosity
- Cohesive
- Hygroscopicity
- Chemical instability
- Electrostatic
- Poor flow properties
- Age/history
- Batch-batch variability

Small Particles, Big Issues
Propellant

CFC Phase-Out
- Triggered major MDI re-development in past decades
    - Phase out ozone-depleting CFCs by 2000 except for essential medical use
  - Kyoto Protocol (1997)
    - Reduce HFA use to baseline 1990 levels by 2012
- CFC Albuterol no longer available in the US, ie. 3 HFA Albuterol MDI products approved

HFA134a and HFA227
- Energy source for production of aerosol plume
- Component compatibility, Surfactant availability, Process complexity, Hygroscopicity

<table>
<thead>
<tr>
<th>Propellant</th>
<th>Trichlorofluoromethane</th>
<th>Dichlorodifluoromethane</th>
<th>1,1,1,2-Tetrafluoroethane</th>
<th>1,1,1,2,3,3,3-Heptafluoropropane</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structure</td>
<td>CFC-11</td>
<td>CFC-12</td>
<td>HFA134a</td>
<td>HFA227</td>
</tr>
<tr>
<td>Vapour Pressure</td>
<td>0.89</td>
<td>1.49</td>
<td>23.7</td>
<td>2.33</td>
</tr>
<tr>
<td>Density (g cm⁻³ at 20 °C)</td>
<td>5.66</td>
<td>1.33</td>
<td>-29.8</td>
<td>2.04</td>
</tr>
<tr>
<td>Boiling Point (°C at 1 atm)</td>
<td>5.72</td>
<td>1.23</td>
<td>-26.1</td>
<td>9.51</td>
</tr>
<tr>
<td>Dielectric Constant at 25 °C</td>
<td>3.9</td>
<td>1.42</td>
<td>-16.5</td>
<td>4.07</td>
</tr>
</tbody>
</table>
Co-solvents

- **Co-solvents can be used as formulation aids in HFA systems**
- **Purpose**
  - Solubility enhancement in HFA
    - Drug, e.g.
      - Qvar® (HFA-134a/EtOH)
    - Surfactants, e.g.
      - Proventil® (HFA-134a/EtOH/Oleic Acid)
      - Symbicort® (HFA-227/PEG/PVP)
    - Excipients, e.g.
      - Atrovent® (HFA-134a/EtOH/Water/Citric Acid)
  - Wetting
    - Improved suspension behaviour, e.g.
      - ProAir® (HFA-134a/EtOH)
    - Reduced drug deposition onto the container closure system
  - Valve function & reduced friction
- Ethanol and PEG 1000 are reported as co-solvents in the marketed products
Surfactants and How They Work

• **Surfactant**: Head/tail structure, molecular weight and chemical composition

• **Surfactants used in the marketed inhaler products:**
  • Oleic acid, Lecithin, Span 85, PVP K25

Assumes continuous phase is an oil, i.e. reverse micelle.

Effects apply equally to:
- Particle-particle interaction
- Particle-surface interaction

Adsorption

Stabilisation

Increasing [Surfactant]

[Diagram showing adsorption and stabilisation processes]
Benefits of Surfactants

No surfactant vs. With surfactant

Add Surfactant

Less variability

Formulations after storage at 40 °C/75% RH for 3 Months
Surfactant Concentration and Suspension Stability

Concentration increases from Bottle 13 to Bottle 16
Surfactant Concentration and Phase Separation

Particle-particle aggregation & settling

Compact sediment
- Difficult to disperse

Loose sediment
- Disperses readily

Homogeneous dispersion
Time, $t_0$

Stable

Unstable
Time, $t_1$

Discrete
Flocculant

$V_0, h_0$

$V_{a}, h_{u}$

Unstable
Time, $t_2$

Compact sediment
Compaction and Product Performance

Example 1
Increased delivered dose variability from retention valve due to compacted sediment with highly stable surfactant mediated formulation
Primeless valve may help

Example 2
Enhanced product performance when surfactant concentration is optimized
Container

Considerations

- **Chemical compatibility**
- **Physical compatibility, e.g. drug deposition onto the can wall**

**Material selection or coating helps resolve both issues**

- **Aluminum**
  - Bare aluminum
  - Anodized aluminum
  - Coated aluminum
    - Polymer coating
      - Heat Cured, e.g. fluoropolymers – PTFE, FEP, PFA, etc
    - Plasma
      - Gaseous monomer, e.g. fluoro, carbon, etc
- **Stainless steel**
- **Glass**
Metering Valves

Valve function
- Sealing mechanism to retain volatile formulation
- Barrier to moisture ingress
- Accurate and reproducible metering, i.e. delivered dose

Type of valves
- Retention valves
- Primeless valves, i.e. Fast fill/fast drain

Metering volume
- Typically 25 µl, 50 µl, 63 µl, 100 µl

Materials of construction
- Elastomeric seals, e.g.
  - EPDM (Ethylene propylene diene monomer); Nitrile; Bromobutyl; Chlorobutyl
- Plastic/metallic body & chamber

Considerations
- Drug/surface interaction
- Extractables and leacheables
- Valve friction
  - Metering function
  - Selection of materials
  - Surfactant/lubricant
- etc
Impact of Seal Integrity and Moisture Ingress

Example 1
Effect of moisture content on flocculation/particle size for different drugs
Östwald ripening &/or Capillary bridging

Example 2
Effect of moisture content on aerodynamic particle size
Reduction in fine particle fraction
Increase in throat deposition
Actuator

**Purpose**
- Mechanism to fire the inhaler
- Mouthpiece/patient interface
- Control aerosol spray behavior, e.g.
  - Spray pattern
  - Plume geometry

**Materials of construction**
- Typically polypropylene

**Actuator geometry**
- Expansion chamber
- Spray orifice, e.g. 0.1 – 0.5 mm

**Requirement for all new MDI products to have a dose compliance device**
- Dose counter
- Dose indicator
Actuator and Spray Pattern/Plume Geometry

Spray Pattern Measured at 3 cm Distance

Plume Geometry Measurement
Summary for MDI Formulation Development

All components, ie. drug particles, surfactant, co-solvent, propellant, can and valve affect formulation performance and stability

Surfactant stabilizes the suspension. However, inappropriate or excessive use of surfactant will result in compacted sedimentation or "creaming", leading to erratic delivered doses. Surfactant also minimizes drug deposition on the can and effect of moisture.

Co-solvent solubilizes surfactant or drug in the propellant (solution formulation) and stabilize suspension formulations.

Selecting an appropriate can or can coating minimizes drug deposition on the can and drug-can interaction.

Selecting an appropriate valve gasket minimize moisture ingresson and drug-valve interaction.

Nozzle orifice size is critical for the aerosol spray pattern and plume geometry.

SUCCESS IN THE FORMULATION RELIES ON ALL ABOVE FACTORS
Formulation Considerations of Inhaled Products

Inhalation Therapy

Metered Dose Inhalers (MDI) and Formulations

**Dry Powder Inhalers and Formulations**

Nebulizers and Formulations

Emerging Technology in Particle Engineering

Conclusions
Dry Powder Inhalers (DPI) and Formulations

- Delivery of dry powder aerosol to the lungs for local or systemic treatment
- Dry Powder Inhaler = Dry powder formulation + Inhaler device

**Product**
- Size reduced API (< 5µm)
- Pre-formulated API size reduced by micronization, spray dry or other technology
- Loose agglomerates of pure API/API diluent
- API/Carrier (Lactose monohydrate) blend

**Process**
- Blending/blender
- Low shear- Turbula® shake mixer, Pharmatech® blender
- “High shear” (high impact) Pharmx®, KG5,Glatt®, Hosakawa® GEA Niro Pharma (PMA), DIOSNA

Quantos is a trademark of Mettler-Toledo AG Corp., Turbula is a registered trademark of Willy A. Bachofen AG Corp., Pharmx is a registered trademark of Spraying Systems Co., Glatt is a registered trademark of Glatt GmbH., Hosokawa is a registered trademark of Hosokawa Mieron Corp., Xcelodose is a registered trademark of Capsugel Belgium BVBA Corp, Omnidose is a trademark of Harro Hoefliger
Dry Powder Inhaler Formulations

Three Types of Formulation

1. Pre-formulated Small Particles
2. Loose Agglomerates of Drug and excipient Particles
3. Drug Particles Carrier (Lactose) Blend

Present in the DPI Device

Aerosolized into individual particles when delivered from the device
Focus on DPI Blend Formulations

**Drug Particles**
- Size reduced to inhalation range (<5 µm, majority 2-3 µm)

**Inhalation α-Lactose Monohydrate**
- Form uniform interactive blend by attaching fine drug particles on to the lactose surface
- Improve flow ability
- Lactohale and Respitose ® Inhalation lactose with different particle size distribution and manufacturing process

**Ternary Agents**
- Enhance aerosolization performance by modifying the interaction forces between drug particles and carrier lactose through competition for high energy sites on the lactose surface
- Fine lactose, Magnesium Stearate, Amino Acids, e.g. L-Leucine
Control the Interaction Force using Ternary Agents, Fine Lactose or by Surface Modification

- **Passivate the lactose surface**

- **Addition of ternary agents or fine lactose to occupy high energy sites**
Key Formulation Considerations

**Interactive blend formulations**
- Drug particles evenly attached to the lactose surface.
- Improved drug content uniformity
- Improved Dose Uniformity

**Free flowing powders**
- Easy for device filling
- Accurately metered
- Improved dose uniformity

**Balanced drug lactose interactions**
- “Strong” binding to improve physical stability; No segregation during device filling and subsequent storage
- “Weak” binding to improve aerosolization performance when delivered from the device
Particle-Particle Interaction and Force Balance

Static and dynamic properties of the dry powder formulation can be manipulated by controlling particle-particle interaction through selection of proper formulation and process conditions.

Weak interactions:
- Poor flow ability – poor delivered dose consistency
- Enhanced aerosolization performance
- Fine lactose; Low shear force blending process; smoother particle surface

Strong interactions:
- More condensed powder, better flow ability – better delivered dose consistency
- Compromised aerosolization performance
- Large carrier lactose; High shear force blending process; less smooth particle surface

Good formulation means Sophisticate balance in particle-particle interaction
Impact on Process

Input Material Consideration
- Drug and lactose particle size distribution and other physical properties

Selection of Mixer
- Low shear or high shear mixer, dependent on the compounds to be processed and ultimate batch size.

Define Process Conditions
- “Time course” study to establish mixing process.
- Good blend content uniformity and aerosolization performance

Formulation Screening
- Selection of lactose; Use of fine lactose; Use of ternary agents; Lactose surface modification

Process Scale up
- Formulation fine tuning may be required to achieve the same performance
Effect of Mixing Time and Speed on the Fine Particle Fraction

- FPF affected by both mixing time and speed
- FPF affected by mixing speed but not the mixing time
- FPF less affected by mixing time and speed
Summary on the DPI Formulation Development

Selecting and controlling input drug particles and lactose are important factors in successful DPI formulation development.

DPI formulation and process conditions are equally important in achieving a good drug content uniformity and aerosolization performance.

Use of ternary agents or modification to the lactose surface improves formulation aerosolization performance.

Emerging particle engineering technology provides a new way of improving DPI formulation performance.
Formulation Considerations of Inhaled Products

Inhalation Therapy

Metered Dose Inhalers (MDI) and Formulations

Dry Powder Inhalers and Formulations

Nebulizers and Formulations

Emerging Technology in Particle Engineering

Conclusions
Nebulizer Solution Formulations

**Sterile Aqueous Solution**

Similar principles for MDI formulations apply

**Marketed Inhalation Solutions, e.g.**

- TOBI® Tobramycin Inhalation solution
- Ventolin® Inhalation Solution

- Drug dissolved in the solution
- Buffer vehicles to match pH in the lungs
- Salts to maintain tonicity
- Surfactants to increase drug solubility
- Stabilizers required for labile molecules
- Viscosity controlled to ensure size and distribution of nebulized droplets
- Package component compatible with the formulation. No drug adsorption
- Manufactured under aseptic conditions
Nebulizer Suspension Formulations

Sterile Aqueous Suspension

Similar principles for MDI formulations apply

Marketed Inhalation Suspension, e.g

PULMICORT RESPULES® (budesonide) Inhalation suspension

- Drug particle size within inhalation range
- Drug suspended in the vehicle suspension
- Buffer vehicles to match pH in the lungs
- Salts to maintain tonicity
- Surfactants to maintain solution stability
- Package component compatible with the formulation.
- Manufactured under aseptic conditions
Formulation Considerations of Inhaled Products

Inhalation Therapy

Metered Dose Inhalers (MDI) and Formulations

Dry Powder Inhalers and Formulations

Nebulizers and Formulations

Emerging Technology in Particle Engineering

Conclusions
Emerging Technology in Drug Particle Engineering

Advanced particle engineering technology has been widely explored for the inhalation application

Purpose: Free flowing particles; Less cohesiveness; Ease of dispersion and aerosolization

- **Spray Drying**
- **Large Porous Particles**
- **Super Critical Fluid**
- **Sonocrystallization**
- **Others, e.g. Pollen/Spores**

Spray Dried Particles

Inhalable Particles are produced by rapid evaporation of drug solution/suspension droplets atomized into the hot air stream.

Suitable for processing hydrophilic (spray drying from the aqueous solution) or hydrophobic (spray dry from the organic solvent solution) compounds.

Particle size can be manipulated by controlling the process conditions.

Particle density, morphology and surface properties can also be manipulated by controlling the process conditions or co-spray drying with excipients, e.g. sugar/polyol/surfactant.

High yield, continuous and scaleable manufacturing process.

Ideal process for producing inhalation particles of labile macromolecules.

Resulting particles can be delivered as a formulation alone or co-formulated with carriers.

Well established equipment from laboratory to production scale.
Large and Porous Particles

Large porous particles have been widely explored for inhalation use since it’s first reported by Edwards et al (Edwards, David A., Abdelaziz Ben-Jebria, and Robert Langer; J. Appl. Physiol. 84(2): 379–385, 1998)

The particles have a large geometric size but small aerodynamic particle size distribution due to their low density

The particles exhibit superior aerosolization performance and handling due to the particle morphology

The particles can be easily suspended in the propellant in the MDI formulation or delivered from DPI without formulation with carrier excipient

Phospholipid, one of the endogenous lung surfactant components, makes the particles “stealthy”, therefore avoids phagocytosis. Retention of the particles in the lungs provide as a good vehicle for sustained release of encapsulated drugs.
Supercritical Fluid (SCF)

Supercritical CO$_2$

SCF is a good solvent for the drug to be precipitated. The Rapid Expansion of Supercritical Solution (RESS), Gas Saturated Solutions (PGSS)

SCF as a poor solvent (Anti-solvent) for the drug to be precipitated; Additional good solvent is needed to introduce SCF into the drug solution to be processed.

Gas Anti-Solvent (GAS); Aerosol Solvent Extraction System (ASES); Supercritical Fluid Anti-Solvent (SAS); Precipitation with Compressed Anti-Solvent (PCA); Solution Enhanced Dispersion by Supercritical Fluid (SEDS).

Pure crystalline with no defects

Particle size well controlled

Suitable for both small and macromolecules
Particles Produced by Sonocrystallization – Prosonix Technology

Sonocrystallization is a technology of producing particles by controlling crystallization through cavitation and acoustic streaming using a high power ultrasound. (Reference: Graham Ruecroft et al, Organic Process Research & Development 2005, 9, 923-932)

Nucleation is induced by a high power ultrasonic probes and sonotrodes to produce uniformity nuclei so that drug crystallizes in a controlled and reproducible way

The technology allows control of crystal size distribution, crystal habit and produces consistent surface morphology

Uniform and smooth surface morphology is reported to improve physical stability of particles

The technology reports to minimize batch to batch variability
Pollen as a Drug Delivery Vehicle

Research was first reported by Alberto Diego-Taboada et al. at the University of Hull (Alberto Diego-Taboada and etc., Pollen: a Novel Encapsulation Vehicle for Drug Delivery; Innovation in Pharmaceutical Technology 24 2007)

Pollen and Spores which are male reproductive elements of flowers or non-flower plants consist of a double layer shell encapsulating grains. The internal shell is made of cellulose and the external shell consists of a nature polymer called sporopollenin. The polymer and sporoplasma can be removed to reserve the shell which becomes no longer allergic.

The pollen or spore shells can then be used a drug delivery vehicle to encapsulate drug particles.

The pollen or spore are mono-dispersed with different size ranges (2 to 250 µm).

Aspergillus Niger Spores were specifically mentioned for use in inhalation drug delivery
SEM images of pollens

**Lycopodium clavatum**

**Ambrosia trifida**

Acknowledgement to Sporomex Ltd for the permission of use of pollen images. © Copyright of this slide belongs to Sporomex Ltd.
Concluding Comments

- Inhalation drug delivery deals with delivery of small drug particles into the lung
- Formulation and process design should focus on ensuring an even and controllable distribution of drug particles (DPI, suspension MDI and Nebules)
- Formulation and process designs should focus on ensuring accurate and reproducible metering or dose delivery for the labeled number of doses throughout shelf-life
- A successful formulation relies on a combination factors including formulation composition, container closure system and delivery device
- Research efforts continue to focus improvements inhalation drug delivery through formulation science, e.g. drug particle engineering, new excipient, process technology, delivery devices, container closure systems, etc
more products. better treatments. reliably supplied.™

Catalent Pharma Solutions
14 Schoolhouse Road, Somerset NJ 08873 USA

(866) 720 3148  info@catalent.com  www.catalent.com