IPAC-RS
International Pharmaceutical Aerosol Consortium on Regulation & Science

NASAL INNOVATION FORUM

Commercializing Nasal Sprays: Overcoming Challenges in Manufacturing and Tech Transfer for Sterile and Non-Sterile products.

Key Factors for successful product launch

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Catalent

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Agenda

Product Fundamentals and Market Landscape

Preservative and Preservative Free

Technical Transfer Considerations

Commercialization Pathway

Real-World Challenges and Common Pitfalls

Launch Strategies and Looking into the Future.

Closing

Product Fundamentals and Market Landscape.

Introduction

History and Opportunity

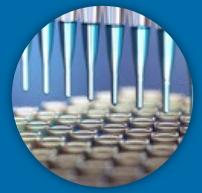
Early years: nasal delivery was mainly focused on administration at a **local level** to support treatments for **decongestion** and **rhinitis.**

Nasal Sprays are increasingly important in modern therapeutics, bridging local treatment and systemic opportunities via CNS, Pain management, and several other indications.

Technical Transfer and Commercialization

Tech transfer is high stakes: poor execution can mean *delays, lost market share, regulatory setbacks and in some instance program cancellation.*

Commercialization is not just “making at scale” – its ensuring safety , reproducibility, regulatory compliance and patient usability. While also managing associated costs.

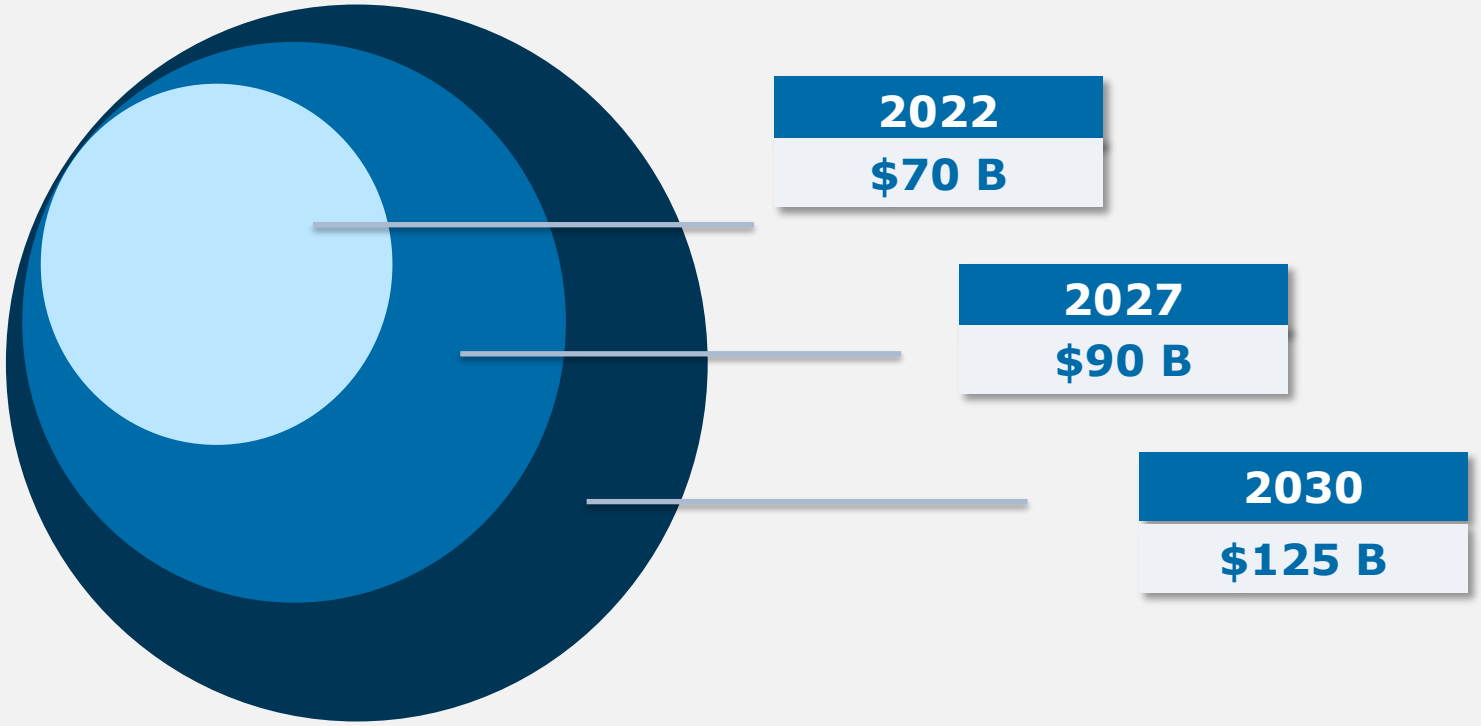


Product Innovation in Inhalation

Nasal sprays are evolving into critical delivery platforms for **vaccines**, **biologics, powders, and CNS therapies**, making commercialization strategies more important than ever.

Ref: Weers et al. Pulmonary Formulations: What Remains to be Done? 2010

Market Trends Driving Growth in Nasal Delivery

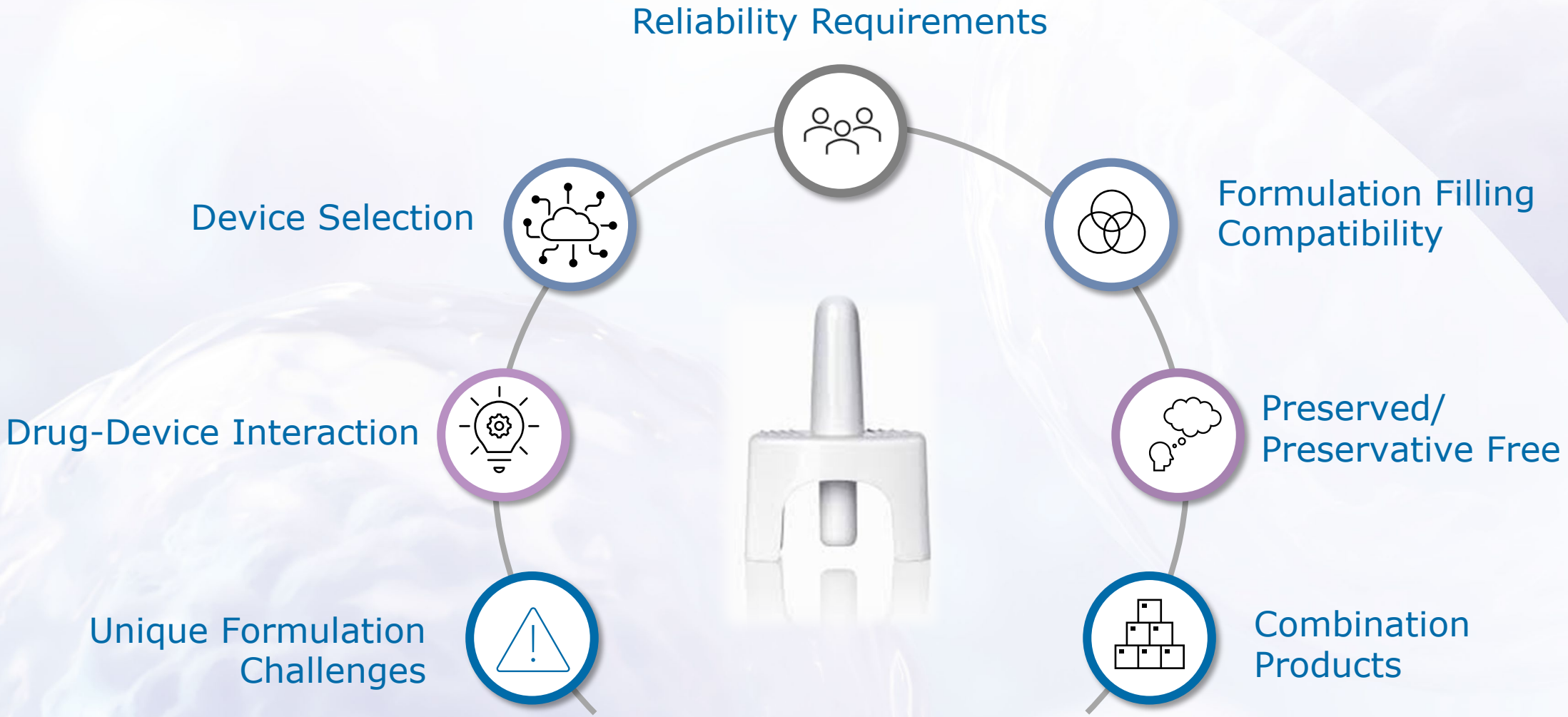


- Wide range of projections reveal underlying differences in methodology, regional focus, therapeutic scope, and technological assumptions
- Despite numerical differences, all reports indicate robust growth and innovation in the nasal drug delivery market, which can inform strategic directions rather than exact targets

Key Growth Drivers	
Largest Market / Highest Growth	United States
Largest Market Segment by Volume	Allergy
Highest Growth Rate by System	Unit Dose

- Innovations in nasal sprays **enhance drug absorption** and **patient compliance**, with **China expected to drive growth** alongside the U.S and Europe

Complexity of Nasal Sprays



Comparison: Preserved Nasal Sprays and Preserved-Free Nasal Sprays

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Preserved Nasal Sprays

Key Components

Device Selection

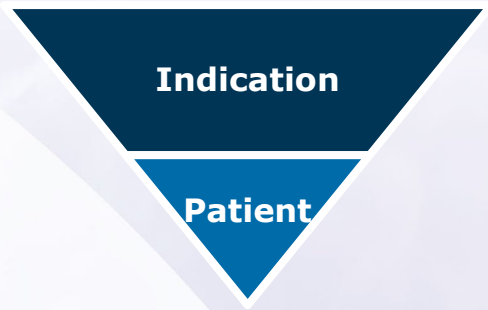
- Unit Dose/Multi-Dose
- Chronic/Acute
- Formulation Compatibility

Formulation

- Preservative selection that balances antimicrobial efficacy and potential irritation
- Consider approved agents in use.

Sponsor User:

- Preservatives with minimal irritation and toxicity.
- Preservative effectiveness over shelf-life for safe usage



Important Notes

Overuse or high concentrations of preservatives could potentially lead to nasal mucosal irritation.

Majority of launched products are still preserved.

Preservative sprays will generally have longer shelf life

Considerations

Packaging must maintain preservative integrity

Microbial Control measures (Sanitization)

Labeling must disclose preservative content

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Preserved Free Nasal Sprays

Key Components

Device Selection

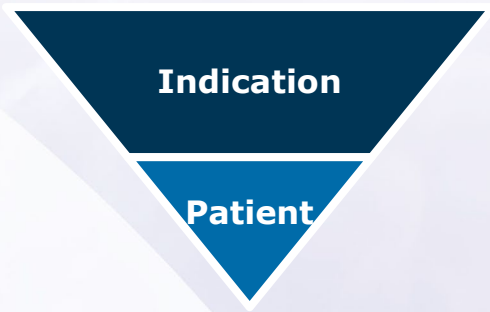
- Unit Dose/Multi-Dose
- Advanced Multi-Dose to maintain sterility

Formulation

- Formulated to maintain chemical and physical stability
- Device/Formulation compatibility

Sterility Assurance

- **Number of aseptic processes will require validation/challenge to support manufacturing (Filter Studies, Cleaning and Sterilization cycles and Autoclave)**
- **Media fills**
- **Sterile Component Receipt**
- **Aseptic material exchanges**



Important Notes

Preservative-free options align with patient safety trends and preservative regulations

On-going Quality assurance to maintain sterility

Emerging device technologies should eventually lead to more cost-effective options.

Considerations

Manufacturing complexities, Media Fills, aseptic handling.

Limited Manufacturing options

Formulation/Process controls

Evaluate terminal Sterilization

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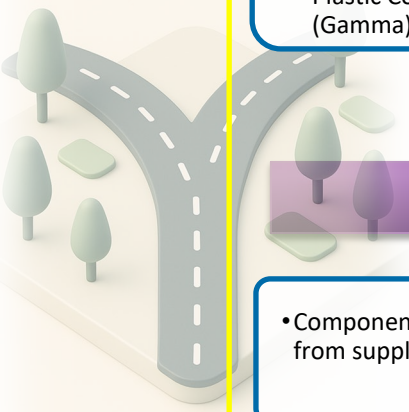
Sterile vs Non-Sterile at a Glance

Sterile

Device	Formulation	Filling	Assembly	Secondary	Testing
• Glass Components – washed/dehydrogenated • Stoppers – Pre-Sterilized or Sterilized on-site(autoclave) • Plastic Components – Sterilized (Gamma)	• Grade A/B • Grade A Personnel Gowning • Equipment preparations as per aseptic requirements. • Sterile Handling for formulation preparation followed by sterile filtration via 0.22µm Aseptic Cleaning Requirements		• Equivalent	• Equivalent labeling, text modification for sterile product.	• Analytical/Spray • Endotoxin • Sterility • MLT

Non-Sterile

Device	Formulation	Filling	Assembly	Secondary	Testing
• Components are ready to use from supplier.	• Grade C • Handled to Grade C conditions. • Equipment preparations per sanitization requirements. • Formulation typical filter via 0.22µm (Bioburden reduction) or 0.45µm (Clarifying)		• Equivalent	• Equivalent labeling,	• Analytical/Spray • MLT



What development path do you choose.

Preserved

- Single/Multi Dose Device
- Lower Cost and Simpler Manufacturing.
- Preservative compatibility and Efficacy
- Potential Safety concerns (Chronic Toxicity/Irritation)

Preservative Free

- Single/Multi Dose Device (Specialized)
- Higher risk of contamination depending on facility configuration (Open Environment, RABS, Isolator)
- Higher Cost and Complexity of Manufacture
- Microbial Control Strategy – Aseptic processing (or terminal sterilization).
- Sterility Assurance over shelf life
- Chronic use and Sensitive populations

•Preserved sprays are attractive for their **simplicity** and **lower cost**, but questions about long-term safety data remain.

•Preservative-free sprays align better with patient safety and perception, but they **require aseptic infrastructure, higher validation burden, and more expensive device solutions.**

•Each approach requires careful **risk–benefit evaluation** depending on indication and target market.

Technical Transfer

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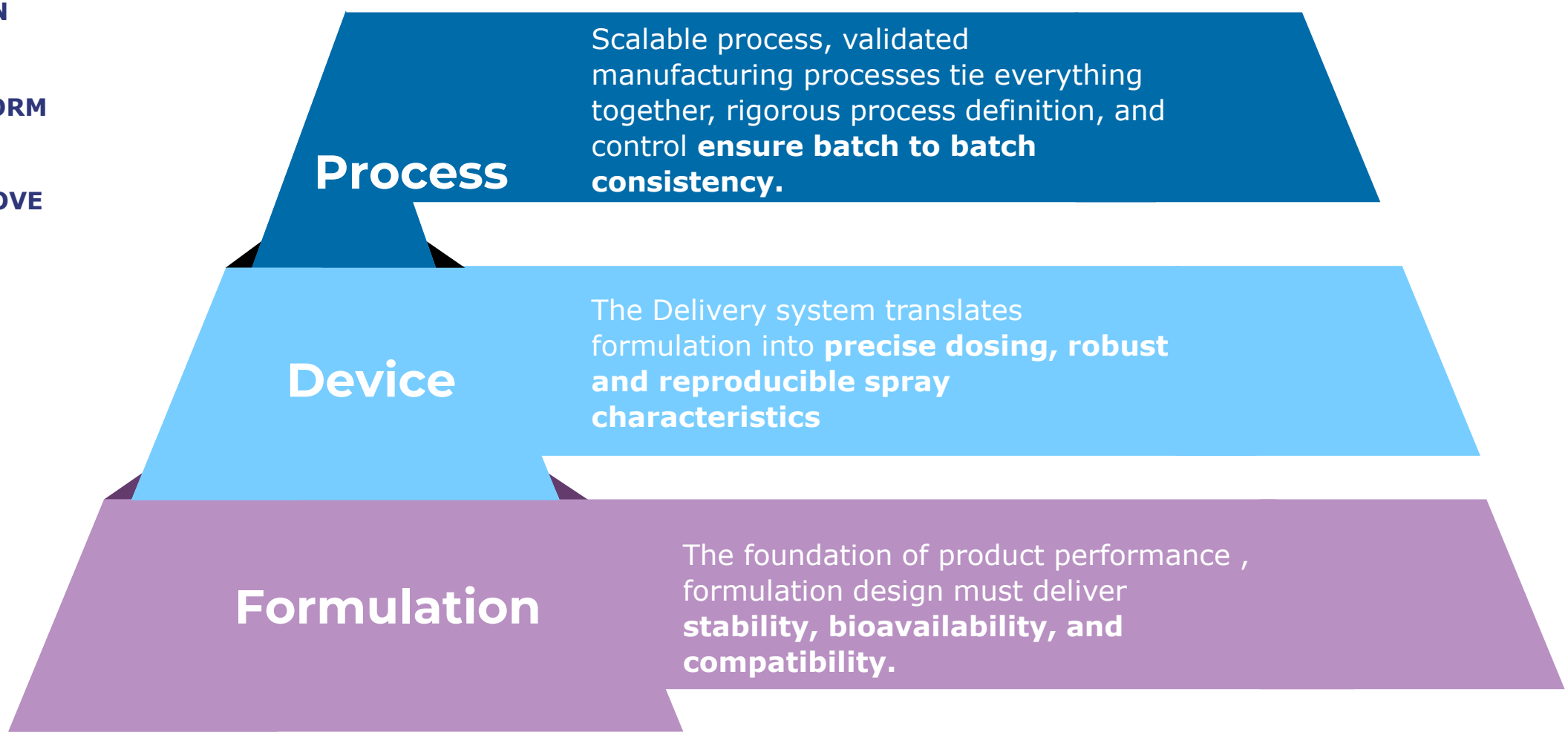
Key Technical Transfer Pillars

ALIGN

PERFORM

IMPROVE



Success requires all pillars to align

Core Elements of a Successful Tech Transfer

Cross Functional Alignment

Clear Ownership & Accountability

Transparent documentation & Metrics

Regulatory Alignment & Early Engagement

Catalent reviews each program across multiple factors to determine an **optimal tech transfer strategy** that is tailored to meet the specific needs of the project and our clients.

Risk Assessment and Mitigation Planning

Device-Formulation Compatibility Assessment

Critical Quality Attribute Definition and Controls

Scalable Submission Batches

Unique Tech Transfer Challenges

Common Pitfalls

- **Drug Device Integration**: Compatibility must be proven for materials, seals, elastomers, which can interact with formulation.
- **Preservative Free Products**: Contamination risk is high; facilities need stringent aseptic controls.
- **Scale-up mismatches**: Mixing and filling equipment at commercial scale behave differently than lab scale setups.
- **Regulatory Hurdles**: Combination product submissions are more demanding , requiring integrated risk profiles and device studies.
- **Supply Chain risks**: Continuity in supply.
- **Reliability:** Achieving 99.999% reliability

Key Notes

Formulation and Device must perform as a unified system. The Physicochemical properties of the formulation (viscosity, surface tension) with spray engineering.

Rigorous control of manufacturing and quality parameters. Precise control utilizing in most cases specialized equipment.

Commercialization Pathway

Commercialization Pathway

Formulation & Feasibility

- Formulation Development
- QbD
- Device Compatibility
- Method Development

Preclinical & Clinical Development

- Define critical process parameters
- Define Critical Quality Attributes

Transfer & Scale-Up

- Review Scale
- Engineering Runs
- Process Qualification
- Registration

Validation & Submission

- Execute PPQ
- Forecasting
- Documentation
- Training

Launch & Lifecycle Mgmt

- Launch
- Lifecycle Management
- Continuous Improvement

Cross-Functional Communication, Risk-based planning , documentation rigor, and proactive regulator engagement.

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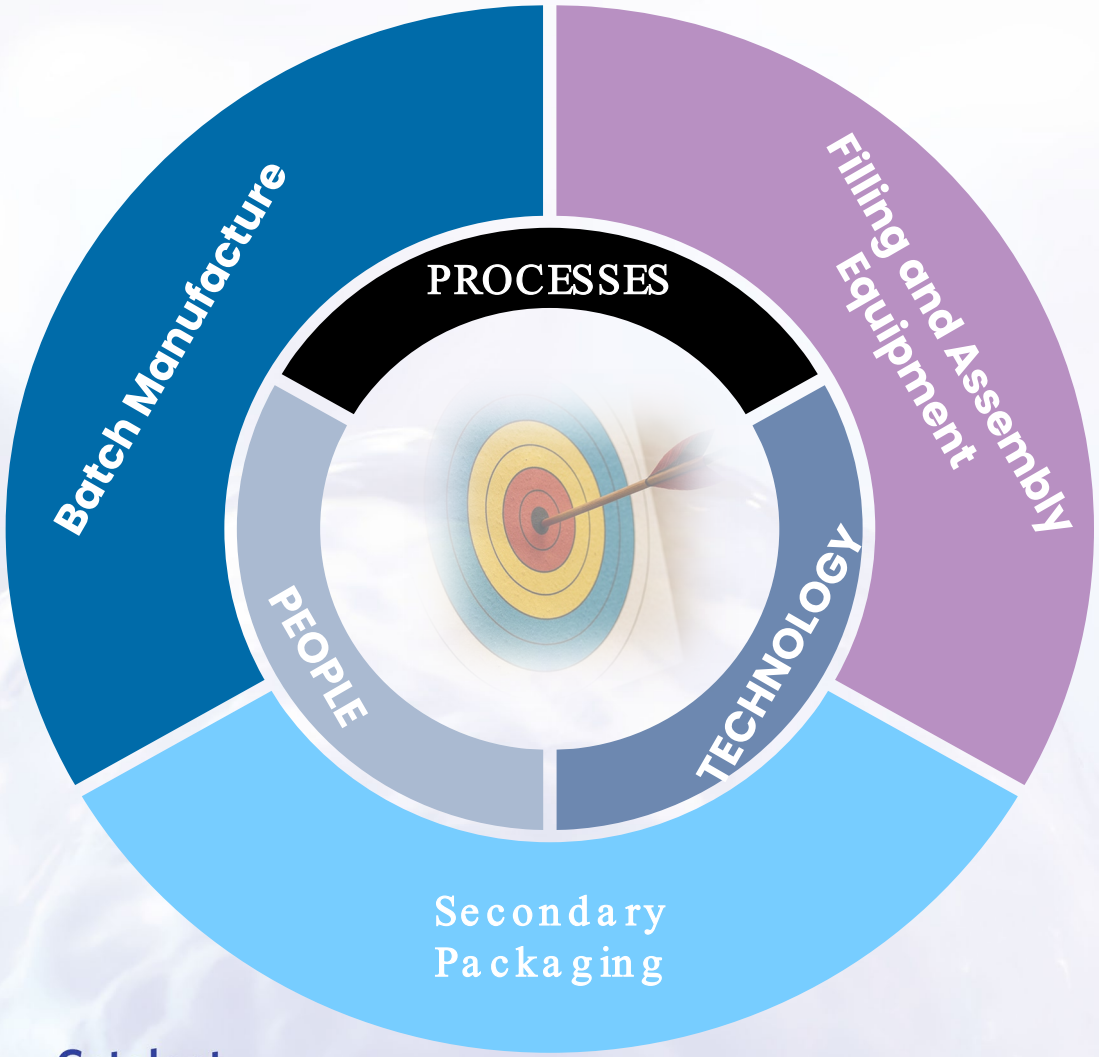
Key Elements to successful Commercial Manufacturing



Key Points

- **Batch Size planning**
- **Review equipment requirements to support forecast and beyond**
- **Secondary Packaging**
- **Supply Chain Continuity (where possible)**
- **Training, Training, Training**
- **Facility Preparedness / Engineering Runs**

Unique Manufacturing Challenges

What appears simple , is truly not

Viscosity

- Operating at the **outer limits** will not only cause **spray characterization issues** but also cause **filling issues**. Fill weight and dripping issues which can lead to stopper/vial integrity issues.

Device Labeling

- Ensure label studies are performed to **support placement**.
- **Adhesive/Device** stability studies should be executed to ensure label integrity is robust.

Automated Inspection

- Determine **acceptable inspection criteria** to allow for reliable filled units.
- Start validation **activities early**, build your reject library and challenge
- This is a process that requires **adequate lead time.**

Reliability

- **Critical** to ensure **proper controls and acceptance criteria for** fill weight, stopper placement and assembly.
- **Variability** in critical parameters will cause **reliability issues, deviations and OOS batches.**

Learn from others' mistakes, not your own

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Real-World Pitfalls

What appears simple , is truly not

CONTROL RISK

Late-Stage Device Incompatibility.

Requiring reformulation/re-execution.

ASSESS RISK

Facility Readiness Gaps.

Inadequate equipment and facility requirements leading to failed inspections

Documentation & Knowledge Transfer Gaps

Incomplete process parameters, poor training. Leading to loss of know how.

Deviating from the typical presentation.

Evaluate line capabilities

Allow for adequate time for evaluation and implementation.

REVIEW CONTROLS

IDENTIFY RISK

Launch Strategies and Looking Forward

Strategic Factors for Launch

Supply Chain Robustness

- Device Sourcing
- Raw Material
- Secondary Packaging
- Distribution channels

Scale-Up Readiness

- Capacity Planning
- Filling Technology Transfer
- Engineering Preparedness

Commercial Readiness

- Demand Forecasting
- Market Entry Strategies

Risk Mitigation

- Stability Readiness
- Regulatory Interactions
- Business Continuity

Successful Launches are an output of proactive and transparent communication

- **Preservative and Preservative Free trending**
- **AI Integration into Manufacturing**
- **Advanced Devices**
- **Nasal Powders**
- **Regulatory Update and Harmonization.**

Closing

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Conclusion: Navigating the Complexities of Nasal Spray Commercialization

Technical Challenges

Successful nasal spray commercialization depends on **overcoming formulation** and **delivery technology challenges.**

Regulatory Compliance

Meeting regulatory requirements is essential for market approval and ongoing product safety.

Manufacturing Excellence

Efficient production processes ensure consistent quality and supply of nasal spray products.

Strategic Collaboration

Teamwork and continuous learning drive innovation and successful market entry.

Commercializing nasal spray drugs requires mastering technical, regulatory, and manufacturing complexities through strategic planning, collaboration, and continuous learning to achieve market success.

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