



Green Chemistry for Inhaled Products – Issues and Opportunities

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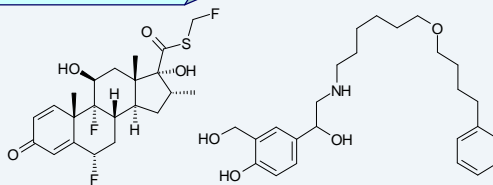
API Manufacturing

Routes developed and fixed by phase II

- Reluctance to introduce more developed routes or processes
 - Stick to tried and tested manufacturing processes that have FDA approval
- Nothing must affect API physical properties or particle characteristics

Respiratory Products are small volume products

- Significant investment in new technology is difficult
- Waste stream incineration is common
- Solvent recovery opportunities



fluticasone

salmeterol

Location of plants

- Primary and secondary manufacturing not co-located
- EU REACH regulations for processing materials and API intermediates

Outsourcing

- Influence over stages that are manufactured at 3rd parties
- Need robust EHS audit programme

Dry Powder Devices (DPI)

FORMULATION

- Micronised Drug
- LABA/ICS
- Excipients



COMPONENTS

- Blister Strip
- Mouthpiece
- Device actuator
- Counter

Pharmacologically active materials at **very low doses**

- Secondary manufacturing operations require **high containment** e.g. sieving, micronising, blending, filling
- API losses to **air extraction** systems
- **Robustness** of technology and process (including PAT)

Real Time Release

- Understand physical property parameters
- Develop methods to **measure and control** to avoid failed batches and off-line testing

Device Issues

- One use product and disposal
- Type of plastics used
- Life Cycle impacts
- Manufacturing rejects

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Metered Dose Inhalers (MDI)

COMPONENTS

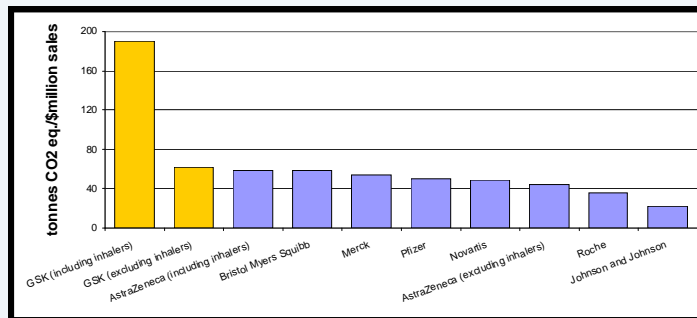
- Can
- Valve
- Device actuator



FORMULATION

- Micronised Drug
- LABA/ICS
- Propellant
- Surfactant

- Complexity in the API combinations
- Propellants and Climate Change
 - GSK historically used CFC's, currently use HFC's
- Manufacturing rejects



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