Environmentally Friendly Plasma Coated Pressurised Metered Dose Inhalers

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Background & Motivation

- Pressurised-metered dose inhalers (pMDIs) have been in medical use since the 1950s and have gone through many improvements and refining since their invention.
- pMDIs are comprised of an aluminum canister, metering chamber, valve, and an actuator.
- Inside the canister is where the pharmaceutical formulation is held and consists of drug(s), excipients and propellant (Fig 1 & 2).

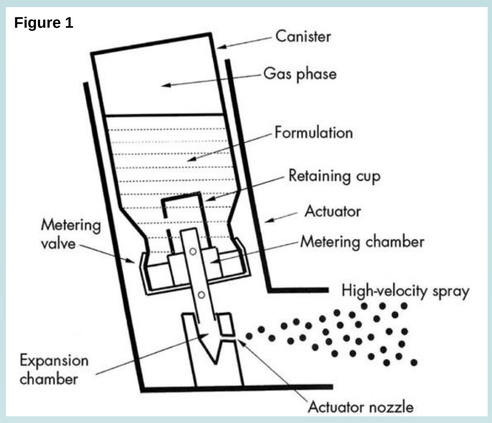


Figure 1


Figure 2

- After the Montreal Protocol in 1987 when CFC propellants were banned. Huge push for alternative inhaler designs
- Development of internal surface treatments to reduce drug-canister adhesion and improve inhaler performance with the new generation of HFA propellants.
- Presspart has developed a new method of applying FCP (fluorocarbon polymer) on canister surfaces (Fig 3 & 3.1)
- Shown to improve FPD (fine particle dose) of inhalers and increase their useable lifespan.
- New method reduces environmental impact of the surface treatment process

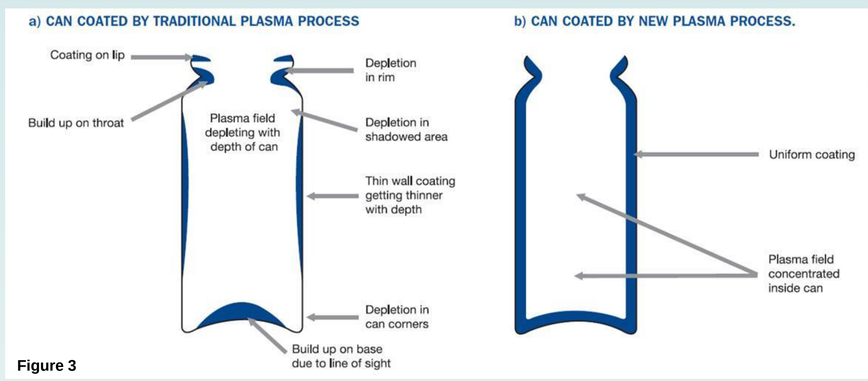


Figure 3

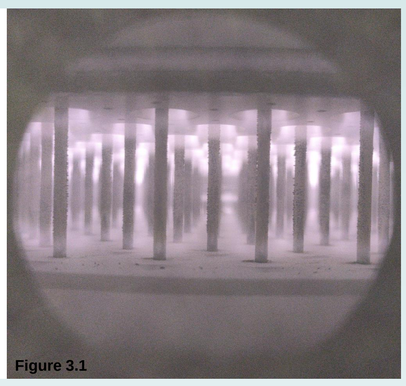


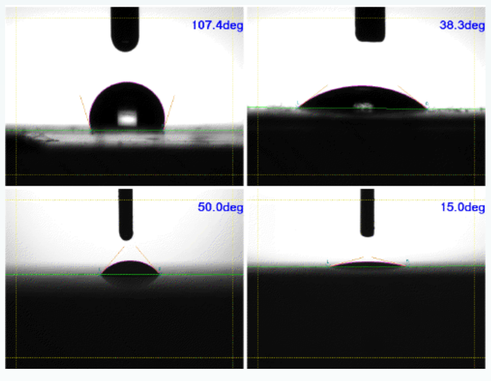
Figure 3.1

Objectives

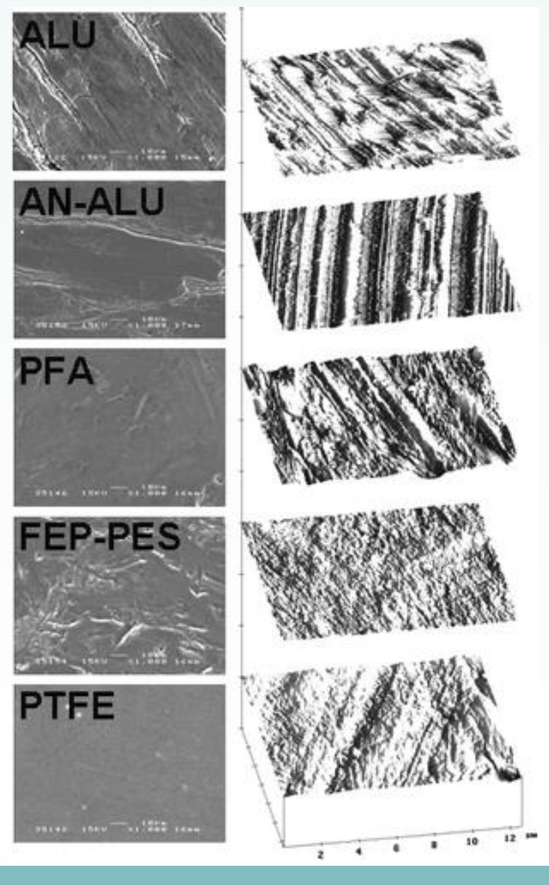
1. Analysis of surface properties
   1. Surface energy
   2. Surface roughness
   3. Coating thickness
   4. Coating uniformity
2. Analysis of surface interactions with different drug candidates
   1. Surface-Drug adhesion properties
3. Analysis of inhaler performance
   1. Delivered dose from full to empty
   2. Inhaler performance when stored in different conditions and durations
4. Data analysis

Phase 1: Surface Properties Analysis

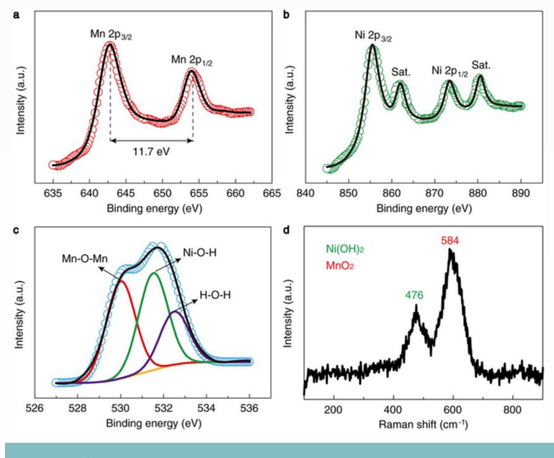
Contact Angle Measurement Using Water



SEM & AFM of Canister Surfaces



XPS & Ramen Spectroscopy Spectra



Phase 2: Surface-Drug Adhesion Measurement

AFM with single drug particle as the surface probe instead of the tip (Fig 8, A & B right)

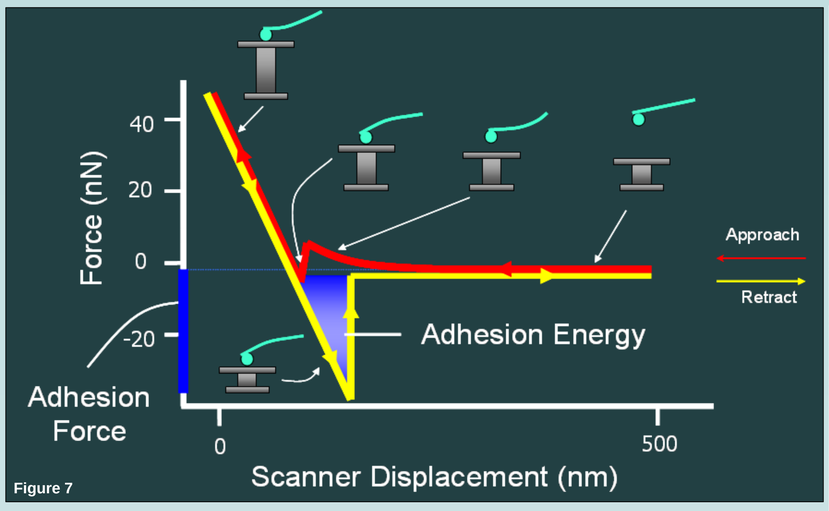


Figure 7

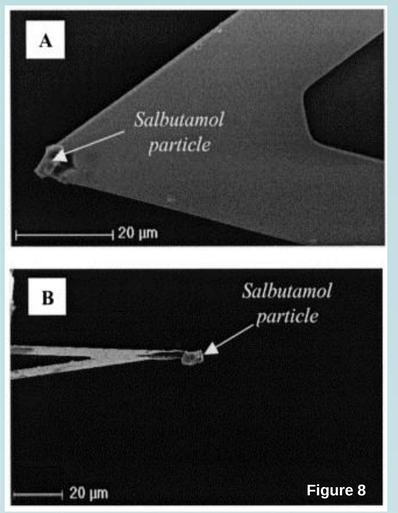


Figure 8

Typical force–distance curves obtained from the interaction of a salbutamol–functionalised tip Fig 7 above left and, 9b below .

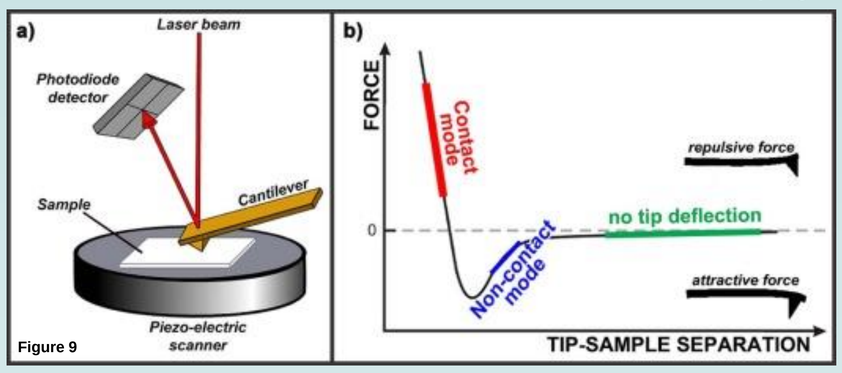


Figure 9

Phase 3: Inhaler Performance Analysis

Utilising Next Generation Impactor coupled with High performance Liquid Chromatography to measure inhaler performance of our test canisters.

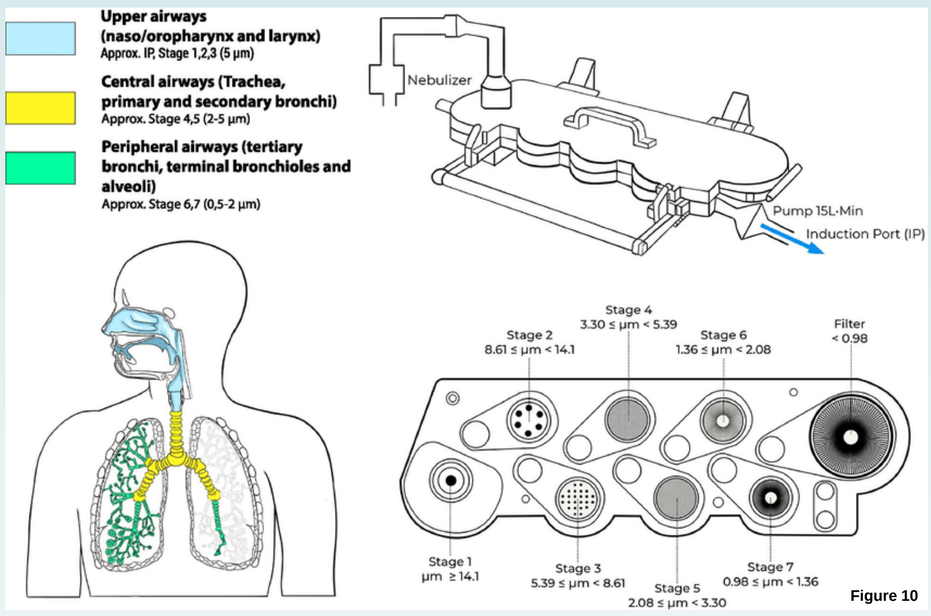


Figure 10

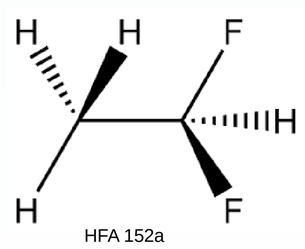
Next Generation Impactor set up and correspondence of the different stages to airway generations (Fig 10)

Responsible Innovation & Policy

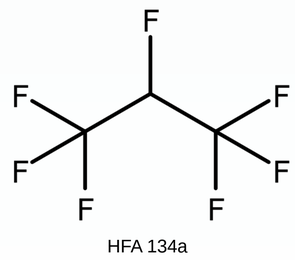
- Close collaboration with Presspart who can review any data before publication
- Limited data in field due in part to pharmaceutical industry desire to protect intellectual property.
- Presspart have agreed to allow research public and encourage peer review
- We have already seen policy changes in the past due to the environmental impacts of CFC propellants
- Feasible that there will be a policy change for canister coating processes to produce less environmental waste in the future.

Challenges

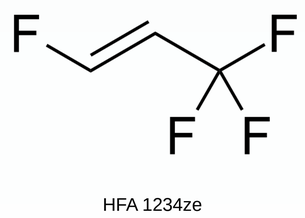
- Current generation of HFAs are in the process of being phased out and replaced with a new generation
- The current roster of candidates include HFA 152a, 134a and 1234ze
- To ensure that this research remains applicable to future inhalers it will require the experiments to use some of these new propellant types.
- No way of ascertaining which propellant the industry will begin to shift to out of the current candidates.
- With close contact with Presspart and pharmaceutical insiders, we can more confidently choose appropriate propellants for use while carrying out phase 1 which does not involve the use of propellant filled canisters.



HFA 152a



HFA 134a



HFA 1234ze

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