Development of HFA-152a as a sustainable pMDI propellant
Stuart Corr PhD. Koura, Thornton Science Park, Chester, CH2 4NU, UK

Summary
In looking to reduce the environmental impact of inhalation medicine delivery, one possible route is to develop a pressurised metered dose inhaler (pMDI) system that maintains all of the therapeutic advantages of the pMDI platform but which has a competitive carbon footprint to alternative technologies, particularly dry powder inhalers (DPI). To achieve this, a new low carbon footprint pMDI propellant will be required.

However, environmental sustainability is only one factor and developing a new pMDI propellant requires the candidate to satisfy a number of essential criteria including:
- Safety - at least as safe for extended inhalation use as the current propellants
- Functionality - effective for a range of solution and suspension pMDI drug formulations and ideally offer performance benefits over the current propellants or other technologies
- Economic - be of acceptable cost and be available at the appropriate scale and purity

P152a (1,1-difluoroethane) is under investigation in an extensive research and development program as a potential pMDI propellant and to date has shown an attractive combination of environmental and formulation performance properties[3].

LCA Study
The cradle-to-grave environmental impact of a HFA-152a pMDI was investigated according to ISO 14040/14044 methodology with the boundaries[8][9].

Life Cycle Analysis (LCA) was used to compare the environmental impacts, particularly the carbon footprint, of a pMDI system using that of the equivalent HFA-134a pMDI and with a representative Diskus®-type dry powder inhaler (DPI[2]). This LCA study shows that the carbon footprint of an HFA-152a pMDI is reduced by >90% compared to an analogous HFA-134a MDI and is essentially equivalent to that of the DPI device. Based on this data and further analyses[1], a transition to HFA-152a pMDIs has the potential to:
- Provide the greatest reduction in inhaler carbon footprint for the UK NHS
- Have the least adverse impact on patient inhaler use

Introduction
It is estimated that over 3 million people die from chronic obstructive pulmonary disease (COPD) each year with over 350 million people suffering from asthma[1] and both are identified as key health targets by the WHO. Pressurised metered dose inhalers (pMDIs) are a common drug delivery platform for treatment of asthma and COPD with an estimated 630 million pressurised pMDIs manufactured annually worldwide, not surprising since pMDIs are acknowledged as an almost universal and cost-effective platform for delivery of respiratory-related medical products.

For example[12],

References
2. Jenkinson, S., Crompton, E.: Avoiding the carbon footprint of national scale inhalers. Inhalation 2012
5. NICE Patient Decision Aid found at https://www.nice.org.uk/guidance/ng80/resources/inhalers-for-asthma-patient-decision-aid-pdf-6727144573
10. Available at: https://www.nhs.uk/conditions/asthma/copes/copes.pdf
11. © Koura 2019. All rights reserved. Not to be reproduced without the consent of the copyright owner. All other trademarks cited herein are the property of their respective owners.

Contact details
Dr Tim Keaikes - Technical Associate
+44 (0)1292 51 8813 /+44 (0)7739 65 7896
tim.keaikes@kouraglobal.com

Dr Stuart Corr - Techno-Commercial Director
+44 (0)1292 51 8811 /+44 (0)7712 01 0762
stuart.corr@kouraglobal.com

P152a GMP Development Timeline

Safety testing expected to be finalised in 2021 with the propellant Drug Master File to be in place by 2022. Propellants-only clinical trials are scheduled with GMP-grade propellant already available in limited quantities for development purposes enabling pharmaceutical companies to progress their research and development activities toward formulated product registration.

NHS Inhaler Footprint Mitigation

The NHS Long Term Plan[2] sets out the NHS’ commitments towards sustainability including a commitment to reducing carbon emissions and adoption of new innovations to reduce waste, water and carbon, in addition to reducing single-use plastics.

Inhaler Footprint Mitigation Options Summary
A pMDI transition to use P152a MDI transition provides:

- Lowest potential for NHS inhaler carbon footprint reduction
- Currently when the essential nature of pMDI is recognised (e.g. 90% per dose MDI scenario)
- Minimal disruption to patients[12]
- Minimal distress of exacerbations due to change in delivery platform
- Minimal patient retraining costs
- Minimal potential cost of treatment of exacerbations due to change in delivery platform

Inhaler Carbon Footprint Mitigation Options Summary

A pMDI transition to use P152a MDI transition provides:

- Greatest potential for NHS inhaler carbon footprint reduction
- Tactically when the essential nature of pMDI is recognised (e.g. 90% per dose MDI scenario)
- Minimal disruption to patients[12]
- Lower patient distress with respect to delivery platform
- Minimal distress of exacerbations due to change in delivery platform
- Minimal patient retraining costs
- Minimal potential cost of treatment of exacerbations due to change in delivery platform

Carbon Footprint (gCO2e/dose)

Scenario

A = Adopt reduced charge pMDI
B = pMDI transition to P152a, reduced charge, recycle
C = pMDI transition to P152a, reduced charge, no recycle
D = pMDI transition to DPI
E = pMDI transition to DPI, no recycle

Carbon footprint for the UK NHS Inhalers of all types account for around 4% of the NHS’ carbon footprint and are seen as one possible area where carbon footprint could be reduced. There are a range of potential inhaler footprint mitigation scenarios including:

- Replace all pMDIs with DPIs
- Replace pMDIs with lower propellant charge per dose
- Recover and recycle propellant from all MDIs
- Replace current propellants (HFA-134a/HFA-227ea) by P152a
- Carbon footprint data from the LCA study in conjunction with analysis of the NHS prescription database, can be used to estimate the potential impact of a range of scenarios on the NHS inhaler sector carbon footprint[10].