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 pressurises 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 - be 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

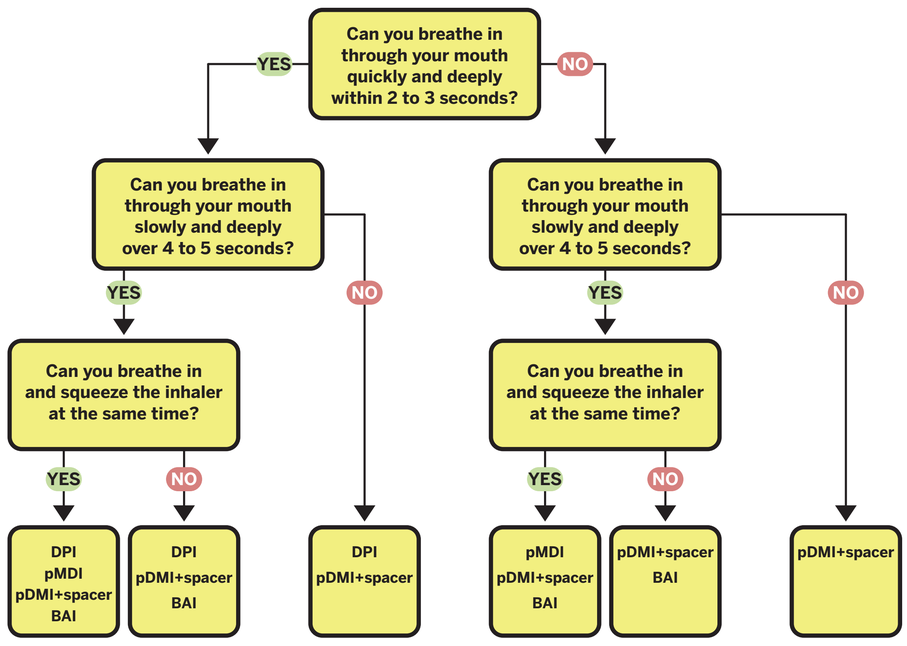
P152a (1,1-difluoroethane) is under investigation in an extensive research and development program as a potential pMDI propellant and to date has shown an attractive combination of environmental and formulation performance properties[1].

Life Cycle Analysis (LCA) was used to compare the environmental impacts, particularly the carbon footprint, of a pMDI system using with 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 analysis[3], 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

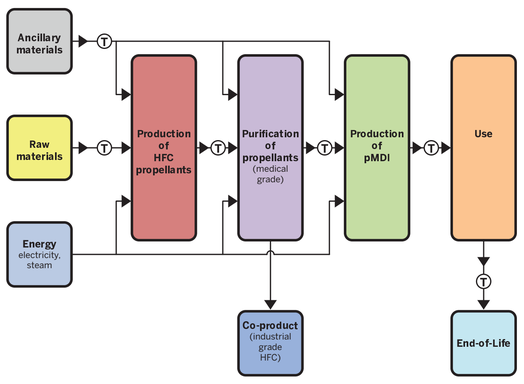
It is estimated that over 3 million people die from chronic obstructive pulmonary disease (COPD) each year with over 330 million people suffering from asthma[4] and both are identified as key health targets by the WHO. Pressurised metered dose inhalers (pMDIs) are a common drug delivery platform for treatment of asthma and COPD with an estimated 630 million pressurised pMDIs manufactured annually worldwide, not surprising since pMDIs are acknowledged as an almost most universal and cost-effective platform for delivery of respiratory-related medical products.
For example[5]:



DPI = Dry Powder Inhaler MDI = Metered Dose Inhaler BAI = Breath Actuated Inhaler (MDI)

LCA Study

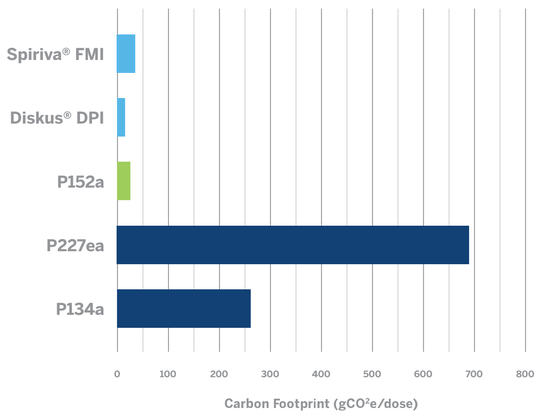
The cradle-to grave environmental impact of a HFA-152a pMDI was investigated according to ISO 14040/14044 methodology with the boundaries [2],[3]:



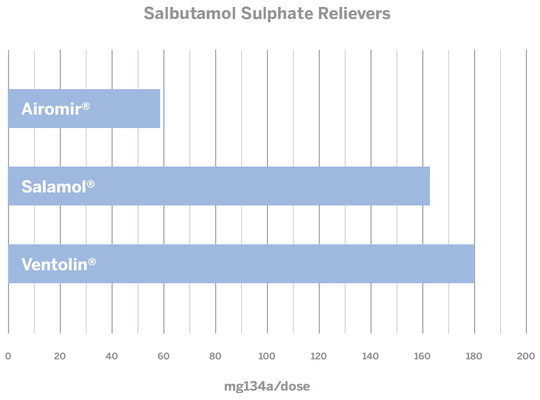
Whilst carbon footprint is regarded as the most significant environmental impact, the comprehensive LCA study also examined a range of other potential impacts including fossil depletion and marine eutrophication with P152a performing well across the range establishing its sound environmental sustainability credentials[3].

Results

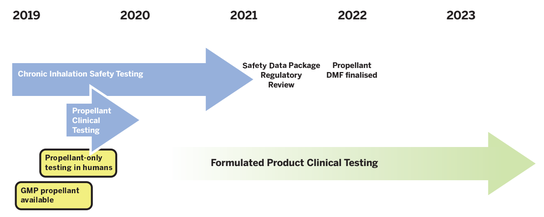
Comparing the carbon footprints of equivalent 100-dose (200 actuation) pMDIs with alternative propellant-free delivery platforms shows P152a to have a >90% reduction in carbon footprint compared to P134a:



Whilst P152a (20gCO2e/dose) is higher than that of the particular DPI examined here (Diskus® at 9gCO2e/dose), the P152a result is clearly within the 8g-60gCO2e/dose range that has been published for the variety of DPI devices by UNEP[6]. Given the variations between device designs and charge sizes across the platforms, the P152a pMDI carbon footprint is equivalent to the DPI and Spiriva® [7] FMI platforms.



P152a GMP Development Timeline



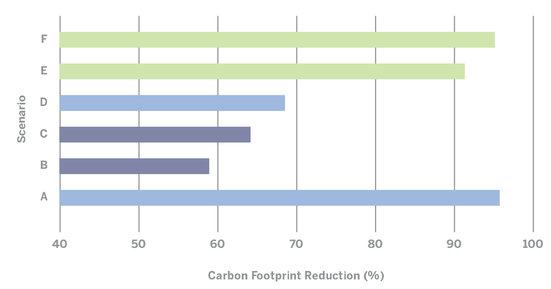
Safety testing expected to be finalised in 2021 with the propellant Drug Master File in place by 2022. Propellant-only clinical trials are scheduled with GMP-grade propellant already available in limited quantities for development purposes enabling pharmaceutical companies to progress their research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

NHS Inhaler Footprint Mitigation

The NHS Long Term Plan[8] 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.
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 number of potential inhaler footprint mitigation scenarios including:

- Replace all pMDIs with DPIs
- Prescribe pMDIs with lower propellant charge per dose
- Recover and recycle propellants at end-of-life
- Replace current propellants (P134a/P227ea) by P152a

Carbon footprint data from the LCA study, in conjunction with an 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[3].



F = pMDI transition to P152a, reduced charge, recycle
E = pMDI transition to P152a
D = Replace most current pMDI by DPI (70:30 DPI:pMDI)
C = Replace P227ea by P134a, reduced charge, recycle
B = Adopt reduced charge pMDI
A = Replace all current pMDI by DPI

Inhaler Carbon Footprint Mitigation Options Summary

A pMDI transition to use P152a MDI transition provides:

- Greatest potential for NHS inhaler carbon footprint reduction
- Especially when the essential nature of pMDI is recognised (eg 70:30 DPI:pMDI scenario)
- Minimised disruption to patients[9],[10]
- Retain patient choice with respect to delivery platform
- Minimised distress of exacerbations due to change in delivery platform
- Minimised patient retraining costs
- Minimised potential cost of treatment of exacerbations due to change in delivery platform

References

1. Noakes, T., Corr, S.: *The future of Propellants for pMDIs*; Drug Delivery to the Lungs 27; The Aerosol Society, Bristol, UK, pp. 61-64, 2016
2. Jeswani H. K., Corr S., Azapagic A. : *Reducing carbon footprint of metered dose inhalers,* ; Inhalation; December 2017.
3. Jeswani H. K., Azapagic A. : *Environmental impacts of Inhalers in the UK*; J Cleaner Production; 237(2019) 117733.
4. World Health Organisation The Global Impact of Respiratory Disease (2nd Edition) 2017 found at https://www.who.int/gard/publications/The_Global_Impact_of_Respiratory_Disease.pdf
5. NICE Patient Decision Aid found at https://www.nice.org.uk/guidance/ng80/resources/inhalers-for-asthma-patient-decision-aid-pdf-6727144573
6. UNEP: *Report of the Medical Technical Options Committee (MTOC) 2014 assessment report*; UNEP Ozone Secretariat; United Nations Environment Programme.
7. Spiriva® data from Hansel M., Bambach T., Wachtel H., 'A comparison of Product Carbon Footprints of Respimat® versus Pressurized Metered Dose Inhalers', Respiratory Drug Delivery 2018, 321
8. Available at https://www.sduhealth.org.uk/about-us/what-we-do/nhs-ltp.aspx
9. Usmani O.S., Scullion J., Keeley D.; *Our planet or our patients - is the sky the limit for inhaler choice?*.; The Lancet; 7(1): pp11-13, 2019
10. Bjermer L.: *The Importance of Continuity in Inhaler Device Choice for Asthma and Chronic Obstructive Pulmonary Disease*, Respiration Vol 88, 2014

Contact details

Dr Tim Noakes - Technical Associate
+44 (0)1928 51 8889 / +44 (0)7739 65 7896

tim.noakes@kouraglobal.com

Dr Stuart Corr - Techno-Commercial Director
+44 (0)1928 51 8811 / +44 (0)7712 01 0762

stuart.corr@kouraglobal.com

Koura

kouraglobal.com