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A Multi-Stakeholder Approach to Minimizing the Environmental Impact of Inhaled Therapies and Improving Patient Care

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SUMMARY

It is recognized that healthcare makes a significant contribution to the overall global carbon footprint. Energy, transportation, supply chain, estates, usage and disposal of medicines all have climate impact. Inhaled medicines form part of this contribution and in this context, the need to improve patient care whilst, in parallel, minimize the environmental impact of inhaled therapies is clear. In particular, the environmental impact of the propellants used in pressurized metered dose inhalers (pMDIs) continues to be a particular focus for global and regional legislation and in national healthcare guidelines, policy, or recommendations.

Healthcare interventions and improvements that positively interact with the patient are the most effective, so a multi-stakeholder approach to minimizing the environmental impact of inhaled therapies, in parallel with improving patient care, is recommended. Engaging patients, healthcare providers, health authorities, environmental agencies and administrative bodies is considered the best approach to balancing patient needs and environmental issues. A case study in the United Kingdom (UK) exemplifying this approach is provided.

INTRODUCTION

Respiratory diseases including asthma and chronic obstructive pulmonary disease (COPD) are amongst the leading causes of death and disability globally [1]. In 2011, costs associated with respiratory disease in the European Union (EU) were estimated to be approximately €380 billion [2]. Inhaled treatments using devices such as pMDIs, dry powder inhalers (DPIs), soft mist inhalers (SMIs) and nebulizers are used across the world as the mainstay of treatment for patients with respiratory conditions.

The climate impact of global warming is an immediate and ever-present issue and it is recognized that healthcare is a major contributor to the global carbon footprint. Globally, this has been calculated to be equivalent to 4.4% of net emissions in 2014 [3]. While more than half of these emissions are from energy use, medicines also contribute. Medical inhalers, particularly pMDIs, have become a particular focus due to the environmental impact of the propellants. For all inhaler types, there is an impact on the environment to consider at each stage of the inhaler lifecycle, from manufacturing, supply, usage by the patient and appropriate disposal when the labelled number of doses have been taken or the inhaler is no longer needed.

Members of the International Pharmaceutical Aerosol Consortium (IPAC) believe that the most effective approach to the global environmental challenge surrounding inhalers is for healthcare systems to adopt a holistic, patient outcome-based approach [4]. This approach would aim to reduce the carbon footprint of patients using inhaled treatments, while simultaneously supporting improvements in patient care together with reducing the environmental impact of medical treatments at all stages of the life cycle. IPAC's mission is to ensure that environmental policies relevant to inhaled therapies are patient-centric and appropriately balance both patient care and sustainability objectives. IPAC members remain committed to the development of innovative treatment solutions that have both near-term and longer-term lower environmental impact.

THE EVOLVING GLOBAL LEGISLATIVE AND REGULATORY LANDSCAPE

Figure 1 summarizes key legislation for the phaseout of ozone-depleting substances and phase-down of hydrofluorocarbons (HFCs). Originally, chlorofluorocarbon (CFC) propellants were used in pMDIs but these were phased out under the Montreal Protocol, due to their ozone depleting behavior and very high global warming potential (GWP, approximately 10,800 for CFC 12). An 'essential use' designation was assigned for the medical use of CFCs, which allowed time for suitable alternatives to be developed. Following confirmation of the suitability for human use and formulation, development of two HFC propellants (HFC-134a and HFC-227ea), pMDIs containing these propellants were developed to ensure treatment continuity. (It should be noted that HFCs as medical propellants are also sometimes referred to as hydrofluoroalkanes (HFAs); these can be used interchangeably and for consistency HFC is used in this paper.) Globally, transition away from CFC use in pMDIs was completed in 2016. However, whilst protecting the ozone layer, HFC 134a and HFC-227ea still possess a high GWP (1300 and 3350, respectively) leading to their inclusion in the global phasedown schedules described in the Kigali amendment to the Montreal Protocol 2016 [5]. These schedules have been put in place to encourage the use of low GWP alternatives and to reduce consumption and emissions of high GWP HFCs. Phase down of HFCs has been embodied in law by specific countries and regions, for example the Fluorinated Gas (F-Gas) Regulation in the European Union (EU) [6], which is currently under review, and more recently the American Innovation and Manufacturing Act (AIM) [7], both of which currently include exemptions or mandatory allocations for medical use.

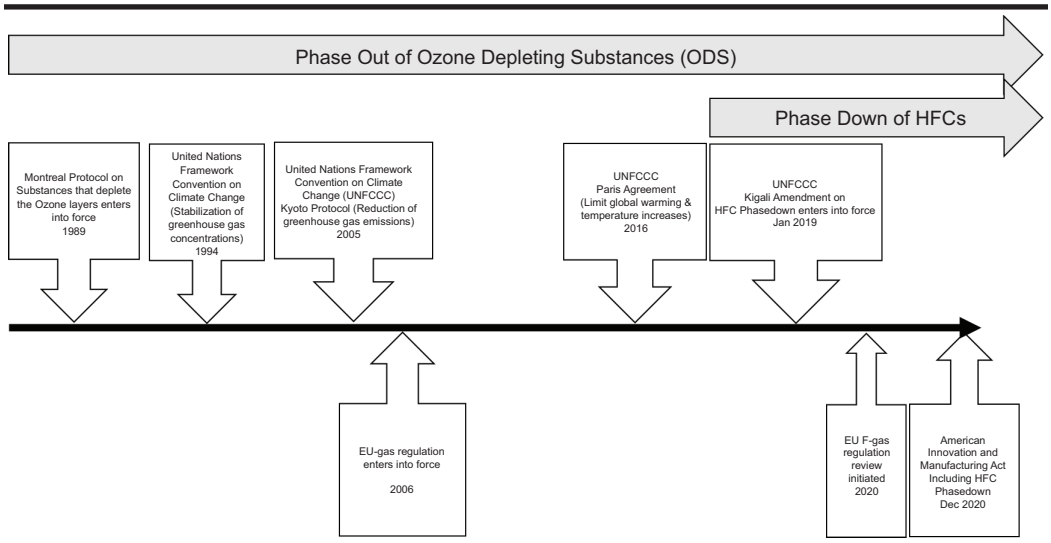

Figure 1. Key legislation and accords for the phaseout of ozone-depleting substances and phasedown of HFCs.

BALANCING PATIENT NEEDS AND ENVIRONMENTAL ISSUES

The detrimental effects of HFCs as greenhouse gases on the environment are well recognized, with many international governments setting strategies for action. Whilst ambitious targets and resourced initiatives relating to reducing the environmental impacts of pMDIs are important, our first priority should be the care and wellbeing of patients with respiratory conditions. Decisions to change a patient's device should not be made solely on carbon emissions and should be balanced with the setting of ambitious carbon reduction targets. Environmental policies are likely to be successful when they undertake a patient-centric approach to reducing carbon impact across respiratory treatment and care pathways.

Choice of inhaled treatment is based on a complex set of factors including the individual patient's needs and clinical condition, side effect profiles of the respiratory medicine, frequency of dosing and sustained efforts to prevent deterioration in care [8]. The focus of attention in carbon reduction policy, solely on inhaler selection, will not only limit the success of carbon reduction initiatives, but also risk unintended clinical consequences for patients whose treatment is highly dependent on stability and continuity with their existing inhaler therapy. All inhalation devices play an important role in patient care and are used in a broad range of patient populations from children to the elderly and across different respiratory diseases and severity of disease states. Studies demonstrate that where patients are involved with the choice of their inhaler, better clinical outcomes follow [9]. Therefore, IPAC believes it is critical for all stakeholders within government (environmental and health), clinical providers, patients and pharmacists to collaborate, with the shared understanding that, 'optimising disease control is essential to minimising the environmental impact of respiratory healthcare'. The Primary Care Respiratory Society (PCRS) describe this collaboration in their published White Paper and Call to Action 'Greener respiratory healthcare that is kinder to the environment' [10].

In response to environmental challenges and the need to sustain a range of delivery options to patients, the inhalation industry and its supply chain partners have invested, and continue to invest, significant resources to innovate new medicines and inhaled delivery systems (such as HFC pMDIs, DPIs, and SMIs), to meet different therapeutic needs. More recently, this work has expanded to lower carbon pMDIs with low global warming potential propellants. Efforts to innovate lower carbon impact therapies continue at pace, with both near-term and longer-term developments providing further solutions to the environmental challenges, whilst maintaining choice for patients and their individual clinical needs.

CONSIDERATIONS FOR MAINTAINING DISEASE CONTROL

Well-managed treatment, appropriate prescribing and device selection, together with ensuring the patient understands their own condition and can use their device effectively, can all potentially help to improve patient outcomes through better control [11]. A patient with deteriorating disease control will likely use more of their pMDI reliever therapy and potentially require additional visits to healthcare services [12].

Adopting a patient-centric approach, policies should take into consideration all the touchpoints for potential action to reduce the environmental burden along the patient journey. At the start of the patient journey, delayed or inaccurate diagnosis has the potential to increase the number of repeat visits to primary care and, potentially, hospital admissions as patients continue to struggle to cope with ongoing or deteriorating respiratory symptoms. Similarly, poor disease control from sub-optimal treatment, inappropriate device choice, over reliance on short-acting beta-agonist (SABA) therapy (sometimes referred to as 'reliever therapy') or poor adherence to treatment also has the potential to increase the number of repeat primary care visits and emergency hospital visits due to acute exacerbations of their condition, with the resulting increased environmental impact. A recent review of the use of SABAs across Europe and particularly in the UK, has shown that implementing guidelines to drive improvements in asthma care, with a focus on reducing the use of SABA, would improve asthma control, thereby reducing the greenhouse gas emissions associated with high reliever medication use and exacerbation frequency, benefitting patients and reducing carbon savings that go beyond the reduction in SABA use alone [13].

In an optimal patient-centric approach, healthcare providers, including pharmacists, should support patients with inhaler device choice, educate patients on their prescribed treatments' aims, and encourage adherence to prescribed maintenance treatment and correct use of devices. This approach should support good control, reducing reliance on reliever medications, many of which are high global warming potential propellant-based pMDIs, whilst empowering patients to seek healthcare advice if demand for their reliever medication increase. Selecting the medicine, device(s), and regimen that is most clinically appropriate for the patient – consistent with existing evidence-based treatment guidelines, as a shared decision between patient and clinician – is the first priority. It is also critical to ensure correct device technique to optimize drug delivery, which combined with discussion, education and understanding by the patient should promote adherence with the prescribed treatment regimen. Treatment decisions are best made by the patient and doctor together in line with clinical evidence. Undoubtedly, patients care about the environment and part of the shared decision-making should include a discussion on environmental implications of inhaler therapy with the appropriate context.

PHARMACEUTICAL INNOVATION IN INHALED THERAPY

The parallel need to balance patient care with environmental sustainability will continue to drive existing and ongoing innovation. The environmental impact of current medical propellants is clear, but this is a short- to medium-term issue, that can be addressed if innovation is adequately supported, without impacting patient health. As such, any steps to reduce the carbon impact should be proportional and appropriate. The transition away from CFC pMDIs contributed to successful innovation in DPIs, SMIs and HFC pMDIs and has also delivered other patient benefits (e.g., dose counters, combination therapies, and refillable containers). Effective maintenance therapies, delivered via DPIs and SMIs and combination pMDIs over the last decade has also limited the growth of HFC emissions by reducing the consumption of propellant-containing reliever inhalers. Manufacturers of inhaled products continue to invest in new technologies, including next generation propellants, which will support the development of pMDIs with a carbon footprint comparable with DPIs [14]. Integrating the next generation propellants into the development and commercialization of new inhalers, designed to optimize sustainability and minimize environmental impact, requires a multidisciplinary approach across pharmaceutics, engineering, polymer science, physical, chemical and biological sciences. Development of a pMDI using a next generation propellant must meet all of the extensive safety, clinical and quality requirements for medical combination products. A typical development pathway for a new pMDI, utilizing a low GWP propellant, will contain several stages and tollgates; see Figure 2.

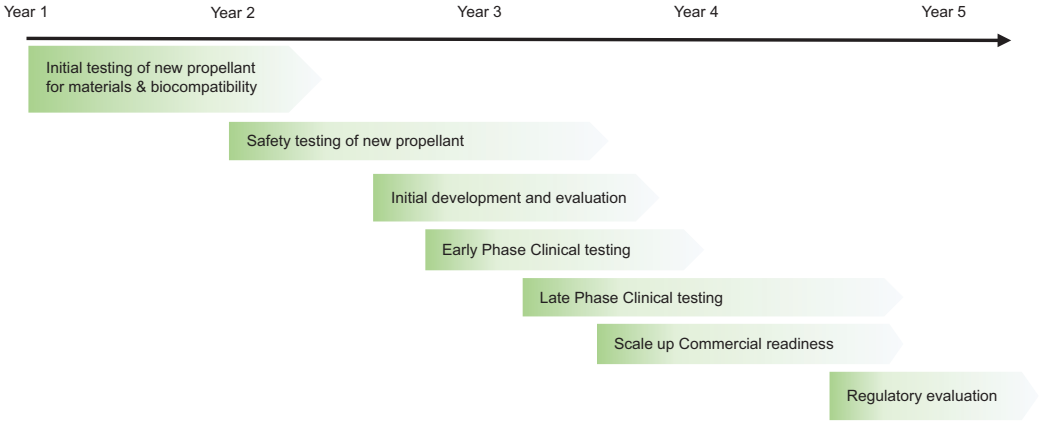

Figure 2. Illustrative development process for a low GWP pMDI.

Health regulatory authorities have an important role to play to ensure that review is timely. It is also important to undertake efforts, in collaboration with national health systems, to encourage uptake of new respiratory therapies using both existing and future innovative, environmentally friendly products. Integration of currently available existing inhalers delivery platforms with digital health applications is also driving innovation and a more holistic approach to respiratory healthcare. Smart inhalers promise to drive greater usability, adherence and compliance, whether in pMDIs, DPIs or SMIs [15].

DEVELOPING A MULTI-STAKEHOLDER APPROACH TO INHALER RETURN

The recovery of inhalers that are no longer needed by patients for environmentally suitable disposal is recognized as an important factor in the overall reduction of the carbon footprint associated with inhaled therapy treatment. Translating this requirement into a feasible proposition that can combine an intervention at an appropriate point in the patient journey, requires a multi-stakeholder, phased approach (Figure 3). This approach allows stakeholders to co-create and shape a model that can support patients to understand their inhaler usage and improve treatment outcomes, whilst encouraging return of inhalers when they are no longer usable (including expired treatments, all labelled doses used, or because of treatment changes). The model needs to be practical and scalable to deliver the expected benefits of improving patient care and reducing the overall carbon footprint of the patient and inhaler journey.

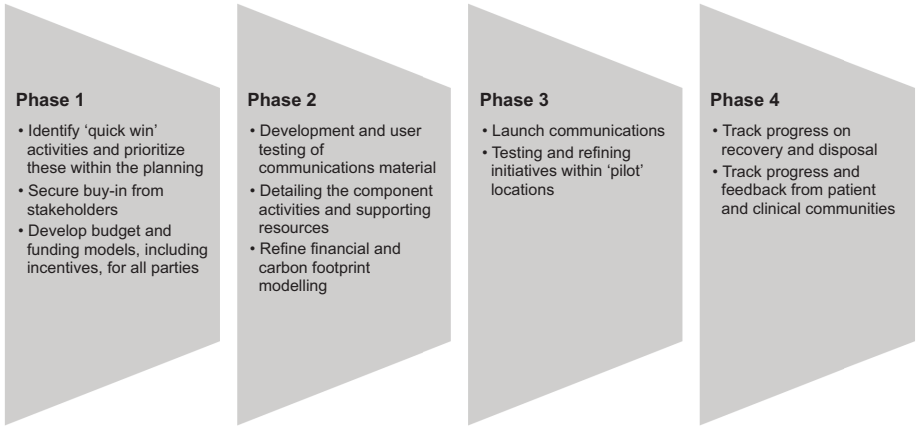

Figure 3. A multi-stakeholder approach to inhaler return.

APPLYING THE APPROACH – A UNITED KINGDOM PILOT STUDY

The UK Government continues to review progress on reducing F-Gas emissions. In April 2018, the UK Parliament Environmental Audit Committee (EAC) published a report highlighting the level of emissions from inhalers and concern over the number of inhalers that are disposed of in domestic waste and consequently finding their way to landfill sites, with only a small proportion of dispensed inhalers being disposed of through recycling or environmentally appropriate routes [16]. The report recommended that the UK Government should work with medical professionals, pharmacists, the pharmaceutical industry and patients to move towards a lower carbon impact for inhaled therapies including diversion of inhaler waste from the domestic system to more environmentally sustainable solutions.

The National Health Service (NHS) Long Term Plan (LTP) [17] and the report published by the Taskforce for Lung Health [18] highlight the need for patients, supported by pharmacists, to choose the best inhaler for their treatment and to have regular reviews to support adherence. The NHS LTP acknowledges the need for patients to be supported to ensure the correct use of inhalers and reduce the use of short-acting bronchodilator inhalers (which currently represent approximately 60% of prescribed pMDIs in the UK). Interventions to support patients with their

inhalers should be linked to supporting efforts to reduce the environmental impact of inhalers at various stages of the patient journey. The NHS LTP also sets clear carbon reduction targets linked to the use of lower carbon inhalers. It references that pharmacists will support patients to reduce the use of short-acting bronchodilator inhalers and incentivize the use of DPIs where clinically appropriate.

IPAC proposes that there are four discrete touchpoints, described below, across the journey, for every patient using inhaler treatments in the UK, with pharmacists (either practice- or community-based) and physicians being at the interface of all points:

- Supporting the selection of the most appropriate drug and device.
- Optimizing the use of the device.
- Ongoing supply.
- Waste disposal.

The multi-stakeholder approach requires all participants involved in the manufacture, prescribing, commissioning, supply, dispensing and waste collection of inhalers to work together to shape a new approach to the challenge and to co-create a comprehensive program. Using the identified touchpoints, the approach can be operationalized further into a framework which centers on establishing a patient engagement and support program combining medicines optimization and waste management communications. The interventions should encourage patients to take active steps, supported by practice-based and community pharmacists, to contribute to helping reduce the impact of inhalers. The framework is structured around four components:

- **Patient-focused education, choice and support**
  Healthcare providers and pharmacists should support patients with inhaler device choice, educate patients on their prescribed treatment aims, and encourage adherence to prescribed maintenance treatment to ensure good control and thereby reduce reliance on reliever medications and to seek healthcare advice should demand for their reliever medication increase. In some instances (e.g., online purchases), solutions such as interactive messages may need to be deployed. Published inhaler choice guidelines should be followed (see for example [19]).

- **Repeat inhaler management**
  Prescription guidance for pharmacies and patients should ensure that ongoing supply is appropriate for the patient's needs. This is an opportunity for discussions with the patient on their use of reliever inhalers and, where appropriate, referrals for support.

- **Returned medicine audit and review**
  An initial assessment can be undertaken at the pharmacy with a review of returned waste inhalers to identify adherence issues, help tackle over-prescribing and/or reliever over-reliance. Where appropriate, patients should be referred for support. Longer-term audits should be undertaken at the waste collection point with a waste analysis reporting function built into the disposal/recovery contract.

- **Waste communication and management**
  Provision of information to patients and the public of inhaler disposal options and locations in order to facilitate environmentally appropriate disposal.

By combining all four components, and associated activities, and integrating them into existing community pharmacy and primary care services, the efforts to reduce the environmental impacts across the patient and inhaler journey have the potential to achieve a greater benefit for treatment and environmental outcomes than each component in isolation (see Figure 4).

Although discussions relating to the implementation of the overall framework have been delayed due to the coronavirus pandemic, IPAC has continued to move forward with one component of the framework, supporting patients to understand how best to dispose of their inhalers via an inhaler return campaign.

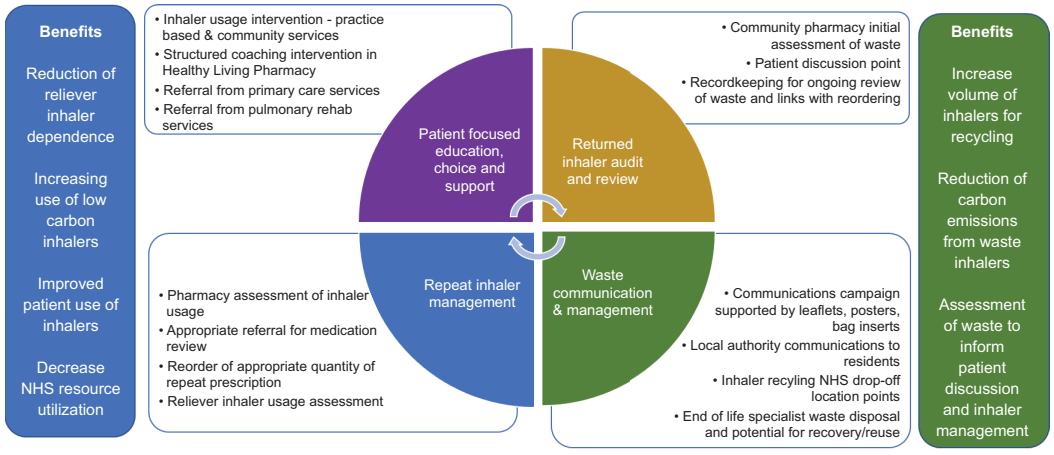

Figure 4. A framework for reducing the environmental impact of the patient and inhaler journey in the UK [4].

IPAC INHALER RETURN CAMPAIGN

As part of the essential services component of the Community Pharmacy Contractual Framework in England, community pharmacies operate a service for the collection and disposal of unwanted medicines [20]. The waste collection and destruction components are provided by designated waste management companies, funded by NHS. The aggregated medicines' waste is destroyed by appropriate incineration methods, although no separation of inhalers takes place. This is a final destruction process and not a recycling process; nevertheless, the incineration method used is the most environmentally appropriate for decommissioning of the fluorinated propellant gas.

A joint industry funded campaign has now been designed with the aim of encouraging patients to return their empty or unwanted inhalers to a community pharmacy for final disposal, utilizing the existing unwanted medicines collection infrastructure. The campaign messages are presented in everyday language, to raise awareness of patients (and their caregivers), of the impact of inhalers on the environment. The campaign is designed to change the behavior of inhaler users, to divert inhalers from domestic waste streams to environmentally appropriate waste disposal processes. The design of the campaign messages and materials has been led by IPAC, in close collaboration with key stakeholders such as Pharmaceutical Services Negotiating Committee (PSNC), Asthma UK–British Lung Foundation Partnership and NHS England. The campaign consists of several visual designs to be shared across social media networks to encourage patients to return their used devices and raise awareness for the impact of inhalers on the environment. This

campaign, whilst developed for the UK healthcare system, can be implemented in other countries. Many countries operate medicines waste collection schemes similar to the one in the UK. Raising public awareness of safe disposal routes can be adopted with limited resources. Using social media, the key messages of returning inhalers to a pharmacy when they are no longer needed or wanted can be transmitted across communities.

CONCLUSIONS

Inhalers are the mainstay of treatment for many patients with lung conditions across the world. Availability of DPIs, SMIs, and the introduction of low GWP propellant pMDIs will significantly reduce the environmental impact of the devices. But in the meantime, as a call to action, we must ensure that efforts to reduce the impact of inhalers on the environment do not undermine patient care and choice and patients continue to receive the inhalers they need. Seeking to improve the outcomes for patients, while reducing the environmental impact of current inhaler devices, needs to be tackled from a multi-stakeholder approach and should include all contributors to the patient and inhaler journey. An approach has been outlined that goes beyond simply addressing the environmental impact of inhalers and focuses on the wider challenge of reducing the carbon footprint of the sub-optimally controlled respiratory patient by considering all touchpoints along the patient journey, ending with effective waste management of inhalers.

The most important lessons learned from the transition away from CFCs under the Montreal Protocol to reduce the impact on the ozone layer, included the need for collaboration across the stakeholders, ensuring that patient care is the priority, encouraging innovation and allowing sufficient time for research and development. We must learn from this experience to play our part. Together we have the opportunity to improve patient care and tackle the global challenge of climate change.

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