FAMILY PHYSICIAN airways group

September 21, 2023

Re: The Family Physician Airways Group of Canada request regarding the European Chemicals Agency (ECHA) public consultation on the per- and polyfluoroalkyl substances (PFAS) REACH restriction proposal.

The Family Physician Airways Group of Canada is committed to helping those with airway diseases lead a full life. The group is dedicated to helping all family physicians and primary care providers maintain and increase their skill in assisting those with airway diseases like asthma and COPD. Our group represents almost 2000 Canadian primary care practitioners and their patients. The strategy of the group is to maintain a speaker bank, a data bank, and practical tools to help physicians and primary care providers attain these skills. You can access our website at www.fpagc.com

We would first like to commend you for this work, as certain PFAS are known to accumulate and have been linked to health risks, including developmental and reproductive toxicity, liver and kidney damage and increased risk of cancer. With over 10,000 chemicals to sort out, it is an enormous accomplishment to have proceeded this far. I am sure that you are getting responses from multiple industries, and we appreciate you taking the time to read our concerns and request.

We do understand that there is a structural basis for the chemicals being chosen. However, you are well aware that not all PFAS chemicals are the same in terms of their effects on the environment. In addition, the rapid timelines being instituted may leave our patients in dismay and distress due to their inability to access certain types of inhalers that they require for their respiratory health. This will place our health care systems at risk as patients may become unstable and have exacerbations of their respiratory conditions.

The active medications (which are exempt from the restriction proposal) are either suspended or solubilised in a propellant which delivers the medicine to the lungs; unfortunately, no propellant means no delivery. Medications delivered by pressurized meter dose inhalers (pMDIs) are an essential therapeutic option for many respiratory patients, as they both acutely treat and may reduce asthma attacks and COPD exacerbations, which can be potentially life-threatening events[i],[ii],[iii]. Maintaining propellant options for pMDIs therefore, is critical to ensuring the flexibility to formulate active therapeutic options of a variety of products each with different properties to allow the delivery of safe and effective medications.

Inhaled medicines are the most used medicines in respiratory care in Europe and worldwide. In 2021, pMDIs accounted for 76% of all inhalers used in Europe, and 78% of global use[iv]. pMDIs are an essential option for patients, particularly use in acute emergent situations, familiarity with the device, limited lung function, young or advanced age or reduced dexterity or cognition are considerations. pMDIs are also currently included in the World Health Organization essential medications list. While there are options for change which I will review below, it is important to state that inhaler regimens are not interchangeable and switching should be driven by clinical need and follow an individual patient assessment. Non-consensual inhaler device switching has been reviewed in a systematic review of the real-world consequences of switching inhaler regimens for non-clinical reasons. This review reported that switching inhaler regimens is a complex issue that can have variable clinical consequences and can harm the patient-doctor relationship and worsen respiratory disease and associated with lower therapeutic adherence and reduced disease control[v]. Poor disease control leads to exacerbations and hospitalizations, which are disastrous on a personal and economic patient level, health care level and even climate issue with higher global warming effects associated with them[vi].

20 Crown Steel Drive, Markham, ON L3R 9X9
Phone: [redacted] – E-mail: [redacted]@secretariatcentral.com – Web: www.fpagc.com

With an anticipated entry into force of the restriction in 2026, followed by an 18-month transition period for non-exempted PFAS uses, our concern would be that both current and certain next-generation propellants in development, intended to have a lower Global Warming Potential, would be banned from use.

Options instead of current pMDIs:

1) Dry powder inhalers (DPIs)

While there have been calls to switch patients to low carbon, propellant-free alternatives, such as DPIs, it is important to note that inhaler medicines are not interchangeable. These are complex and difficult to treat diseases and it will also require significant medical manpower to go through the processes of changing an individual patient's inhaler device[vii].

pMDIs remain the mainstay inhaler for patients with asthma or COPD in most countries, particularly for those with limited lung function, such as the elderly, the very young, or those undergoing an acute exacerbation[viii],[ix],[xxi]. In addition to patient preference, cost is an important factor in considering a wholesale switch from pMDIs to DPIs, as DPIs are more expensive than pMDIs, in addition to costs incurred to healthcare systems such as retraining of healthcare professionals[xii]. It is worth noting that there are two current medications delivered by pMDIs on the World Health Organization essential medication list at this time[xiii], and that in many developing countries, there are no alternatives to pMDIs available at all!

We are also concerned that even if mass switching could be clinically achieved, manufacturing capacity of DPIs may not be scalable to a level that would serve the 76% of patients in the EU currently relying on pMDIs[xiv].

Switching from pMDIs to DPIs could cause a significant worsening of other environmental impacts due to the high plastic and aluminum content in some of the current DPIs, and lead to human and marine toxicity[xv].

2) HFA-152A:,

The two current propellants being used HFA-227ea and HFA-134a, while being vastly superior to the previous CFC propellants, have GWP (global warming potential) to warrant a change happening. There are two current propellants being worked on by industry, with apparently NOTHING new in the pipeline to alleviate the concerns we have. There is some debate as to whether this is a PFAS substance, so we await your decision, but it still does produce F Gas and will have improved cf previous, but still does have some GWP.

3) HFO-1234ze(E)

The fluorinated substance HFO-1234ze(E), a novel propellant under development for use in pressurised metered-dose inhalers (pMDIs) that has near-zero Global Warming Potential (GWP); having up to 99% less Global Warming Potential than propellants currently used in respiratory medicines. In addition, while chemically a PFAS, evidence is clear that this is a safe substance with it being non-persistent[xvi],[xvii],[xviii],[xix], non-bio accumulative and non-toxic.

We feel that an exemption for this substance, though considered a PFAS based on its chemical structure, provides the best balance of environmental safety (due to its benign effects) and patient and health care concerns. This would allow time for companies working to get this propellant into devices to allow essential therapies to be maintained. The major crisis that the world faces this century is how it is going to limit the worst consequences of climate change and achieve the targets set out in the Paris Agreement. It means reducing carbon emissions as fast and as deeply as possible without the changes significantly disrupting societies. This includes safeguarding access for patients to essential medicines. The unintended consequence of this well-intentioned legislation is unfortunate in this case because it stifles exactly the type of innovation it was drafted to stimulate.

FAMILY PHYSICIAN
airways group

As a primary care organisation, we represent each of our patients individually, dealing with their illnesses, but also their fears, hopes and concerns. We listen to them wheeze and cough and commiserate with their sufferings. Many of our patients have had a lifelong attachment to their pMDIs and are terrified of being without them. Even if appropriate alternatives do exist, change can be hard, and frankly dangerous to them if done improperly. The ECHAs current inclusion of all pMDIs leave us at risk of our patients not having the medications they depend upon.

No longer having a pMDI available for their treatment, patients may end up having an acute exacerbation of their lung condition. Exacerbations of COPD and asthma can be quite terrifying. Symptoms of lung exacerbations include shortness of breath, gasping, choking, coughing and feeling like they cannot breathe. The lucky one will make it to an emergency facility and get treated. The unlucky ones will die! Data is quite clear that greenhouse gas emissions are created in much more significant amounts with a hospitalization than would ever occur with the use of pMDIs[xx].

We applaud the concern driving this proposal. But how will it look for your organization when asthma deaths start to accrue, and when the patient is asked 'Where is your puffer?". The unfortunate answer will be "The ECHA took them away". Nobody wins if we are dogmatic and not recognizing that exclusions to your proposal are necessary for our patients suffering from obstructive airways disease.

It is the goal of FPAGC to join with ECHA to both ensure our patients' safety and to avoid undue embarrassment for ECHA going forward. Together, a minor adjustment in the proposed legislation can save potentially millions of lives in the near future, without putting the future of the earth at risk in the longer term. We humbly submit our request to create the proper exclusions for the propellants in question for your consideration.

Regards,

Alan Kaplan MD CCFP(EM) FCFP
Chairperson, Family Physician Airways Group of Canada

For the Family Physician Airways Group of Canada

20 Crown Steel Drive, Markham, ON L3R 9X9
Phone: [redacted] – E-mail: [redacted]@secretariatcentral.com – Web: www.fpagc.com

[i] GOLD. Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2023. Available at: https://goldcopd.org/2023-gold-report-2/. Accessed: August 2023.
[ii] The Global Asthma Report 2022. Available at: http://globalasthmareport.org/. Accessed: August 2023.
[iii] National Asthma Education and Prevention Program, Third Expert Panel on the Diagnosis and Management of Asthma. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Bethesda (MD): National Heart, Lung, and Blood Institute (US); 2007 Aug. Section 2, Definition, Pathophysiology and Pathogenesis of Asthma, and Natural History of Asthma. Available at: https://www.ncbi.nlm.nih.gov/books/NBK7223/. Accessed August 2023
[iv] Bell J, et al. An Assessment Of Pressurized Metered-dose Inhaler Use In Countries In Europe And The Rest Of The World. Poster Presentation at American Thoracic Society (ATS) international congress, 2023 19-24 May.
[v] Usmani OS, Bosnic-Anticevich S, Dekhuijzen R, Lavorini F, Bell J, Stjepanovic N, Swift SL, Roche N. Real-World Impact of Nonclinical Inhaler Regimen Switches on Asthma or COPD: A Systematic Review. J Allergy Clin Immunol Pract. 2022 Oct;10(10):2624-2637. doi: 10.1016/j.jaip.2022.05.039. Epub 2022 Jun 22. PMID: 35750323.
[vi] Wilkinson AJK et al. Presented at: ERS 2021 International Virtual Congress; September 5−8, 2021
[vii] Kaplan A, van Boven JFM. Switching Inhalers: A Practical Approach to Keep on UR RADAR. Pulm Ther. 2020 Dec;6(2):381-392. doi: 10.1007/s41030-020-00133-6. Epub 2020 Oct 13. PMID: 33051824; PMCID: PMC7672131.
[viii] Lavorini F. The challenge of delivering therapeutic aerosols to asthma patients. ISRN Allergy. 2013; 102418.
[ix] Roche N, et al. The evolution of pressurized metered-dose inhalers from early to modern devices. J Aerosol Med Pulm Drug Deliv. 2016; 4: 311–27.
[x] 4 Laube BL, et al. What the pulmonary specialist should know about the new inhalation therapies. Eur Respir J. 2011; 37 (6):1308-31.
[xi] Lavorini F, et al. Optimising inhaled pharmacotherapy for elderly patients with chronic obstructive pulmonary disease: the importance of delivery devices. Drugs Aging. 2016; 33 (7): 461–73
[xii] Keeley D, Scullion JE, Usmani OS. Minimising the environmental impact of inhaled therapies: problems with policy on low carbon inhalers. Eur Respir J. 2020;55(5):2001122.
[xiii] https://www.who.int/groups/expert-committee-on-selection-and-use-of-essential-medicines/essential-medicines-lists Assessed August 2023
[xiv] European Commission. Feedback from: International Pharmaceutical Aerosol Consortium. Available at: https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12479-Fluorinated-greenhouse-gases-review-ofEU-rules-2015-20-/F3317512_en. Accessed June 2023.
[xv] Jeswani, H.K. & Azapagic, A. Life cycle environmental impacts of inhalers. Journal of Cleaner Production, 237, 117733.
[xvi] Chiappero MS, Malanca FE, Argüello GA, et al. Atmospheric chemistry of perfluoroaldehydes (CxF2x+1CHO) and fluorotelomer aldehydes (CxF2x+1CH2CHO): quantification of the important role of photolysis. J Phys Chem A. 2006;110(43):11944-11953.
[xvii] Javadi, M. S. et al. 2008. Atmospheric chemistry of trans-CF3CH=CHF: products and mechanisms of hydroxyl radical and chlorine atom initiated oxidation. Atmos. Chem. Phys. Discuss., 8, 1069–1088.
[xviii] Nilsson E.J.K., Nielsen O.J., Johnson M.S., Hurley M.D., and Wallington T.J. (2009): Atmospheric chemistry of cis-CF3CH=CHF: Kinetics of reactions with OH radicals and O3 and products of OH radical initiated oxidation. Chemical Physics Letters 473 (4-6), 233-237.
[xix] Sulbaek Andersen, P & Nielsen, OJ. Tropospheric photolysis of CF3CHO, Atmospheric Environment, Volume 272, 2022, 118935, ISSN 1352-2310.
[xx] Tennisson I et al. Health care's response to climate change: a carbon footprint assessment of the NHS in England. The Lancet Planet Health 2021; 5: e84–92. DOI:https://doi.org/10.1016/S2542-5196(20)30271