

PERSPECTIVES FROM IPAC ON CFC-FREE METERED DOSE INHALERS (MDIs)

FOR THE 22ND MEETING OF THE PARTIES TO THE MONTREAL PROTOCOL
ON SUBSTANCES THAT DEplete THE OZONE LAYER

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The International Pharmaceutical Aerosol Consortium (IPAC) is a group of companies that manufacture medicines for the treatment of respiratory illnesses, such as asthma and chronic obstructive pulmonary disease (COPD). IPAC has long supported and remains firmly committed to a timely and effective MDI transition that balances patient health and environmental concerns.

IPAC urges the Parties to be mindful of the following points as they consider “essential use” nominations for MDIs and the possible control of hydrofluorocarbons (HFCs) under the Montreal Protocol:

- When authorizing and licensing essential use chlorofluorocarbons (CFCs) at the domestic level, it is important that the Parties adhere to the following core principles: (i) allocate CFCs only for use in the few MDIs that remain essential for patients, and (ii) effectively manage existing stockpiles of pharmaceutical-grade CFCs pursuant to Decisions of the Parties – particularly Decisions XVI/12, XVII/5, and XVIII/7 – and within commercial constraints, to ensure that new essential use CFCs are produced only when truly necessary.
- Adequate, safe, and secure supplies of HFCs must remain available over the long term to meet patient needs. Therefore, any amendment to phase down HFCs should include a self-implementing mechanism to protect HFCs for MDIs. Ensuring patient care by maintaining HFC-based treatment options should be an overriding objective when evaluating controls on HFCs. As TEAP/MTOC conclude in this year’s Progress Report (Volume 1): *“Healthcare professionals continue to consider that a range of therapeutic options is important. Any consideration of policy measures to control HFCs should assess carefully the patient health implications with the goals of ensuring patient health and maintaining a range of therapeutic options.”*

► Essential Use Nominations For 2011

IPAC commends TEAP/MTOC for their commitment and hard work in evaluating the essential use nominations submitted this year. In general, IPAC supports the MDI essential use recommendations set forth in the 2010 TEAP Progress Report (Volume 2) and wishes to highlight the points noted below.

Non-Article 5 Parties

IPAC congratulates the United States (US) and European Community (EC) on their progress in the CFC MDI transition and notes that neither Party submitted essential use nominations for 2011. The US recently achieved a significant milestone by establishing final deadlines for the phase-out of all CFC MDIs remaining on its market.

Article 5 Parties

IPAC does not have access to the six Article 5 Party nominations (Argentina, Bangladesh, China, India, Iran, and Pakistan), and therefore is not in a position to independently assess them. However, IPAC finds the conclusions and recommendations on the nominations described in the 2010 TEAP Progress Report to be reasonable and sound. As detailed in their Report, TEAP/MTOC carefully reviewed each nomination and, in particular, endeavored to fully understand the availability and affordability of alternatives to CFC MDIs in each Party.

IPAC notes that TEAP/MTOC highlight two significant positive developments relevant to the transition in Article 5 Parties: (i) “substantial progress in the development and marketing of affordable CFC-free MDIs, especially those manufactured by Article 5 Parties” and (ii) an adequate range of technically satisfactory and affordable CFC-free alternatives for beta-agonists (particularly salbutamol) and inhaled corticosteroids (particularly beclomethasone propionate) is now available in many developing countries. For example, TEAP/MTOC note that Cipla, the largest MDI manufacturer in India, markets 51 different CFC-free inhaled products.

In spite of these developments, IPAC is concerned that the Article 5 transition is not moving as rapidly as it could, and in that regard, wishes to express particular support for the following TEAP/MTOC conclusions and recommendations:

- “Essentiality should not be linked necessarily to the completion of all [MLF] phase-out projects, but rather to the satisfaction of essential use criteria. Some companies have been successful in transition. Market leaders in HFC MDIs should not be penalized for fast transition by competing against lower priced CFC MDIs in the same markets. These circumstances also arose in non-Article 5 Parties, and this was an important factor in delaying salbutamol CFC MDI transition in some countries.”
- “Parties may wish to consider ‘implementing fast track regulatory processes to expedite approvals’ of CFC-free products.”
- “A cautious approach to CFC production is advisable since transition is moving so quickly and Parties may wish to avoid CFC production that is surplus to actual needs, which subsequently would require costly destruction. The welfare of patients with asthma and COPD and of the environment would be best served by a rapid transition to CFC-free inhalers.”
- “Parties may wish to remind all Parties to collect data on CFC and CFC-free MDIs and provide it annually to the Ozone Secretariat, in accordance with Decision XIV/5.”
- “Parties may wish to remind all Parties to notify the Ozone Secretariat of any MDI products determined to be non-essential, pursuant to Decision XII/2(3), so that the Secretariat can post the information to its website in a timely manner.”
- “Parties may wish to consider requesting nominating Parties to demonstrate that they have received informed consent of the government of any importing country for imports of CFC MDIs.”

IPAC also strongly supports TEAP/MTOC's conclusion that they are unlikely to recommend approval of essential use CFCs intended for products not yet on the market in Article 5 Parties (e.g., ciclesonide for China). Approving CFCs for such products is both unnecessary and wholly counterproductive to achieving a timely transition.

TEAP 2010 Progress Report (Volume 1) Chapter 14 on Inhaled Therapy For Asthma and COPD

In response to Decision XXI/9, TEAP/MTOC provided an update to the chapter on Inhaled Therapy contained in the Decision XX/8 Task Force report issued during 2009. Although the chapter highlights a number of important points relevant to MDIs and other inhaled therapies for the treatment of asthma and COPD, IPAC is especially supportive of the following observations and conclusions:

- “Metered dose inhalers (MDIs), dry powder inhalers (DPIs), and novel delivery systems play an important role in the treatment of asthma and chronic obstructive pulmonary diseases (COPD). No single delivery system is considered universally acceptable for all patients. Similarly not all active ingredients are available equally as either an MDI or DPI. For example, there is currently no single-moiety salbutamol DPI available in the United States.”
- “The choice of the most suitable inhaler is a complex decision taken between the doctor and the patient. Healthcare professionals continue to consider that a range of therapeutic options is important. Any consideration of policy measures to control HFCs should assess carefully the patient health implications with the goals of ensuring patient health and maintaining a range of therapeutic options.”

The chapter also projects that total annual consumption of HFCs for MDIs will be 7,000 to 10,500 tonnes by 2015 (approximately 11 to 17 MMtCO₂-eq). IPAC believes this is a reasonable estimate, and wishes to emphasize that it represents an infinitesimal percentage of overall projected greenhouse gas emissions. Global greenhouse gas emissions are projected to be on the order of 44 *billion* tonnes by 2015 (44 GtCO₂-eq).¹

The CFC MDI transition under the Montreal Protocol was an unprecedented undertaking presenting numerous and substantial challenges for patients, policymakers, MDI companies, and the medical community. Reformulating CFC MDIs to use HFCs was a complex and resource-intensive effort taking close to two decades. As climate change policies are considered that could impact the HFC MDI sector, it is extremely important to keep in mind the lessons learned under the Montreal Protocol. A 2004 paper published in the JOURNAL OF DRUG ASSESSMENT provides useful background and context – *The Importance of Preserving Choice in Inhalation Therapy: The CFC Transition and Beyond* (Volume 7, pp. 45-61).

¹ See <http://www.epa.gov/climatechange/emissions/globalghg.html>, at Figure 3, and Figure 3.1 of the Synthesis Report of the IPCC's Fourth Assessment Report: http://www.ipcc.ch/pdf/assessment-report/ar4/syr/ar4_syr.pdf.

▶ Amending The Montreal Protocol To Control HFCs

In April, the US, Canada, and Mexico submitted a proposed amendment to the Montreal Protocol to control HFCs (the so-called “North American Proposal”). IPAC believes that the proposal is thoughtful and constructive, and shows promise as a workable path forward.

The “Summary Points” accompanying the North American Proposal note that one of its key elements is the recognition that “there may not be alternatives for all HFC applications and therefore utilizes a gradual phase-down mechanism with a plateau, as opposed to a phase-out.” IPAC believes that avoiding a phase-out is essential, and any phase-down must be structured to ensure that adequate, safe, and secure supplies of HFCs remain available to meet patient need over the long term. To date, no alternative medical propellant to HFCs has been shown to be suitable for use with existing active ingredients or components, let alone proven to be safe for patients. This is in contrast to the circumstances under which the international community agreed to phase-out CFCs for MDIs, where work had been completed demonstrating HFC-134a and HFC-227 as promising alternatives to CFCs in terms of their safety profile and technical/performance characteristics. Absent a self-implementing exception for MDIs, even a phase-down of HFCs generally could pose unintended consequences for patient care (e.g., shortages of medicines or increased costs). Existing data illustrates that asthma, COPD, and other respiratory illnesses are undertreated in many Parties. It is a fundamental public health goal to expand the availability of medicines and encourage appropriate treatment for patients. Restrictive policies are inappropriate in this context. This is a particularly important consideration in establishing baselines, especially for Article 5 Parties.

It is critical that the Parties ensure there will be no negative implications for patient health or for the ongoing CFC MDI transition *before* adopting measures that could phase-down HFCs. This evaluative process should include expert advice from the MTOC, national health experts, and all impacted stakeholders taking into account the important “lessons learned” in the CFC MDI transition. The essential use process created for the CFC MDI phase-out is resource intensive and requires significant effort from Parties, TEAP/MTOC, and MDI companies. It would not be prudent or necessary to impose a restrictive and burdensome process in the context of a HFC phase down, especially given the minimal emission reduction opportunities for the MDI sector and important patient care considerations.

In conclusion, IPAC recommends that any amendment to control HFCs should provide unambiguous and self-implementing protections for medical uses of HFCs. For example, a paragraph could be inserted in Article 2J of the North American Proposal (as paragraph 9) stating: “The calculated level of consumption under this Article shall not include amounts used by the Party for metered-dose inhalers.” As needed, subsequent decisions of the Parties could address a process for further consideration of the use of HFCs for MDIs (e.g., essential use process).

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