

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

FOR THE 32<sup>nd</sup> MEETING OF THE OPEN-ENDED WORKING GROUP OF THE PARTIES TO THE MONTREAL PROTOCOL ON SUBSTANCES THAT DEplete THE OZONE LAYER

BANGKOK, THAILAND (23-27 JULY 2012)

*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 adhere to the following core principles 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: (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.
- Ensuring patient care by maintaining HFC-based treatment options should be an overriding objective when evaluating controls on HFCs. As TEAP/MTOC concluded in their most recent Assessment Report (2010): “*Healthcare professionals continue to consider that a range of therapeutic options is important. Any consideration of policy measures to control HFCs should carefully assess the patient health implications with the goals of ensuring patient health and maintaining a range of therapeutic options.*” This can only be accomplished if adequate, safe, and secure supplies of HFCs 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.

## ► Essential Use Nominations For 2013

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 2012 TEAP Progress Report. IPAC also congratulates the Parties for achieving substantial progress toward the global goal of completion of the MDI transition. IPAC notes that the United States (US) and European Community (EC) are no longer seeking essential use CFCs and have either completed the transition (in the case of the EC) or established firm transition deadlines for all CFC MDIs. Numerous Article 5 Parties have ceased making essential use nominations and appear to be managing the essential use process efficiently based upon Reporting Accounting Framework data summarized in the TEAP Progress Report. These are very positive developments. IPAC notes the MTOC’s observation that there “have been significant reductions from about 2400

tonnes of authorized essential use CFCs in 2010 to about 697 tonnes of CFCs for 2013.” This is an encouraging trend and it is important to sustain the momentum towards a successful and complete global CFC MDI transition.

IPAC does not have access to the two Party nominations for 2013 (China and the Russian Federation), and therefore is not in a position to independently assess them. However, IPAC finds the conclusions and recommendations on the nominations described in the 2012 Progress Report to be reasonable and sound. As detailed in their Report, TEAP/MTOC carefully reviewed both nominations and, in particular, endeavored to fully understand the availability and affordability of alternatives to CFC MDIs in each Party. MTOC’s evaluation of the Chinese and Russian transitions is comprehensive, thoughtful and pragmatic.

IPAC wishes to express particular support for the following TEAP/MTOC conclusions and recommendations aimed at bringing the transition to a timely conclusion:

- “Technically satisfactory alternatives to CFC MDIs to treat asthma and COPD are available in all countries worldwide except China. ... CFC-free inhalers manufactured in developing countries are now substantially increasing the range of affordable alternatives.”
- “China may wish to consider a future final campaign production of CFCs in 2014 to satisfy its total essential use requirements until final phase-out of all CFC MDI products. This may require an essential use nomination in 2013 to cover multiple years.”
- “China may wish to critically assess the use of isoprenaline, and the feasibility of achieving the reformulation and launch of a CFC-free inhaler before the end of 2016, China’s strategy phase-out date.”
- “Russia may wish to consider its domestic arrangements (market and pricing) to facilitate an increased use of imported products.”

## ▶ 2010 Assessment Report Of The Medical Technical Options Committee

The TEAP and its Technical Options Committees issue periodic assessment reports on the status of the Montreal Protocol’s control measures and the current state of knowledge on technical, scientific, environmental, and economic issues relevant to protection of the stratospheric ozone layer. The MTOC’s 2010 Assessment Report provides a comprehensive review of the status of the global CFC MDI transition and reviews important technical and medical context on the key patient health and environmental considerations relevant to the MDI sector.

IPAC considers it important to highlight the following observations and conclusions from the Assessment Report:

- “It is estimated that about 4,000 tonnes of HFCs are used to manufacture MDIs, accounting for a very small proportion of total HFC usage (estimated at 1-2 per cent). Based on current consumption and projected growth rates of MDI use, annual consumption of HFCs for MDIs

is estimated to be between 7,000-10,500 tonnes by 2015. By moving from CFC MDIs to HFC MDIs and DPIs, not only have emissions of ozone depleting substances been eliminated, but there have also been benefits for climate change. According to rough estimates of carbon footprints of inhaler products, HFC MDIs have about 10 times less climate impact than CFC MDIs. DPIs have an even lower comparative climate impact, about 100 times less than CFC MDIs and 10 times less than HFC MDIs.” [The MTOC also provides some carbon footprint data for consumer products and activities that provides useful context for the impact of life-saving medications such as HFC MDIs (see pages 15-17 of the Assessment Report).]

- “It is important to note that MDIs, DPIs and novel delivery systems play an important role in the treatment of asthma and COPD, and no single delivery system is considered universally acceptable for all patients. Healthcare professionals continue to consider that a range of therapeutic options is important. Any consideration of policy measures to control HFCs should carefully assess patient health implications with the goals of ensuring patient health and maintaining a range of therapeutic options. Each country has its own unique and complex makeup in terms of availability of medicines, overarching health care systems, and patient preferences.”

The MTOC also assesses the possibility of novel medical propellants other than HFCs, and accurately illustrates the formidable risks and technical and development challenges associated with an effort to transition to one of these propellants. For example, with regard to hydrofluoroolefins which have become commercially available for some non-medical sectors, the MTOC notes:

“However, this does not mean that unsaturated HFCs represent a viable alternative to saturated HFCs as propellants in MDIs. These new chemicals are not as advanced for pharmaceutical usage as were HFCs -134a and -227ea when the Montreal Protocol was introduced. For a new propellant development programme, there is major risk, significant investment, and no guarantee of success. Substantial time and resources would be required to (i) test the safety of unsaturated HFCs for direct and chronic human inhalation, and (ii) research, develop, reformulate and conduct safety and efficacy testing of whole new products with unsaturated HFCs, followed by regulatory review. For existing products, it would likely be particularly difficult for a pharmaceutical company to justify an investment in unsaturated HFCs given the limited benefit to patients (i.e., the active ingredient will remain the same and the performance characteristics are likely to be comparable to saturated HFCs), and in light of the large investments they have already made over the past two decades in developing and marketing saturated HFC MDIs.”

## ▶ Amending The Montreal Protocol To Control HFCs

In May, the US, Canada, and Mexico re-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. Therefore, IPAC encourages the Parties to formally consider the proposal during the Meeting of the Open-Ended Working Group and the Meeting of the Parties.

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 phasedown mechanism with a plateau, as opposed to a phaseout.” 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 threats to patient care. For example, shortages of medicines and/or increased costs for medicines could result from overall diminished demand for HFCs and related supply chain disruptions or challenges. 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 addition to the important observations and technical background provided by the MTOC in this year’s Assessment Report (and prior Reports), a 2004 paper published in the JOURNAL OF DRUG ASSESSMENT provides useful background and context on patient care issues – *The Importance of Preserving Choice in Inhalation Therapy: The CFC Transition and Beyond* (Volume 7, pp. 45-61).

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).