

# Metered Dose Inhaler Transition Issues at the 25th Meeting of the Open-Ended Working Group of the Montreal Protocol

**Montreal, Canada (27 to 30 June 2005)**

## INTRODUCTION

The International Pharmaceutical Aerosol Consortium (IPAC) is committed to a timely, effective transition to CFC-free products that are safe and effective for patients. IPAC appreciates the work of the Technology and Economic Assessment Panel (TEAP) and its Medical Technical Options Committee (MTOC) in considering issues surrounding the transition to CFC-free metered dose inhalers (MDIs). In its May 2005 Report, TEAP made recommendations concerning essential use nominations for MDIs and reviewed the status of the MDI transition around the world. IPAC supports many of these recommendations, as discussed herein.

## STATUS OF MDI TRANSITION IN NON-ARTICLE 5(I) COUNTRIES

Virtually every major developed country has made great strides toward completion of the MDI transition at the national level by establishing firm deadlines for phasing out CFC MDIs. For example, Australia, Canada and Japan have phased out CFC salbutamol MDIs<sup>1</sup> and other CFC MDI products. As a result, these Parties no longer request any essential use volumes. Similarly, the European Union has declared salbutamol MDIs to be non-essential effective January 1, 2006 and is progressing the phase-out of other therapeutic categories of CFC MDIs.

The United States presents a distinct contrast to this progress. The US Food and Drug Administration (FDA) recently established a delayed phase-out date of 31 December 2008 for salbutamol MDIs. As detailed below, the 2008 phase-out date is two to three years longer than needed in the US. Moreover, it is inconsistent with Decision IV/25, and other Decisions of the Parties, and is not supported by the information presented to FDA.

CFC salbutamol MDIs represent a significant proportion of the essential use nominations submitted by the US (2006: 70%/2007: 62%). In addition, more than one-third of the European Union's nomination (180 tonnes) is for use in production of salbutamol MDIs to be exported to the United States.

Three CFC-free salbutamol products are currently on the market in the US, and a fourth CFC-free alternative to CFC salbutamol was recently approved. Two of the currently available salbutamol products have been on the market together for more than three years (and one of these products has been available for more than eight years). Yet, CFC MDIs still represent 90% of the domestic salbutamol market.

In determining non-essentiality for CFC salbutamol MDIs, FDA concluded that patients would be adequately served by the CFC-free products – *i.e.*, the cost of these products would not be detrimental to patient health or safety. FDA's primary stated reason for choosing the

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<sup>1</sup> In this document, the term "salbutamol MDIs" refers only to single-moiety products. Salbutamol is referred to as "albuterol" in the United States and other Parties.

December 31, 2008 effective date was not concern for patient care, or cost of the new products, but rather because FDA appears to have concluded that close to four years would be needed for adequate HFA salbutamol MDI production capacity to be ready. In doing so, FDA chose to ignore the commitments of the three HFA MDI manufacturers to have adequate production capacity in place by the end of 2005.

By contrast with US FDA, TEAP concluded that only up to 18 months would be required to complete the ramp-up of production capacity. IPAC agrees with TEAP that adequate production will be ready – likely in 2006 and almost certainly in 2007. Therefore, and considering the ample CFC stockpile in the US, IPAC believes that it is unnecessary for the United States to continue to receive essential use allocations for use in salbutamol MDIs for 2006 and thereafter. In fact, FDA's choice for an end-2008 date could cause HFA salbutamol manufacturers to delay or cut back on their ramp-up of production capacity.

## ESSENTIAL USE NOMINATIONS

### European Community's Nomination

TEAP recommended approval of 539 metric tonnes (MT) for the EC in 2006, including 181 MT for salbutamol CFC MDIs to be exported to non-Article 5(1) countries (180 MT for salbutamol CFC MDIs to be imported to the US<sup>2</sup>). As noted above, IPAC believes that there is no need for CFCs for salbutamol for the US market for 2006. Therefore, IPAC recommends that the Parties approve a reduced quantity for the EC of 358 MT. IPAC notes that the European company currently importing CFC salbutamol into the US is one of the three companies with an approved CFC-free salbutamol MDI on the market in the US, and so there is no need for it to continue to manufacture CFC salbutamol MDIs for the US market.

### United States' Nomination

MTOC recommended approval of 637 MT for the US for 2006, and TEAP revised that into a formula, rather than a single number, that takes into account pre-1996 stockpiles. As noted above, IPAC believes that only the non-salbutamol portions of the US nomination be approved, since technically and economically feasible alternatives are now available for salbutamol products. IPAC estimates that approximately 450 MT are needed for the US for non-salbutamol MDIs.<sup>3</sup> TEAP's formula could yield a level close to consistent with that volume. Therefore, IPAC supports the MTOC and TEAP recommendations, subject to the following qualifications:

- an amount certain of pre-1996 stockpiles satisfying US regulatory requirements and actually sold into the US market should be known by the Parties at MOP-17; and
- during licensing of approved volumes first priority should be given to uses for which there are no CFC-free alternatives and for which there is a real medical need.

In addition, while TEAP's review of the extent of CFC stocks in the US is important and relevant, IPAC notes that TEAP did not address the key issue of whether CFC salbutamol MDIs in the US are essential under Protocol criteria. US FDA considered this issue only with respect to US domestic essential use criteria. However, TEAP has a long-standing obligation under Decision IV/25 not to recommend approval of essential use volumes if “technically and economically feasible alternatives” are available. In addition, Decision XV/5 requests TEAP to make its recommendations on essential use nominations with reference to the active ingredient of the MDI in which the CFC will be used and the intended market for that active ingredient. IPAC therefore requests that in its report next year, TEAP consider this key question of whether CFC salbutamol MDIs are an essential use under Protocol criteria.

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2 IPAC notes that this request is inconsistent with the European Community's action plan on salbutamol which clearly states that it will cease after 2005 nominating CFCs for salbutamol MDIs for non-Article 5(1) markets.

3 IPAC fully supports its member companies' portion of the US nomination for 2006, all of which is for use in non-salbutamol MDIs.

## **CFC Stockpile Issues**

IPAC notes that MTOC and TEAP have undertaken a detailed analysis of CFC stockpiles. Now that the CFC MDI transition is entering its final phase, it is timely to consider more carefully the need for new CFC production in light of stockpile volumes. In particular, IPAC believes it is quite appropriate to reduce the amount authorized for the US at MOP-17 by the amount of available CFC stockpile which satisfies US regulatory requirements sold into the US market for use in MDIs, subject to the above important qualifications. The IPAC member company holding 605 MT of pre-1996 pharmaceutical-grade CFC stock has confirmed that it intends to make its entire stockpile available for MDI use in the United States.

IPAC also agrees with TEAP's recommendation that each Party granted essential use volumes should reduce the amounts licensed to each company by the amount that the company's stockpile exceeds a one-year operational supply.

IPAC questions, however, why TEAP restricted its recommendations solely to pre-1996 stock. The US has reported 279 MT of post-1995 CFC stock in excess of a one-year operational supply (1521 MT – 1242 MT). Under the terms of Decision IV/25, this should be taken into account the same as pre-1996 stock.

Finally, IPAC concurs with TEAP's request to the Parties that future nominations report the quantity, quality, and availability of any pre-1996 stockpiled material that has not previously been included in a Party's accounting framework. The IPAC member company that reported to MTOC on its pre-1996 CFC stockpile did so at the request of the MTOC co-chairs, after first offering to report to US EPA.

## **Availability of CFC-Free Alternatives**

IPAC shares TEAP's strong concern that "companies continue to request essential use quanti-

ties for CFCs when they also manufacture HFC MDI alternatives for salbutamol." IPAC concurs with TEAP's assessment that if these companies "took the immediate decision to transition their production, this would result in an approximately 90% reduction in CFC volumes for salbutamol MDI use in the United States (equivalent to ~900 tonnes of CFCs)." IPAC also believes that continuing to allocate CFC volumes to companies that have approved alternatives is inconsistent with Decision IV/25 paragraph 1(b) (i), which states that production and consumption should only be permitted if "all economically feasible steps have been taken to minimize the essential use." IPAC therefore recommends that the Parties at MOP-17 only authorize essential use volumes to individual Parties on the condition that such volumes may only be licensed to companies for products for which there are no corresponding CFC-free alternatives on the market.

## **Research and Development of CFC-Free Alternatives**

Pursuant to Decision VIII/10(1), the Essential Use Handbook requires each nominating Party to assure that all MDI companies applying for essential use nominations "demonstrate ongoing research and development of alternatives to CFC MDIs with all due diligence and/or collaborate with other companies in such efforts." IPAC is concerned that past essential use nominations have included amounts for companies that have not demonstrated ongoing research and development as required by Decision VIII/10, and believes that the 2006 nominations under consideration from the Parties—the United States in particular—fail to adequately address this requirement. IPAC therefore recommends that when the Parties approve essential use volumes at MOP-17, they do so on the condition that such volumes may not be licensed to any company that has not demonstrated an ongoing commitment to research and development of CFC-free alternatives to its own products.

## IPCC/TEAP SPECIAL REPORT

On 8 April 2005, the Intergovernmental Panel on Climate Change (IPCC) adopted the final version of the Special Report entitled *Safeguarding the Ozone Layer and the Global Climate System: Issues Related to Hydrofluorocarbons and Perfluorocarbons*. The “Summary for Policymakers” section of this report notes that the “reduction potential for medical aerosols is limited due to medical

constraints, the relatively low emission level and the higher costs of alternatives” and states that the major contribution to a reduction of greenhouse gas emissions for MDIs would be the completion of the transition from CFC to HFC MDIs. IPAC fully concurs with this conclusion and believes it illustrates the imperative need to conclude the MDI transition as soon as possible and refrain from allowing the use and production of CFCs for non-essential MDIs.

## IPAC RECOMMENDATIONS

- 1. At MOP-17 the Parties should not authorize essential use volumes for use in single-moiety salbutamol MDIs intended for non-Article 5(1) markets. Therefore, it is IPAC’s strong view that the US and EU requests should be reduced to 450 and 358 MT, respectively.**
- 2. Alternatively, at MOP-17, the Parties should approve the TEAP recommendation, but with the qualifications that: (i) the US authorization should be reduced by pre-1996 stockpiles actually sold for MDI use prior to MOP-17 (amount certain) and (ii) first priority should be given to uses for which there are no CFC-free alternatives and for which there is real medical need.**
- 3. In either case, essential use volumes should be authorized only:**
  - (a) to companies that have demonstrated ongoing commitment to research and development of CFC-free alternatives for their products;**
  - (b) for products for which there are no corresponding CFC-free alternatives; and**
  - (c) to the extent that each company’s stockpile would not exceed a one-year operational supply.**



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