

IPAC

INTERNATIONAL PHARMACEUTICAL AEROSOL CONSORTIUM

1301 K Street NW § Suite 900 § East Tower § Washington DC § 20005-3317

Telephone +1 202 230 5133 § Telefax +1 202 230 5333

Internet: <http://www.ipacmdi.com>

10 March 2006

Dr. Helen Tope
Mr. Jose Pons Pons
Dr. Ashley Woodcock
Co-Chairs, UNEP Medical Technical Options Committee

Dear Dr. Tope, Mr. Pons Pons, and Dr. Woodcock:

We are pleased to provide you with this *IPAC SUBMISSION TO THE MEDICAL TECHNICAL OPTIONS COMMITTEE: TRANSITION TO CFC-FREE METERED-DOSE INHALERS*. These comments are submitted for your consideration in the development of MTOC's 2006 Report.

We appreciate the opportunity to make this submission and look forward to continuing our work with MTOC on the transition to CFC-free MDIs.

Sincerely,



Dr. Paul Wright (AstraZeneca)
Chair

INTERNATIONAL PHARMACEUTICAL AEROSOL CONSORTIUM

IPAC SUBMISSION

TO THE MEDICAL TECHNICAL OPTIONS COMMITTEE:
TRANSITION TO CFC-FREE METERED-DOSE INHALERS

10 March 2006

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I. INTRODUCTION AND SUMMARY OF RECOMMENDATIONS

The International Pharmaceutical Aerosol Consortium (IPAC) is an association of leading manufacturers of metered dose inhalers (MDIs) and other devices used for the treatment of asthma and chronic obstructive pulmonary disease (COPD). Its members include: AstraZeneca, Boehringer Ingelheim, Chiesi Farmaceutici, GlaxoSmithKline, and Inyx.

The purpose of this Submission is to:

- § provide quantitative information on market trends for CFC-free alternatives;
- § comment on the Essential Use Nominations of the European Union and United States for 2007 and 2008;
- § review issues concerning the MDI transition in Article 5 Parties; and
- § discuss IPAC's efforts to bring the MDI transition to a timely conclusion consistent with patient care.

For the reasons set forth in this submission, IPAC recommends that TEAP recommend against approval of essential use volumes for 2007 or 2008:

- § for salbutamol MDIs¹ intended for sale and distribution in non-Article 5 Parties;
- § for any company for a CFC MDI product for which that company has an approved and launched CFC-free alternative (after an adequate post-marketing period); and
- § for any company for a CFC MDI product for which that company is not conducting adequate research and development on a CFC-free alternative.

TEAP's recommended authorization amount should clearly articulate the conditions noted in the bullets above. This level of specificity is critically important to ensure that essential use CFCs remain available for products where CFC-free

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

alternatives have not yet been launched and where the manufacturer is undertaking diligent efforts to develop an alternative.

In addition, IPAC recommends that TEAP assess the nominating Parties' implementation of paragraph 3 of Decision XVII/5 (on stockpiles) and, if necessary, seek clarification to ensure that national implementation is consistent with that provision. Finally, with respect to transition in Article 5 Parties, IPAC acknowledges the Parties' suggestion (in Decision XVII/15) that the Executive Committee of the Multilateral Fund consider hosting regional workshops to raise awareness and educate stakeholders on the MDI transition.

II. QUANTITATIVE INFORMATION ON MARKET TRENDS FOR CFC-FREE ALTERNATIVES

A valuable aspect of TEAP's reports has been the review of available data on the uptake of CFC-free alternatives. IPAC wishes to support TEAP's efforts by providing some recent global market data summarising the current trends in the major inhaled devices: CFC MDIs, HFA MDIs, and DPIs. This data was produced by IMS Health, a respected company that has been gathering and analysing pharmaceutical market data for decades.²

Figure 1 illustrates the current world-wide market for CFC MDIs and HFC MDIs (as of the 3rd Quarter of 2005, Moving Annual Total (MAT): Q3 2004 – Q3 2005, based on 31 countries). Of a total market of 47.7 billion Standard Units (SUs) of MDIs, CFC MDIs represented approximately 60% and HFC MDI approximately 40%. Please note the explanation below defining "Standard Units."

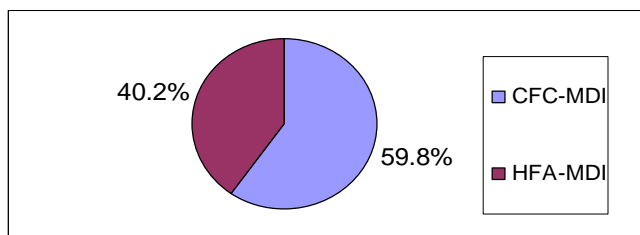


Figure 1: Distribution of Worldwide Sales of Respiratory Devices in Units

IMS definition of SUs: "These are the number of dose units, such as the number of inhalations/puffs, tablets, the number of 5ml doses, or the number of vials, sold for a particular product".

Note: For SU comparisons of DPIs vs MDIs it is important to know, that for DPIs: 1 puff (1 SU) = 1 dose, whereas in general for MDIs: 2 puffs (2 SUs) = 1 dose. Translating SUs into the absolute number of actual MDIs or DPIs can be a challenging, complex exercise because different devices provide a range of doses. A very rough estimate could be made for MDIs by dividing the SUs by 200 and for DPIs by 60.

Figure 2 summarises the global sales volume performance in SUs of CFC MDIs, HFC MDIs, nebulized solution inhalants, and DPIs. This data illustrates that the DPI market has dramatically increased, while the MDI products in total (HFC- and CFC-MDIs) have fallen in the past five years. Because DPIs do not require an aerosol

² Source for all data in this section: IMS Health, IMS MIDAS (permission granted for IPAC to submit to MTOC/TEAP).

propellant this trend is positive for mitigating both ozone depletion and global climate change.

It is also important to note that the Special Report prepared by TEAP in collaboration with the Intergovernmental Panel on Climate Change (IPCC) – *Safeguarding the Ozone Layer and the Global Climate System* – concluded 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.³ As TEAP has recognized, however, “the availability of CFC-free products alone will not lead to a timely conclusion of the transition” and additional regulatory steps are needed, particularly “ceasing the supply of CFC MDIs where alternatives exist.”

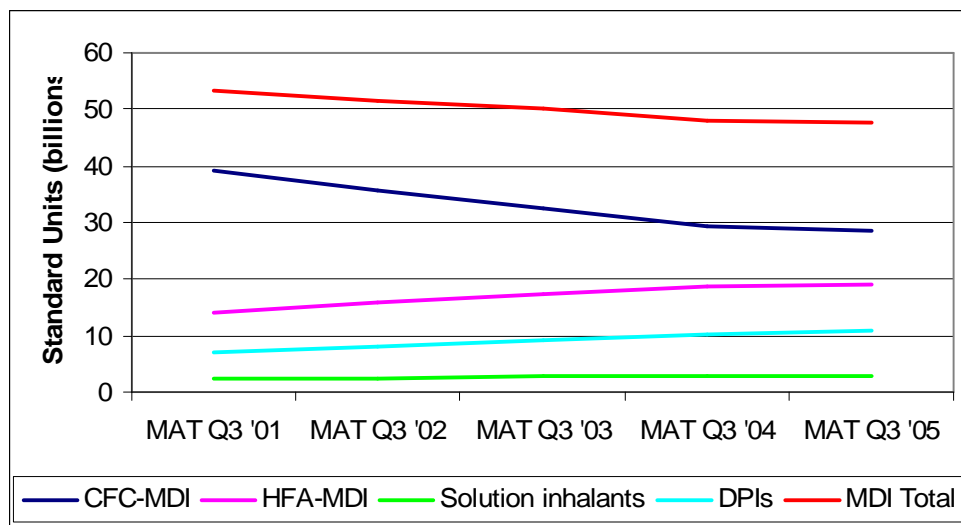


Figure 2: Development of Respiratory Device Market in Units

Figures 3 through 9 (in Appendix I) provide market trend information for the sales volume performance in SUs of CFC MDIs, HFC MDIs, nebulized solution inhalants, and DPIs in several key regions:

- § Top 5 European Markets (Figure 3)
(Germany, Italy, France, Spain, and UK)
- § North America (Figure 4)
- § Latin America (Figure 5)
(Argentina, Brazil, Colombia, Ecuador, Mexico, Venezuela)
- § Australia (Figure 6)

³ See IPCC/TEAP Special Report at 14 (*Summary for Policymakers*).

- § New EU Entrants (Figure 7)
(Poland, Czech Republic, and Slovak Republic)
- § Japan (Figure 8)
- § Africa/Asia (Figure 9)
(Korea, Philippines, South Africa, Taiwan, Turkey)

This data illustrates that the MDI market in these key regions is either constant or declining, with the exception of the Africa/Asia region, where the MDI market is slightly growing during the last five years, but on a relatively low level.

III. ESSENTIAL USE NOMINATIONS FOR 2007 AND 2008

At the request of MDI manufacturers, including some IPAC companies, the European Union and the United States have nominated the MDI for the treatment of asthma and COPD as an essential use of CFCs for the years 2007 and 2008. The chart below summarises the requests:

UNITED STATES	EUROPEAN UNION
2007	2007
Total request (submitted last year): 1493 MT <i>Note: 1000 tonnes authorised by Parties in Decision XVII/5 (December 2005)</i>	Total request: 535 MT No CFCs requested for single-moiety salbutamol MDIs to be exported to non-Article 5(1) Parties.
2008	2008
Total request: 384.97 MT No CFCs requested for use in single-moiety salbutamol MDIs.	<i>Will submit nomination, if necessary, in January 2007.</i>

UNITED STATES NOMINATIONS

TEAP Review of 2007 US Nomination

In January 2005, the United States submitted a 2007 essential use nomination for 1493 MT, of which 932 was intended for salbutamol. In its report last year, TEAP concluded that it was unable to recommend any CFCs for use in 2007, stating that “given the rapidly changing technical and economic environment in these final stages of transition, TEAP believes it would be better able to make its technical assessment in accordance with essential use Decisions if it could consider a nomination for 2007 in 2006.” Despite that prudent conclusion by TEAP, the Parties approved 1000 MT for the US for 2007. However, under Decision VII/28 (par. 2), TEAP has an obligation to “review, annually, the quantity of controlled substances authorized” and “review, biennially, whether the applications for which exemption was granted still meets the essential use criteria”. Thus, TEAP is obliged to review the 2007 US nomination, even though the Parties have approved certain volumes for 2007.

Some may argue that it would be unprecedented for TEAP to recommend, and for Parties to adopt, reductions in essential use volumes after they are approved by the Parties. However, IPAC notes that the approval of the 2007 volumes without TEAP

even having reviewed, let alone having recommended approval of, the volumes was itself unprecedented. This is a disturbing precedent that risks undermining the essential use process. As discussed below, absent the MTOC/TEAP's expert advice and recommendations, there is a risk that CFCs could be allocated by the Parties in a manner that is inconsistent with patient need. Specifically, CFCs could continue to be allocated to non-essential products, possibly reducing the amounts available for products that remain essential and where diligent efforts are underway to develop and launch CFC-free alternatives. In order to preserve the integrity of the essential use process, it is incumbent upon MTOC and TEAP to review the 2007 US nomination and report its findings to the Parties. When it does so, IPAC recommends that TEAP recommend that the 2007 authorisation be reduced so as not to include volumes for (a) salbutamol MDIs, (b) products of companies for which the company has launched a corresponding CFC-free alternative; and (c) products of companies for which the company is not conducting adequate R&D or not using the results of the R&D.

Salbutamol MDIs

As TEAP noted in its 2005 Report, four CFC-free alternatives to salbutamol CFC MDIs are available in the United States. Two of these products have been marketed for several years – one for nearly a decade. FDA, the health authority in the United States, has concluded that patients will be adequately served by these two alternatives. Nevertheless, the United States chose to delay the effective date for salbutamol non-essentiality until the end of 2008. This lengthy phase-out period is not supported by the rationale set forth in the United States' salbutamol action plan.⁴ Moreover, the inordinately-delayed date chosen by the US for salbutamol non-essentiality is inconsistent with Decision IV/25 and other Protocol decisions on the essential use process.

Decision IV/25 (par. 1(a)(ii)) states that a product is “essential” only if there are no “technically and economically feasible alternative” available. With four CFC-free salbutamol MDIs on the market, salbutamol CFC MDIs do not meet this condition. Last year, when TEAP considered the US salbutamol market, the third CFC-free product (IVAX's) had not yet been on the market for a year, and the fourth product (Sepracor's Xopenex) had just been approved but not yet launched. Now, four products are on the market – three of those for over a year – and have demonstrated post-market safety.

Decision XV/5 (par. 3) requests TEAP and MTOC to “make recommendations on nominations for essential-use exemptions for CFCs . . . with reference to the active ingredient of the metered-dose inhalers in which the CFCs will be used and the intended market for sale and distribution” IPAC agrees with TEAP's discussion of this provision in its 2004 Report, that it would be impractical to assess every single

⁴ For a detailed analysis of the United States' salbutamol action plan, please see 11 April 2005 correspondence from IPAC to MTOC Co-Chairs. (Attachment A hereto).

active ingredient in every single market. However, salbutamol is not a “small niche” product; indeed it is the largest single use of CFCs in the United States. Thus, TEAP has an obligation to assess whether salbutamol is still essential in the United States.

Furthermore, in Decisions IV/25 and XV/5, the Parties established that neither TEAP, nor the Parties, may simply defer to an individual Party's decision as to whether Protocol essentiality criteria are met. A TEAP recommendation that CFC salbutamol in the US is no longer essential under Protocol essential use criteria would not be “second guessing” the United States’ domestic decision – it would simply recognize that Protocol essentiality criteria are different from US essentiality criteria.

Therefore, IPAC recommends that TEAP recommend that the Parties reduce the 2007 US essential use authorization, with an explicit condition that the recommended authorisation be clearly designated as only for non-single-moiety salbutamol use (the 2007 nomination for the US was for 1493 metric tonnes and included 932 metric tonnes for single-moiety salbutamol). Simply reducing the authorization without designating the remainder for non-salbutamol could put patients at risk, because it could result in insufficient allocations for some CFC MDI products for which there are not yet CFC-free alternatives. As noted above, IPAC agrees with TEAP’s prior conclusion that it is impractical for them to individually assess each active ingredient that is part of the non-salbutamol portion and this is unnecessary.

MDIs Other Than Single-Moiety Salbutamol

In July 2005, the United States initiated a process to assess the continued essentiality of CFC MDIs other than single-moiety salbutamol MDIs. This is an important first step. The United States has confirmed that, consistent with Decision XVII/5, it will inform the Parties of the estimated timing of regulatory rulemaking(s) on the non-essentiality of these products prior to the Eighteenth Meeting of the Parties. IPAC will closely monitor the regulatory process in the United States, and would be pleased to provide the TEAP and MTOC with further information, as available.

As noted above, IPAC supports approval of volumes for the 2007 US nomination strictly for non-salbutamol use subject to the other conditions as outlined herein. Similarly, IPAC supports the approval of the 384.97 MT nominated by US for 2008, provided that is approved only for the specific active ingredients listed in the US nomination (flunisolide, metaproterenol, ipratropium and salbutamol (in combination), pirbuterol, epinephrine, triamcinolone, cromolyn and nedocromil). Such approval is consistent with the US domestic process: if FDA determines that any of these active ingredients are non-essential, then under US law, sale and distribution of such products would be prohibited, notwithstanding the availability of essential use CFCs. Also, as noted above, MTOC/TEAP should re-review these volumes next year.

EUROPEAN COMMUNITY

Status of MDI Transition

The European Community has made significant progress in transitioning away from CFC MDIs. All twenty-five Member States have declared salbutamol CFC MDIs non-essential, and as of December 2005, the European Community ceased allocating CFCs for salbutamol MDIs intended for sale or distribution in the Member States. The European Community's 2007 nomination does not request any CFCs for use in salbutamol MDIs for sale or distribution in non-Article 5(1) Parties.

With regard to non-salbutamol CFC MDIs, the Commission has facilitated non-essentiality determinations of several products by Member State health authorities. A chart summarising the non-essentiality determinations can be accessed at the Ozone Secretariat's website.

2007 Nomination

Over the past several years, the European Community has achieved substantial reductions in the use of CFCs for MDIs and its nomination requests have decreased accordingly. IPAC supports the European Community's progress, to date, and supports its commitment to continue encourage further reductions in annual licenses, consistent with the European Phase-Out Strategy.

Based upon the representations in the European Community's 2007 nomination, and IPAC's knowledge of the European MDI market and its member companies' expected needs for 2007, the 535 MT nominated appears reasonable. However, IPAC notes that this is only 4 MT less than its 2006 nomination (539 MT). IPAC also notes that a substantial portion of the nomination is for products to be exported outside of the Community. TEAP should have received detailed data on the export markets from the European Community, and has access to the information available from the Global Database on MDIs and DPIs required by Decision XIV/5. We urge the TEAP to carefully evaluate the Community's nomination based upon the most current data available and consistent with Decision IV/25 and other relevant decisions.

MDI TRANSITION ISSUES APPLICABLE TO BOTH NOMINATIONS

Allocating CFCs to Companies That Have Launched a CFC-free Alternative

In its report last year, TEAP expressed strong concern that "companies continue to request essential use quantities for CFCs when they also manufacture HFC MDI alternatives for salbutamol." This is primarily an issue in the United States where the company that launched a CFC-free alternative to salbutamol nearly a decade ago

continues to request and receive the largest annual essential use allocation.⁵ It is inconsistent with several existing Protocol decisions for CFCs to be authorized for use in an MDI for which a corresponding CFC-free alternative has been launched in that market (after an adequate post-marketing period). For example, as noted above, under Decision IV/25 par. 1(a)(ii), a use is only essential if there are no “technically and economically feasible alternatives”. Similarly, par. 1(a)(i) of Decision IV/25 states that a use is essential only if it is “necessary for the health, safety or is critical for the functioning of society”. If a company is marketing a CFC-free alternative, it cannot claim that either of these criteria are met for its CFC product in that market. In addition, par. 1(b)(i) of Decision IV/25 states that production and consumption of CFCs for essential uses should be permitted only if “[a]ll economically feasible steps have been taken to minimize the essential use and any associated emission of the controlled substance”. A company cannot argue that it would be economically infeasible (as opposed to merely commercially disadvantageous) to withdraw its CFC product from the market – thus minimising CFC emissions – when it has a CFC-free alternative to that very product on the market.

Therefore, we suggest that TEAP/MTOC recommend, as a general matter, that at the time of licensing Parties should not allocate essential use CFCs to companies for CFC products for which those companies have launched a corresponding CFC-free alternative (after an adequate post-marketing period). IPAC requests that TEAP/MTOC give attention to, and make a recommendation regarding, this issue in its own right, whether or not TEAP/MTOC also find that salbutamol is non-essential under Protocol criteria.

Active Pursuit of Alternatives

Decision VIII/10 par. 1 calls on each company to conduct "ongoing research and development on alternatives to CFC MDIs with all due diligence and/or collaborate with other companies in such efforts". It was not the intent of the Parties in adopting this provision that R&D should be conducted simply for the sake of advancing scientific knowledge. Rather, as revealed by the title of Decision VIII/10, it was the Parties' intent that the R&D results be used "to promote industry's participation on a smooth and efficient transition away from CFC-based MDIs". In its 2007 nomination, the US stated that “[a]ll companies requesting essential use exemptions submitted information demonstrating their ongoing research and development of alternatives to CFC MDIs” (emphasis added). Although IPAC is not privy to confidential information submitted to EPA, this statement appears to be contradicted by existing circumstances based on publicly available information. For example, continuing to market a CFC

⁵ Schering Plough was licensed 937 tonnes of CFCs in 2003 (67 FEDERAL REGISTER 79508; Dec. 17, 2002); 918 tonnes in 2004 (69 FEDERAL REGISTER 4059; Jan. 28, 2004); and 816 tonnes in 2005 (70 FEDERAL REGISTER 49836; Aug. 24, 2005). These CFCs were requested solely for use in the production of CFC salbutamol MDIs.

product after launching a corresponding CFC-free alternative (e.g., Schering Plough's CFC salbutamol) clearly violates the intent of Decision VIII/10 par. 1.

It was also the intent of the Parties, in adopting this provision, that each company conduct R&D "with all due diligence" – that is, each company should conduct R&D at a level commensurate with getting results within a reasonable timeframe. Therefore, in addition to companies that have CFC-free alternatives, but continue to use CFCs, IPAC believes that TEAP/MTOC should carefully review the portion of the nominations intended for companies that may be conducting only limited research and development on alternatives. Although the US nominations for both 2007 and 2008 state that "all companies" requesting essential use volumes had demonstrated ongoing R&D, IPAC notes that EPA's 2005 domestic allocation included – in addition to significant quantities to Warrick (a generic subsidiary) – such companies as Armstrong (a generic company) and Wyeth (the manufacturer of OTC epinephrine MDIs). Generic companies typically do not conduct research and development. IPAC suggests that MTOC inquire to the US whether either its 2007 or its 2008 nominations include volumes for Wyeth or Armstrong. If these companies are included, MTOC should request that EPA substantiate that these companies are conducting R&D at an adequate level. Absent such information, MTOC could conclude that there is insufficient information for it to make a recommendation on those volumes.

Management of Stockpiles

Decision XVI/12 requires Parties to give due consideration to existing CFC stockpiles when preparing their essential use nominations "with the objective of maintaining no more than one year's operational supply." Decision XVII/5 (2) supplements this requirement by making it clear that non-Article 5(1) Parties must take into account both pre- and post-1996 stockpiles at the licensing and allocation stage so that individual MDI manufacturers maintain no more than a one-year operational supply. IPAC has long supported limiting stockpiles to this level, and commends the Parties for adopting these provisions to promote effective and efficient management of stockpiles. It is important for these Decisions to be proactively and effectively implemented by the Parties. IPAC urges TEAP to carefully assess the Parties' nominations to ensure that stockpiles are well-managed consistent with Decisions XVI/12 and XVII/5.

In this regard, IPAC believes the US response to question 5 of the Essential Use Handbook (2005 version) may require clarification. This question requires each nominating Party to confirm that it has given due consideration *inter alia* to whether:

- (a) Each company's existing stock of pharmaceutical-grade CFCs (including CFCs the company possesses or has title to, pre- and post- 1996) aims not to exceed one year's operational supply (the amount used by the company to produce CFC MDIs in the preceding year);

(d) All available pre-1996 stockpiles have been, or will be, depleted by companies before drawing on essential use quantities and thereby assure that pre-1996 stockpiles are taken into account in making essential use requests.

In responding to this question, the US stated that it “aims to ensure no more than a one-year operational supply of stocks (aggregate pre and post 1996) available to companies and makes reductions to the amount nominated and allocated to reflect this calculation in accordance with the language in Decision IX/6 [sic] and related decisions.”⁶ IPAC urges TEAP to seek clarification to ensure that Decisions XVI/12 and XVII/5 are being effectively implemented.

Finally, IPAC believes that in implementing Decision XVII/5, Parties should take into account not only stocks of bulk CFCs, but also the CFC content of stocks of manufactured CFC MDIs held by individual companies. Many MDI products have a shelf life of up to two years. Companies should not be allowed to circumvent the one-year operational supply requirement by producing and storing excessively large inventories of actual MDI product. IPAC therefore recommends that TEAP ask both nominating Parties whether they have included the CFC volume of MDI inventories in their stockpile data reported to TEAP, and, if not, request that they provide such information to TEAP. TEAP should also ask nominating Parties to take MDI inventories into account in their respective implementation of Decision XVII/5’s stockpile limitation provision.

⁶ It should be noted that Decision IX/6 concerns only the critical use exemption, not the essential use exemption. The US statement that it was reflecting the one-year supply calculation in essential use volumes allocated is contradicted by EPA’s public statements in the August 2005 final rule allocating essential use volumes for 2005 (which was issued before Decision XVII/5). In that final rule, EPA stated that it was not required to apply the one-year rule to domestic allocations (see 70 FED. REG. 49836, at 43839-43840).

IV. MDI TRANSITION IN ARTICLE 5(1) PARTIES

TEAP's 2005 Report provides some information on the status of the MDI transition in several Article 5(1) Parties, noting that it can be difficult to make a full assessment in light of insufficient information. The attached database summarises the availability of CFC-free alternatives produced by IPAC companies in Article 5(1) countries.⁷ IPAC acknowledges the challenges in evaluating the state of transition in these Parties and will consider additional ways that it might support TEAP's efforts to assess the progress of the transition and encourage positive momentum forward.

IPAC also notes that at MOP-17 the Parties adopted Decision XVII/14: *Difficulties faced by some Article 5 Parties with respect to chlorofluorocarbons used in the manufacture of metered-dose inhalers*. The Decision recognizes that some Article 5(1) Parties may encounter difficulties in obtaining sufficient supply of CFCs for MDIs during 2007-2009 in light of the phase-out schedules under the Protocol. The Parties agreed to consider these issues at their 2006 meetings and requested that the Executive Committee of the Multilateral Fund address certain issues. IPAC agrees that this is an important issue and will provide further input as consideration of this issue evolves. IPAC acknowledges the Parties' suggestion that the Executive Committee of the Multilateral Fund consider hosting regional workshops to raise awareness and educate stakeholders on the MDI transition.

⁷ See Attachment B.

V. IPAC'S EFFORTS TO FACILITATE THE TRANSITION

Transition Activities

IPAC continues to actively support the transition at the national level in the United States, European Union, and other Parties. IPAC actively engaged in the FDA rulemaking process on salbutamol MDIs, as appropriate, and supported removing salbutamol's essential use designation effective 31 December 2005 – a step that would have achieved a significant reduction in overall CFC usage. In light of the wide availability of CFC-free salbutamol MDIs, IPAC has continued to advocate the cessation of allocations of CFCs for salbutamol MDIs in all non-Article 5(1) Parties.

In Europe, IPAC has actively supported the transition of short-acting beta agonists, such as salbutamol, and has supported the Commission in its efforts to transition other classes of products and hopes that these efforts occur in a timely and efficient manner, consistent with patient care.

Approval and Launch of CFC-Free MDIs and DPIs

Decision XII/2 asks Parties to urge each MDI company to seek approval for its CFC-free alternatives in the company's domestic and export markets. IPAC has prepared a database reviewing the world-wide availability of CFC-free products. This data indicates that at least one CFC-free MDI is now available in at least 120 countries and DPIs are available in more than 100 countries. The database can be viewed on IPAC's website at www.ipacmdi.com.

For well more than a decade, IPAC companies have expended significant resources to research and develop CFC-free alternatives to CFC MDIs. Rather than waiting for national governments to force a transition, IPAC companies have worked to launch CFC-free alternatives on the market as soon as possible after approval by health authorities. This voluntary, proactive approach represents an important contribution to a timely and effective transition in the marketplace and all companies should be encouraged to undertake a similar approach. However, IPAC is fully aware of and concurs with TEAP's conclusion (noted above) that market forces alone are insufficient, and regulatory intervention is necessary to fully accomplish the transition.

VI. CONCLUSION

IPAC greatly appreciates the leadership that MTOC and TEAP have exhibited in facilitating the MDI transition under the Montreal Protocol. We thank you for your attention to the issues addressed in this submission and look forward to continued cooperation with MTOC and TEAP.

APPENDIX I

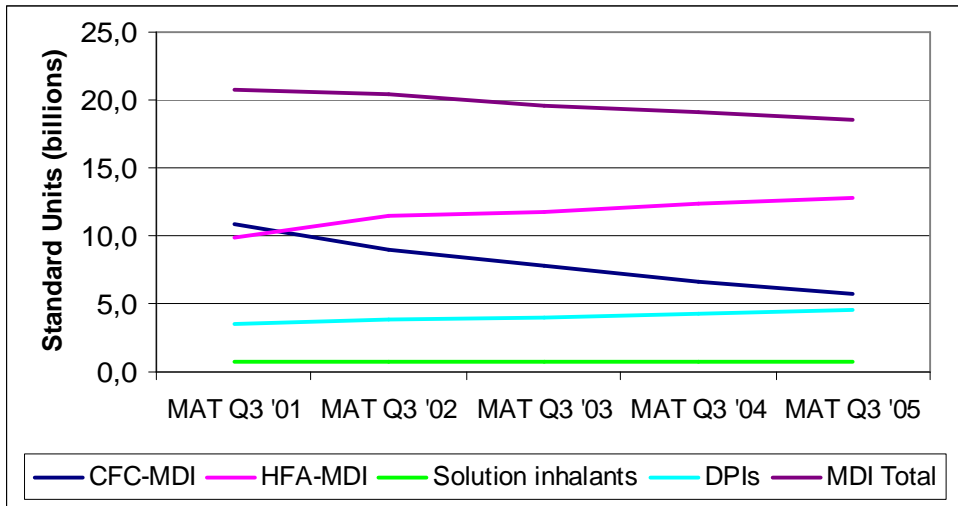


Figure 3: Performance of Device Market in Top 5 European Pharma Markets

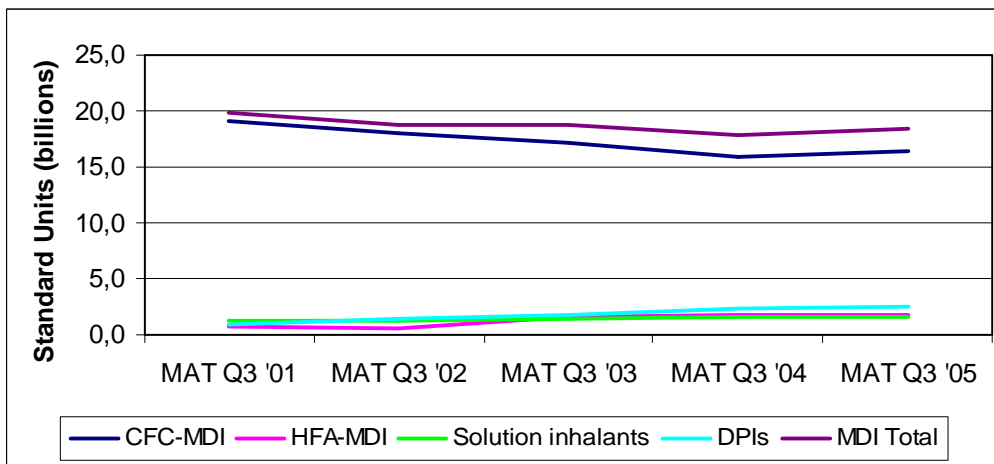


Figure 4: Performance of Device Market in North America

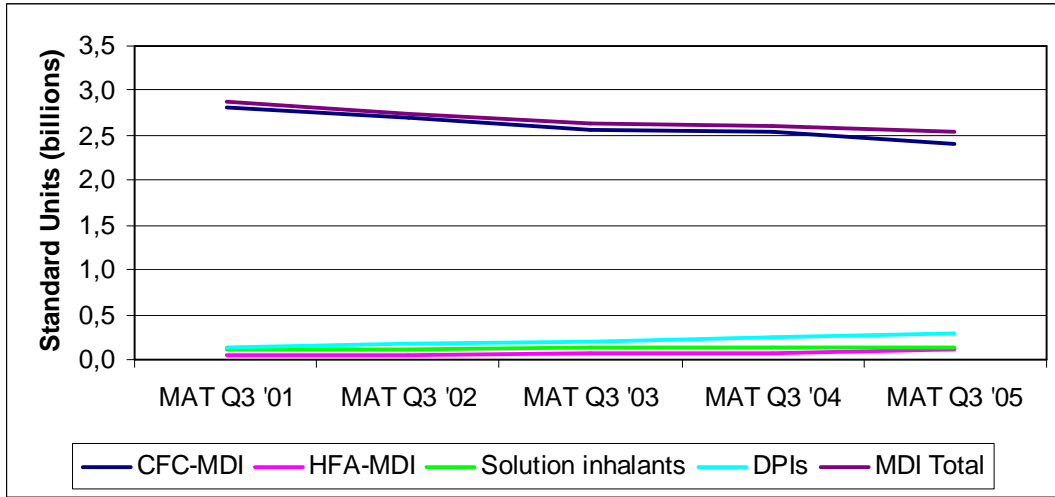


Figure 5: Performance of Device Market in Latin America

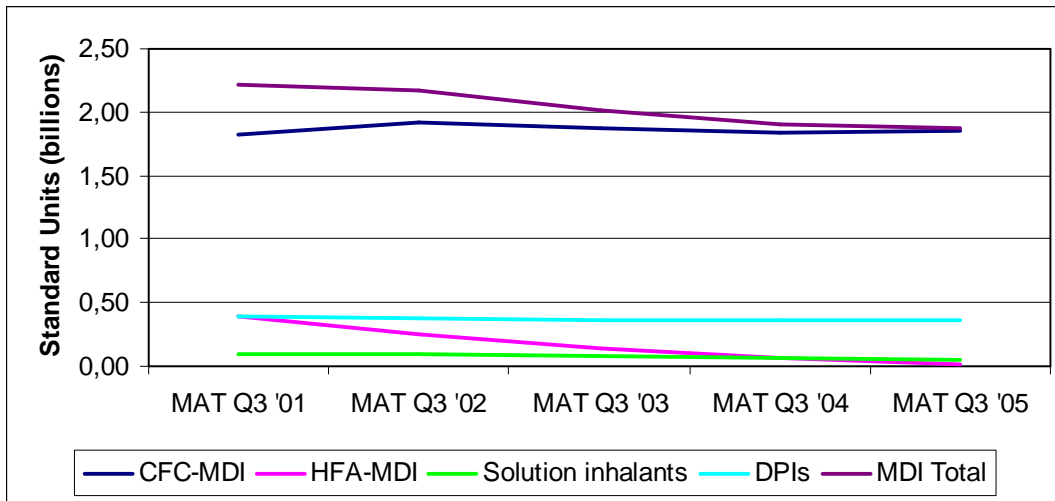


Figure 6: Performance of Device Market in Australia

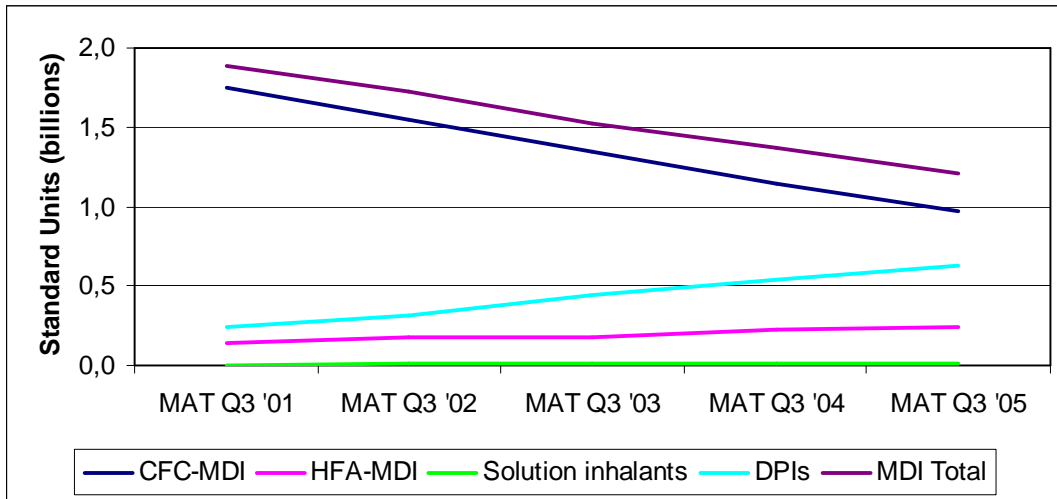


Figure 7: Performance of Device Market in New EU Entrant Countries

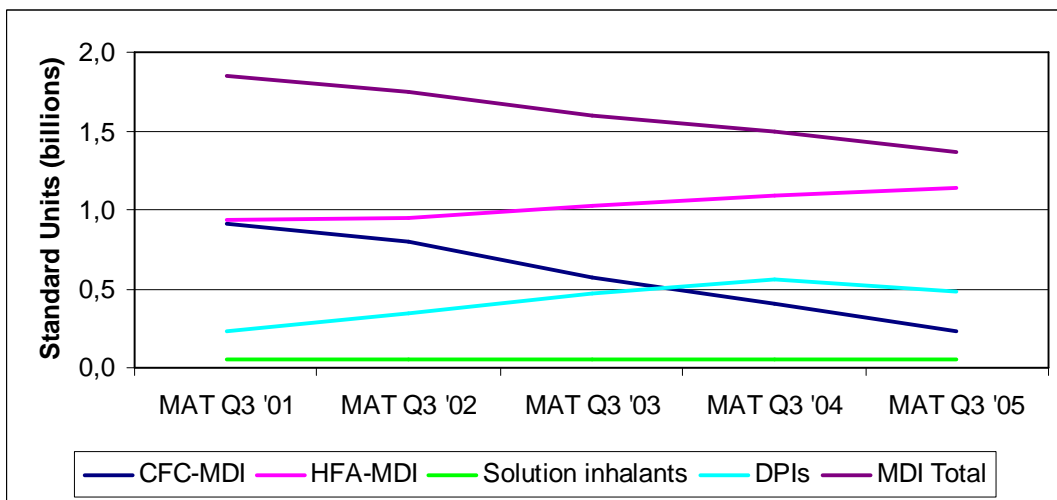


Figure 8: Performance of Device Market in Japan

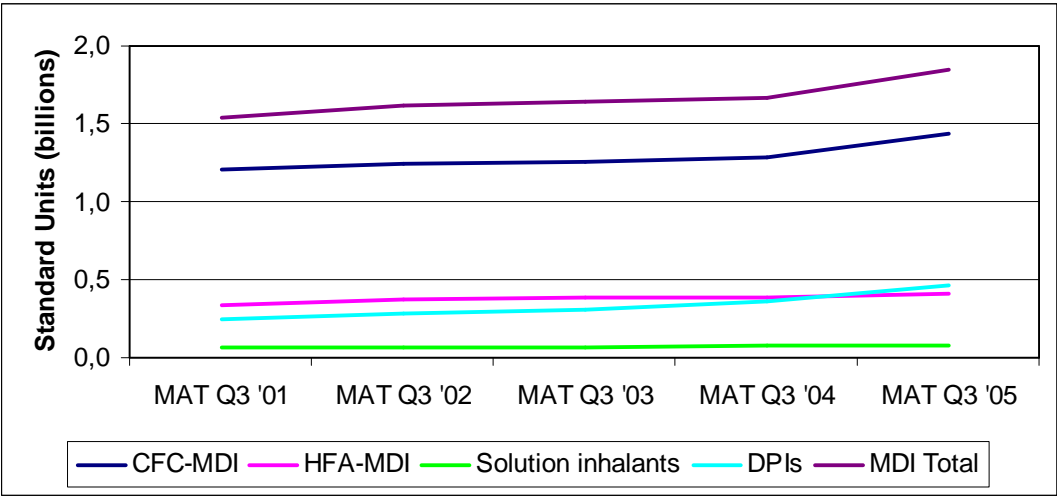


Figure 9: Performance of Device Market in Asia/Africa Market (without Japan and Australia)