

ADDENDUM (OCTOBER 2009)
ESSENTIAL USE NOMINATIONS FOR MDIS
REVISED NOMINATION FROM THE UNITED STATES FOR 2011

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1 Essential Uses

1.1 Revised Essential Use Nomination for Metered Dose Inhalers from the United States for 2011

During the 29th Meeting of the Open Ended Working Group, representatives of the United States' delegations held bilateral discussions with the co-chairs of the Medical Technical Options Committee about the United States' essential use nomination for CFC metered dose inhalers for 2011. Based on newly available information, the United States submitted a revised nomination in August 2009, which reduced its request from 67 tonnes to 52 tonnes of CFCs and provided additional information justifying its nomination.

This Report includes the Medical Technical Options Committee's assessment of, and recommendations for, the revised nomination from the United States. The nominations from and recommendations for other nominating Parties for CFC metered dose inhalers for 2010 remain unchanged from the Technology and Economic Assessment Panel's May 2009 Report.

1.1.1 *Criteria for Review of Essential Use Nominations for MDIs*

Decision IV/25 of the 4th Meeting and subsequent Decisions V/18, VIII/9, VIII/10, XII/2, XIV/5, XV/5, XVI/12, XVII/5, XVIII/7, XVIII/16, XIX/13 and XX/3 have set the criteria and the process for the assessment of essential use nominations for MDIs for Parties to the Protocol.

1.1.2 *Review of Revised Nomination*

The revised nomination was assessed according to the guidelines for essential use contained within the *Handbook on Essential Use Nominations* (TEAP, 2005) and subsequent Decisions of the Parties.

Concurrent with the evaluation undertaken by the MTOC, copies of nominations are provided to the Technology and Economic Assessment Panel (TEAP). The TEAP and its TOCs can consult with other individuals or organisations to assist in the review and to prepare TEAP recommendations for the Parties.

1.1.3 *Committee Evaluation and Recommendation*

Quantities are expressed in metric tonnes.

1.1.3.1 *United States*

Year	Quantity nominated
2011	52 tonnes

Specific Use: MDIs for asthma and COPD for the active ingredient epinephrine for use solely within the United States.

Recommendation: Unable to recommend.

In August 2009, the United States submitted a revised nomination of CFCs for MDIs for the active ingredient epinephrine for use solely within the United States for the year 2011. The United States reduced its original request from 67 tonnes to 52 tonnes of CFCs and provided additional information justifying its nomination and an update on the transition to alternative products.

Epinephrine CFC MDI

In its original assessment in the May 2009 report, MTOC did not consider CFCs for epinephrine MDIs to be essential due to the availability of alternatives.

The United States, in its revised nomination, states that it “*fundamentally agrees with the MTOC that CFC-propelled epinephrine inhalation aerosol is not essential, but the issue is the timing of ceasing production of the product.*” The United States notes that the FDA published final rule removes the essential designation for CFC-propelled epinephrine inhalation aerosol effective December 31, 2011 (73 FR 69532). Thereafter, CFC-epinephrine cannot be sold, distributed or offered for sale or distribution in the United States pursuant to Section 610 of the Clean Air Act. However, the United States maintains that epinephrine CFC MDIs need to be produced and available through the end of 2011 to safely complete the transition to therapeutic alternatives.

The United States detailed the history and background to epinephrine use in its market and the uniqueness of its role as an over-the-counter (OTC) medication rather than as a prescription drug. While epinephrine is intended only for use by patients for the temporary relief of asthma and is not considered the drug of choice by physicians treating patients with asthma, the United States states that the product serves an important and unique role for as many as 1.7 to 2.3 million asthma patients. Some of these patients are low-income and other patients without access to adequate health care who rely on epinephrine as their sole asthma medication or as a back-up to their prescription medication during an acute asthma episode. The United States argues that the forced removal of this product before the planned end date of December 31, 2011, due to unavailability of CFCs, raises serious issues with respect to patient access to asthma treatment.

The manufacturer of epinephrine CFC MDIs, Armstrong, believes that it will be able to bring a CFC-free epinephrine inhaler to the market by the beginning of 2011. The FDA final rule does not require, nor is it dependent on, the development of a replacement CFC-free epinephrine inhaler. The United States maintains that epinephrine CFC MDIs need to be available through the end of 2011 to safely complete the transition to therapeutic alternatives.

The phase-out of epinephrine CFC MDIs is expected to be complicated. As the product is sold OTC, many users of this product may not interact with health care providers who would normally assist the patients in transitioning to alternative therapies. Salbutamol is considered a suitable alternate bronchodilator from a clinical pharmacology standpoint; however, salbutamol is only available with a physician prescription. It is anticipated that patients currently using epinephrine CFC MDIs will probably need to be brought under physician care and transitioned to an alternate product. The FDA held a public workshop in September 2009 to discuss this transition. The United States maintains that availability of CFCs through the end of 2011 will provide the additional time required to prevent a sudden and serious treatment disruption to the patients who currently rely on this OTC product. The United States asserts that the availability of prescription salbutamol as an alternative bronchodilator should not, by itself, be assumed sufficient to meet the public health needs of this population with immediate effect.

Quantity Requested

According to the United States, the quantity requested is influenced by the possible increased production and consumption of epinephrine CFC MDIs until removal of essential designation effective December 31, 2011 (73 FR 69532). The United States maintains this is due to the changed availability of short-acting beta-agonist bronchodilators in the United States with the phase-out of CFCs. Before the CFC-phase-out started, the United States had multiple short-acting beta-agonist bronchodilators in the market, such as salbutamol (called albuterol), metaproterenol, pirbuterol, and epinephrine, some of which had multiple manufacturers. Salbutamol was available in generic products that provided substantial price competition. Of the short-acting beta-agonist bronchodilators, only salbutamol MDIs have until now been reformulated with an HFC propellant. Salbutamol CFC MDIs, including generic products, were removed from the domestic market effective December 31, 2008 (70 FR 17168). The manufacturer of metaproterenol has recently announced that it will not reformulate metaproterenol and will stop production of the CFC MDI product, and the future of pirbuterol remains uncertain at present. However the volume of sales of these two products is relatively small.

With these market changes, the United States asserts that there will be increased demand for epinephrine CFC MDIs in the near term. The United States argues that some patients may temporarily purchase epinephrine CFC MDI as an alternative for economic reasons with the removal of generic salbutamol CFC MDI products. The revised nomination suggests that patients who were using metaproterenol and pirbuterol may also seek alternative short-acting beta-agonist bronchodilators, and epinephrine is one such option that patients may temporarily use. The United States contends that, with the announced end date of December 31, 2011 for the market availability of epinephrine CFC MDIs, patients may acquire multiple canisters and keep them for their personal use beyond the end date. The United States therefore considers that it is possible that the production and consumption of epinephrine CFC MDIs will increase to meet this increased temporary demand until the end of 2011 after which the ban on sale and distribution becomes effective.

Stockpile

In its assessment in the May 2009 report, MTOC did not consider the original nomination to be essential, asserting that the nominated quantities might be supplied from existing stockpiles, including from the manufacturer's one-year strategic reserve that might be available for the final year of manufacture of epinephrine CFC MDI until the ban on sale and distribution becomes effective.

The United States asserts that CFC stocks are not available and not adequate for the manufacture of epinephrine CFC MDIs for 2011 for two reasons.

Firstly, individual manufacturers hold CFC stocks in the United States; therefore, relying on aggregate stock amount is not reflective of the manufacturing need of an individual manufacturer. In accordance with Decision XVII/5(2) and Decision XIX/13(2), the one-year operational supply of CFC stock applies on a manufacturer-by-manufacturer basis and not as an aggregate. CFC stocks held by manufacturers are confidential business information and this information cannot be shared. However, the United States assures that a calculation of its CFC stock situation by

individual manufacturer in accordance with Decisions XVII/5(2) and XIX/13(2) leads to the conclusion that CFC stocks are not available.

Secondly, during allocation of CFCs to manufacturers, the FDA considers previous production history rather than possible future production in applying the one-year operational supply provision of Decision XVII/5(2) and Decision XIX/13(2). For example, during allocation of CFCs in 2009, historical productions in the previous years were taken into consideration for the operational supply need for 2010. Due to a possible increase in the production and consumption of epinephrine CFC MDIs, the one-year operational supply stock for the future year is likely to fall short of the stock needed for one year of production. The United States assures that it will apply strict calculations and only allocate CFCs that are essential through domestic licensing. In the past, the United States has allocated less than the exempted amount authorized by Parties based on such strict calculation.

MTOC Comments

MTOC took the unanimous view that it could not recommend the revised nomination on the grounds that it did not meet the criteria for essential use. MTOC is unable to find reason to reverse its decision not recommending exemption.

MTOC does not consider epinephrine CFC MDIs to be an essential use due to the available alternatives to which patients are being transitioned.

The revised nomination states that the manufacturer's one-year operational supply would not be adequate to supply the CFCs for the manufacture of epinephrine CFC MDIs for 2011. The revised nomination provides no specific information about the transferability and accessibility of stockpile between manufacturers, other than to say that stockpiles in the United States are non-fungible and calculated on an individual manufacturer basis. There would appear to be market inflexibility and commercial or other barriers to stockpile transfers. Pre-1996 stockpile may be available to supply the request for 52 tonnes without the need for an essential use exemption but this may not occur for reasons of commercial competitive advantage by other manufacturers. The Protocol's essential use Decision IV/25(1)(b), against which TEAP and its TOCs are instructed to make recommendations, clearly states that a use is essential only if existing stocks are not available in sufficient quantity and quality. Information is not provided to know whether this will be the case or not in 2011, but a stockpile currently exists in the United States and in 2008 nearly 200 tonnes of pre-1996 stockpile was destroyed by a manufacturer no longer producing CFC MDIs.