# ADDENDUM (OCTOBER 2010)
# ESSENTIAL USE NOMINATIONS FOR MDIS
# REVIEW OF REVISED NOMINATION FROM BANGLADESH FOR 2011

TABLE OF CONTENTS ..... PAGE

# 1 Essential Uses

## 1.1 Review of Revised Essential Use Nomination for Metered Dose Inhalers from Bangladesh for 2011

During the 30th Meeting of the Open Ended Working Group, representatives of the delegation of Bangladesh held bilateral discussions with the attending co-chairs of the Medical Technical Options Committee about Bangladesh's essential use nomination for CFC metered dose inhalers for 2011. In those discussions, Bangladesh requested that TEAP and its MTOC reassess Bangladesh's nomination. MTOC requested additional information from Bangladesh in order to undertake this review. Subsequently, information was submitted by Bangladesh along with a revised nomination in September 2010, which reduced the request from 113.73 tonnes to 85 tonnes of CFCs, and provided additional information justifying its nomination in September and October.

This Report includes the Medical Technical Options Committee's assessment of, and recommendations for, the revised nomination from Bangladesh. MTOC can also report that the essential use nomination from Iran for 2011 for 105 tonnes has been withdrawn since CFC MDIs have been successfully phased out in that country. MTOC wishes to commend to the Parties the transition efforts of Iran and its technology transfer partners. The remaining nominations and recommendations for CFC metered dose inhalers for 2011 remain unchanged from the Technology and Economic Assessment Panel's May 2010 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, VII/28, VIII/9, VIII/10, XII/2, XIV/5, XV/5, XVI/12, XVIII/16, XX/3 and XXI/4 have set the criteria and the process for the assessment of essential use nominations for MDIs for Parties not operating under paragraph 1 of Article 5 and Parties operating under paragraph 1 of Article 5 of the Protocol. Other essential use decisions relevant to these Parties are Decisions XVII/5, XVIII/7 and XIX/13.

### *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, 2009).

The TEAP and MTOC can consult with other individuals or organisations to assist in the review and to prepare recommendations for the Parties.

### *1.1.3 Committee Evaluation and Recommendation of Bangladesh Nomination for 2011*

Quantities are expressed in metric tonnes.

| Year | Quantity nominated |
|---|---|
| 2011 | 85 tonnes |

*Specific Use:* MDIs for asthma and COPD.

Active ingredients and intended markets for which the nomination applies:

| Active Ingredient | Intended market | Nomination in January 2010 Quantity (Tonnes) | Revised Nomination in September 2010 Quantity (Tonnes) |
|---|---|---|---|
| Beclomethasone | Bangladesh | 8.89 | 5.0 |
| Ciclesonide | Bangladesh | 0.48 | 2.5 |
| Fluticasone/Salmeterol | Bangladesh | 9.78 | 8.0 |
| Ipratropium | Bangladesh | 1.34 | 2.0 |
| Ipratropium/Salbutamol | Bangladesh | 25.32 | 21.5 |
| Levosalbutamol | Bangladesh | 0.87 | 3.0 |
| Salbutamol | Bangladesh | 65.32 | 40.0 |
| Salmeterol | Bangladesh | 1.10 | 2.0 |
| Tiotropium | Bangladesh | 0.63 | 1.0 |
| **Total** | | **113.73** | **85.0** |

*Recommendation*:

Recommend 37.0 tonnes of CFCs for MDIs for use in Bangladesh only for ciclesonide, fluticasone/salmeterol, ipratropium, ipratropium/salbutamol, salmeterol and tiotropium.

Unable to recommend CFCs for MDIs for active ingredients beclomethasone, levosalbutamol and salbutamol.

*Comments*

In September 2010, Bangladesh submitted a revised nomination of CFCs for MDIs for the year 2011. Bangladesh reduced its original request from 113.73 tonnes to 85 tonnes of CFCs following further consultation with manufacturers, and provided additional information justifying its nomination. There are increased quantities of CFCs requested now for ciclesonide, ipratropium, levosalbutamol, salmeterol, tiotropium, and decreased quantities requested for other active ingredients.

The requested CFCs are for the manufacture of MDIs for domestic consumption only, as Bangladesh states that it does not export CFC MDIs. There are multiple HFC MDIs on the market in Bangladesh for salbutamol and beclomethasone and there are single HFC or DPI inhalers for budesonide, fluticasone/salmeterol, ipratropium, ipratropium/salbutamol and salmeterol. Locally made CFC-free MDIs were first introduced in 2006, and their introduction and adoption has continued to expand. Currently, three companies are manufacturing HFC MDIs while two companies manufacture DPI inhalers. In general, the pricing of these alternatives is comparable to their CFC counterparts. MTOC believes that uptake has been slower than

expected due to the continued market presence of CFC MDIs. There are as at yet no CFC-free alternatives for ciclesonide and tiotropium.

Total combined capacity of HFC MDI manufacture of salbutamol and beclomethasone among Bangladesh MDI manufacturers by the end of 2010 will be 25 million HFC MDI units per year. Bangladesh MDI consumption is estimated at 5 million per year. MTOC believes that the combined capacity for salbutamol and beclomethasone HFC MDIs is more than adequate to supply Bangladesh's needs.

Bangladesh claims that while the HFC MDI capacity is adequate, physicians and patients need more time to get accustomed to HFC inhalers. Twenty per cent of Bangladesh patients have converted to using salbutamol HFC MDIs. Bangladesh claims that some older patients rarely visit their doctor and would rather buy their medicine themselves. Bangladesh explains its concern that if patients find any problems with using HFC inhalers, they could stop visiting their doctors and switch to oral steroids in the absence of CFC inhalers. Bangladesh also states that many doctors are not convinced of the benefits and needs of shifting to HFC inhalers. Therefore, in the interests of a smooth transition, Bangladesh argues that CFC inhalers are needed in the market for some time. Bangladesh wishes to complete its awareness activities before deregistering CFC inhalers in about 2012.

*MTOC Comments*

The main difference between CFC and HFC MDIs, as perceived by the patient, is a mild difference in taste of the HFC formulations. To date, the withdrawal of CFC MDIs has occurred safely in most markets within a year of HFC MDIs becoming available. In most countries, the experience has been of a smooth and easy transition for patients, including in developing countries such as Iran and other Middle East countries. Experience has also shown that the parallel presence of CFC MDIs on the market stagnates the uptake of CFC-free alternatives, probably through reluctance for change. Physicians and patients accept a change in therapy once there is no alternative but to change to a new asthma therapy. Once the change is made, there have been very few, if any, medical issues.

Generally educational activities have been through the pharmaceutical companies and prescribing doctors, to assure the patient that the pharmacological outcome of alternatives is the same as with CFC MDIs. Furthermore the mild alcohol taste has been found to help to remind patients that they have received an effective dose.

MTOC understands that in Bangladesh physicians prescribe most patients their medication. It seems unlikely to MTOC that a patient, accustomed to MDI therapy, would revert to a reliance on oral therapy in the absence of CFC MDIs, despite HFC and DPI inhalers being available. Oral therapy results in obvious adverse systemic side effects, arguably significantly less acceptable to a patient than a mild difference in taste with a HFC inhaler. Also, per dose, MDI therapy is far cheaper than any oral therapy.

MTOC understands that national educational activities in Bangladesh started in earnest at least as early as March 2009, and that Bangladesh's educational initiatives are progressing well. MTOC sees little benefit in postponing transition of salbutamol and beclomethasone CFC MDIs for a further 12 months. This would also penalise the pharmaceutical companies that have made significant investment in developing and launching the alternatives. MTOC is confident that

transition will continue to proceed smoothly as CFC MDIs are withdrawn. With the essential use exemption quantity approved for 2010, there should be sufficient CFC in the supply chain to satisfy any remaining needs for salbutamol and beclomethasone for 2011, while patient education continues and HFC MDI capacity becomes fully utilised.

For Bangladesh's original nomination, MTOC recommended 38.65 tonnes of CFCs for the manufacture of MDIs for the active ingredients ciclesonide, fluticasone/salmeterol, ipratropium, ipratropium/salbutamol, salmeterol and tiotropium. However, with the availability of alternatives for salbutamol and beclomethasone CFC MDIs, MTOC was unable to recommend CFC quantities for these products. Also, MTOC does not regard levosalbutamol (an isomer of salbutamol) as essential given the availability of multiple salbutamol products.

For Bangladesh's revised nomination, taking into account the changed quantities nominated, MTOC recommends 37.0 tonnes of CFCs for MDIs for use in Bangladesh only for ciclesonide, fluticasone/salmeterol, ipratropium, ipratropium/salbutamol, salmeterol and tiotropium. However MTOC is unable to recommend CFCs for MDIs for active ingredients beclomethasone, levosalbutamol and salbutamol due to the availability of alternatives.