ADDENDUM (AUGUST 2013)
ESSENTIAL USE NOMINATIONS FOR MDIS
ADDITIONAL INFORMATION FOR
THE RUSSIAN FEDERATION ESSENTIAL USE NOMINATION 2014

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1 Essential Uses

1.1 Additional Information relating to the Essential Use Nomination for Metered Dose Inhalers from the Russian Federation for 2014

During the 33rd Meeting of the Open-ended Working Group (OEWG), representatives of the Russian Federation's delegation provided additional information regarding its Essential Use Nomination for CFC metered dose inhalers (MDIs) for 2014. An informal group held discussions at the OEWG, which was attended by present co-chairs of the Medical Technical Options Committee. On 25th June, the Russian Federation provided additional information justifying its nomination for review by MTOC. On 27th June, UNIDO provided supporting information regarding an updated tentative schedule for the GEF co-funded conversion project undertaken by UNIDO with the two Russian CFC MDI manufacturers, Moschimpharmpreparaty and Altayvitaminy.

This Addendum Report includes the Medical Technical Options Committee's assessment of, and recommendations for, the nomination from the Russian Federation based on the additional information provided. The nominations from and recommendations for China for CFC metered dose inhalers for 2014 and 2015 remain unchanged from the Technology and Economic Assessment Panel's May 2013 Report.

1.2 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, XXI/4, XXII/4, XXIII/2 and XXIV/3 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.

1.3 Review of Nominations

Nominations are assessed according to the guidelines for essential use contained within the *Handbook on Essential Use Nominations* (TEAP, 2009) and subsequent Decisions of the Parties. Recommendations are made in accordance with Decision XV/5(3), which requests TEAP and its TOC to make recommendations on nominations for essential use exemptions for CFCs for MDIs with reference to the active ingredient of the metered-dose inhalers in which the CFCs will be used and the intended market for sale or distribution.

1.4 Committee Evaluation and Recommendation of the Russian Federation's Essential Use Nomination for 2014

Quantities are expressed in metric tonnes.

Year	Quantity nominated
2014	212 tonnes

Specific Use: MDIs for asthma and COPD

Nominated quantities, active ingredients and intended markets for which the nomination applies:

Year	Active Ingredient	Intended market	Quantity (Tonnes)
2014	Salbutamol	Russian Federation	212.0

Recommendation: 212 tonnes CFCs for MDIs for intended use in the Russian Federation for the active ingredient salbutamol for 2014.

Additional information

In the TEAP Report May 2013, MTOC recommended 106 tonnes of CFCs for the manufacture of MDIs containing salbutamol, for domestic use in the Russian Federation for 2014, to provide time for market transition to imported CFC-free inhaler products. At the Open-ended Working Group, the Russian Federation restated its request for 212 tonnes of CFCs for MDI manufacture to allow time to complete conversion of two domestic MDI manufacturers to HFC MDIs, and for patient safety. The Russian Federation provided additional information in support of its original nomination of 212 tonnes, in conjunction also with information provided by UNIDO, with a request for MTOC to review the 2014 nomination in light of this additional information.

The Russian Federation elaborated that an exemption of 106 tonnes, half of the quantity nominated of 212 tonnes, would create a gap of 6 months between the production of Russian-made CFC MDIs and HFC MDIs. The Russian Federation indicated that during this period Russian patients would be required to change their usual MDI to a different, imported, MDI. The Russian Federation indicated that most physicians would not recommend this approach.

In addition, the Russian Federation explained that Russian-made salbutamol CFC MDIs occupies 80 per cent market share and is included in the list of medicines provided free of charge by the Government. According to the Russian Federation, almost all of the CFC MDIs made by the Russian manufacturers are supplied to patients free of charge, if a patient uses the special form received from a physician to be supplied free medicine. According to the Russian Federation, some patients may go to the pharmacy without the form, and purchase the medicine themselves, but this is not common. Reportedly, there is a large proportion of low-income patients that cannot afford to buy the imported MDIs and rely on the free medicine. The Russian Federation indicated that more imported MDIs would not be added to the list of free medicines.

In July, the Russian Federation further reported its efforts to investigate global CFC stockpiles to supply its CFC requirements for MDI manufacture in 2014. The Russian CFC importer has contacted the owners of available stockpile of pharmaceutical-grade CFCs in the United States (the Boehringer-Ingelheim and Honeywell stockpile of 280 tonnes CFCs reported in the TEAP Report May 2013). The Russian Federation indicated that the exporter and importer might find it more commercially desirable to sell/purchase all 280 tonnes in one transaction. The Russian Federation signalled the possibility that the full 280 tonnes might eventually be required to complete transition. However, it is not adjusting its nomination for 2014.

The tentative revised schedule provided by UNIDO in June indicates completion of the conversion project by the end of 2014, with the commencement of commercial manufacture. This is unchanged from the original project document approved by GEF regarding the duration of the project. Another important milestone, equipment delivery and installation, is now scheduled

for February to April 2014. In the TEAP Report May 2013, MTOC reported that UNIDO predicted completion of equipment installation by mid-2014, with a new bidding process for a revised tender and a final contract expected in May 2013. Due to some delays, the new schedule revises the timelines for contract finalisation to the end of July 2013, but this has since been completed 2 weeks ahead of schedule. The revised schedule for equipment installation indicates efforts to accelerate activities to keep the original milestones and completion date on track.

MTOC Comments

The Russian Federation is concerned that changing over patients within a short period of time from Russian-made CFC MDIs to imported salbutamol HFC MDIs could have adverse outcomes for Russian patients. However, experience with global transition has shown that, with appropriate medical supervision, there are few if any impacts on adherence to the new medicines or on health, in moving patients from one salbutamol inhaler to another, including from CFC MDIs to HFC MDIs.

The information provided by Russia regarding the proportion of patients accessing Russian-made asthma medicine free of charge differs from information reported previously by MTOC. In 2010, MTOC reported, "In the government reimbursement sector, imported SABA HFC MDIs have 98 percent and Russian-made salbutamol CFC MDIs have 2 percent market share. The average price for reimbursed products in this sector is $6.43 per unit. The implications of these data are that most sales on the Russian market of MDIs are without government reimbursement and paid at full retail cost by the consumer at a pharmacy." This reported information was queried with the Russian Federation in the light of the additional information provided in June 2013. The Russian Federation stated its belief that MTOC's previously reported information was not realistic, and that in 2012/2013 almost all of the MDIs made by Russian manufacturers are supplied free of charge.

Following concerns raised by the Russian Federation at the Open-ended Working Group meeting about the suitability of stockpile for MDI manufacture in the Russian Federation, MTOC confirmed that the available stockpile of pharmaceutical-grade CFCs in the United States, owned by Boehringer-Ingelheim and Honeywell, has been used recently (and for many years) to manufacture MDIs for sale into the United States and other global markets. The CFCs in this stockpile were produced post-1996 and meet US regulatory pharmaceutical standards. If they are not committed for use to manufacture MDIs in the near future, they will be destroyed.

Noting the requirements of essential use decisions to consider CFC stockpiles, and that the supply of CFCs produced in China will become increasingly uncertain with associated risks to patients, MTOC considers the stockpile a suitable option for consideration by the Russian Federation. Use of available stockpile would avoid unnecessary CFC production. It would also provide an additional reserve of 68 tonnes in case conversion is further delayed beyond the end of 2014. Any unwanted surplus would need to be destroyed by the stockpile's owner.

MTOC is encouraged to see the recent efforts to accelerate the schedule for the GEF co-funded UNIDO conversion project. MTOC remains concerned that the challenging schedule, and any unexpected problems, may result in further delays in project completion. In May, MTOC reported that it anticipated a further 12-24 months from equipment installation in mid-2014 to validate and launch HFC MDIs at full capacity. The revised schedule indicates commercial production of HFC MDIs by the end of 2014, only 8 months after equipment installation, which

may or may not be production at full capacity. MTOC believes that its original predictions for the production of HFC MDIs at full capacity are still practical and credible estimates for complete transition to salbutamol HFC MDI manufacture in the Russian Federation.

MTOC asked for clarification whether Russian MDI manufacturers have any existing HFC MDI manufacturing lines. The Russian Federation reported that Russian manufacturers do not have existing HFC lines installed or available to manufacture salbutamol HFC MDIs in the Russian Federation. With installation of the new equipment, the UNIDO project anticipates sufficient HFC MDI production to replace CFC MDIs completely at project completion.

MTOC made its original recommendation of 106 tonnes CFCs for 2014 to allow six months during the first half of 2014 for some domestic production of CFC MDIs while imported CFC-free inhalers were increased. MTOC based this recommendation on:

- The potential for further project delays and an uncertain completion date;
- A potential completion date as late as 2016, based on MTOC predictions;
- The uncertainty of relying on future CFC production;
- The availability of affordable imported HFC MDIs compared with Russian-made CFC MDIs on a dose-for dose basis; and
- The potential to increase the proportion of imported HFC MDIs.

Given the preferential inclusion of Russian-made CFC MDIs on the list of free medicines, and the reliance of almost 80 percent of Russian patients on receiving medicines free of charge, MTOC does not believe that the import of HFC MDIs will be actively increased in the short term by the Russian Federation. Consequently, there would appear to be potential risks to patients in ceasing the supply of Russian-made CFC MDIs by limiting the quantity of CFCs authorised for 2014.

Decision IV/25 states in paragraph 1(b)(ii) that the essential use exemption can be permitted only if "*the controlled substance is not available in sufficient quality and quantity from existing stocks of banked or recycled controlled substances, also bearing in mind the developing countries need for controlled substances*". MTOC recommends 212 tonnes of CFCs for MDI manufacture in the Russian Federation for 2014, preferably utilising existing available global pharmaceutical-grade CFC stockpiles of suitable quality, rather than new CFC production.