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COMITÉ EJECUTIVO DEL FONDO MULTILATERAL
PARA LA APLICACIÓN DEL
PROTOCOLO DE MONTREAL
Quincuagésima séptima Reunión
Montreal, 30 de marzo al 3 de abril de 2009

# INFORME SOBRE LA SOLICITUD DE LA 20ª REUNIÓN DE LAS PARTES EN EL PROTOCOLO DE MONTREAL ACERCA DE LA SITUACIÓN DE LOS ACUERDOS PARA CONVERTIR LAS INSTALACIONES DE FABRICACIÓN DE INHALADORES DE DOSIS MEDIDAS DE LOS PAÍSES QUE OPERAN AL AMPARO DEL ARTÍCULO 5 Y DE LA EJECUCIÓN DE LOS PROYECTOS APROBADOS (DECISIÓN XX/4).

**Antecedentes**

1. En su 20ª Reunión, las Partes en el Protocolo de Montreal pidieron específicamente a la Secretaría del Fondo que informe al Grupo de Trabajo de composición abierta en su 29ª Reunión (julio de 2009) sobre el estado de los acuerdos para convertir las fábricas de inhaladores de dosis medidas y sobre la ejecución de los proyectos aprobados en los países que operan al amparo del Artículo 5. Las Partes también pidieron al GETE que presente un informe sobre el posible calendario de la producción unificada final, tomando en cuenta, entre otras cosas, las designaciones para usos esenciales de las Partes que operan al amparo del Artículo 5 como de las que no operan al amparo dicho artículo, opciones para el almacenamiento a largo plazo, la distribución y la gestión de las cantidades producidas de clorofluorocarbonos de calidad farmacéutica antes de que las Partes las necesiten y para reducir al mínimo la posibilidad de que en el marco de la producción unificada final se fabrique una cantidad excesiva o insuficiente de clorofluorocarbonos (decisión XX/4). En el Anexo I a esta nota de estudio se adjunta una copia de la decisión.

2. La Secretaría del Fondo ha preparado esta nota de estudio en respuesta al párrafo 2 de la decisión XX/4. Para preparar esta nota de estudio, la Secretaría del fondo pidió a los organismos de ejecución pertinentes que suministraran un informe sobre la marcha de las actividades de la situación de la ejecución de los proyectos de inhaladores de dosis medidas, incluidas las cantidades anuales de CFC utilizados en los inhaladores de dosis medidas hasta que se logre la conversión a alternativas que no utilizan CFC. Se envió un borrador de la nota de estudio a los organismos de ejecución pertinentes para su revisión. Los comentarios remitidos por los organismos se han incorporado en la versión final.

3. La nota de estudio se presenta a esta Reunión para que sea considerada por el Comité Ejecutivo, a fin de que la Secretaría pueda presentarla puntualmente a la 29ª Reunión del Grupo de Trabajo de composición abierta.

**Proyectos de eliminación de inhaladores de dosis medidas que utilizan CFC que se están ejecutando actualmente**

4. El Comité Ejecutivo ha aprobado financiación para la conversión de las plantas que fabrican inhaladores de dosis medidas que utilizan CFC a alternativas sin CFC en 12 países que operan al amparo del Artículo 5. La ejecución de estos proyectos permitirá eliminar más de 1 800 toneladas PAO de CFC. La Tabla 1 siguiente enumera todos los proyectos de eliminación de inhaladores de dosis medidas que utilizan CFC que se están ejecutando actualmente. En el Anexo II a esta nota de estudio se adjunta información adicional sobre el sector de inhaladores de dosis medidas en estos países.

**Tabla 1. Proyectos de eliminación para la conversión de inhaladores de dosis medidas que utilizan CFC a tecnologías de alternativa aprobadas por el Comité Ejecutivo**

| País | Proyecto | Organismo | CFC (toneladas PAO) | | | Fechas | |
|---|---|---|---|---|---|---|---|
| | | | CFC-11 | CFC-12 | CFC-114 | Aprobación | Terminación |
| Argentina | Eliminación del consumo de CFC en la fabricación de inhaladores de dosis medidas en aerosol | Banco Mundial | 35,5 | 82,9 | | Nov-08 | Ene-12 |
| Bangladesh | Eliminación del consumo de CFC en la fabricación de inhaladores de dosis medidas en aerosol (Beximco, Square Pharmaceutical y Acme Pharmaceutical) | PNUD | 21,8 | 54,5 | | Jul-07 | Jul-11 |
| China | Plan sectorial de eliminación de consumo de CFC en el sector de | ONUDI | 48,4 | 274,1 | | Nov-08 | Dic-13 |

| País | Proyecto | Organismo | CFC (toneladas PAO) | | | Fechas | |
|---|---|---|---|---|---|---|---|
| | | | CFC-11 | CFC-12 | CFC-114 | Aprobación | Terminación |
| | inhaladores de dosis medidas | | | | | | |
| Colombia | Eliminación del consumo de CFC en la fabricación de inhaladores de dosis medidas | PNUD | | 7,4 | | Nov-08 | Nov-11 |
| Cuba | Eliminación del consumo de CFC en la fabricación de inhaladores de dosis medidas en aerosol | PNUD | 37,6 | 71,5 | | Dic-03 | Abr-2009 |
| Egipto | Eliminación del consumo de CFC en la fabricación de inhaladores de dosis medidas en aerosol | ONUDI | 4,1 | 153,0 | 2,4 | Nov-06 | Dec-09 |
| India | Plan para la eliminación de los CFC en la fabricación de inhaladores de dosis medidas de uso farmacéutico | Italia/PNUD | 215,7 | 488,6 | | Nov-08 | Nov-13 |
| Indonesia | Asistencia técnica para aplicar la estrategia de transición nacional a inhaladores de dosis medidas sin CFC | Banco Mundial | | 16,3 | | Nov-08 | Dic-10 |
| República Islámica del Irán | Eliminación del consumo de CFC en la fabricación de inhaladores de dosis medidas en aerosol | ONUDI | 28,9 | 67,5 | | Jul-07 | Sep-10 |
| México | Eliminación del consumo de CFC en la fabricación de inhaladores de dosis medidas en aerosol | ONUDI | 25,7 | 65,2 | 6,1 | Nov-07 | Ene-10 |
| Pakistán | Plan para la eliminación de los CFC en la fabricación de inhaladores de dosis medidas de uso farmacéutico | PNUD | 25,0 | 58,8 | | Nov-08 | Nov-11 |
| Uruguay | Eliminación del consumo de CFC en la fabricación de inhaladores de dosis medidas en aerosol | PNUD | 3,0 | 7,0 | | Jul-04 | Dic-2009 |
| Total | | | 445,7 | 1 346,8 | 8,5 | | |

5. También se fabrican inhaladores de dosis medidas que utilizan CFC[1] en los siguientes tres países que operan al amparo del Artículo 5. El Comité Ejecutivo decidió que dichos proyectos no resultan admisibles para recibir financiación del Fondo Multilateral:

a) Argelia: Producción de 0,5 millón de inhaladores de dosis medidas con salbutamol por año, con un consumo de CFC de 11 toneladas PAO de CFC;

b) República Árabe Siria: Producción de 1,9 millón de inhaladores de dosis medidas con salbutamol, beclometasona, salmeterol, fluticasona, salmeterol por año, con un consumo de CFC de 41,3 toneladas PAO de CFC; y

c) Venezuela: Producción de 2,0 millones de inhaladores de dosis medidas con salbutamol, fenoterol/ipratropio, beclometasona y budesonida por año, con un consumo de CFC de 43,4 toneladas PAO de CFC.

[1] Inhaladores de dosis medidas que utilizan CFC que se convertirán a inhaladores de dosis medidas con HFA.

**Cantidades estimativas de CFC para la producción de inhaladores de dosis medidas después de 2009**

6. Las cantidades estimativas de CFC que requerirán los países que operan al amparo del Artículo 5 para la producción de inhaladores de dosis medidas que utilizan CFC después de 2009 se presentan en la Tabla 2 a continuación. Estos datos fueron proporcionados por los países que operan al amparo del Artículo 5 pertinentes por intermedio de los organismos que brindan asistencia para la conversión de las líneas de fabricación a alternativas que no utilizan CFC.

**Tabla 2. Cantidades estimativas de CFC para la producción de inhaladores de dosis medidas después de 2009 (toneladas PAO)***

| País | 2010 | 2011 | 2012 |
|---|---|---|---|
| Argelia | 11,0 | 8,0 | 0,0 |
| Argentina | 178,0 | n/d | n/d |
| Bangladesh | 156,7 | 0,0 | 0,0 |
| China | 977,2 | n/d | n/d |
| Colombia | 0,0 | n/d | n/d |
| Cuba | 0,0 | 0,0 | 0,0 |
| Egipto | 264,0 | 0,0 | 0,0 |
| India | 360,0 | n/d | n/d |
| Indonesia | 0,0 | 0,0 | 0,0 |
| República Islámica del Irán | 105,0 | 0,0 | 0,0 |
| México | 0,0 | 0,0 | 0,0 |
| Pakistán | 130,0 | n/d | n/d |
| República Árabe Siria | 41,0 | 25,0 | 0,0 |
| Uruguay | 0,0 | 0,0 | 0,0 |
| Venezuela | 0,0 | 0,0 | 0,0 |
| **Total** | **2 222,9** | | |

* Mezcla de CFC-11 y CFC-12, generalmente con una relación de 30:70.
(n/d) No disponible.

7. A partir de los datos presentados en la Tabla 2 anterior y las deliberaciones con los organismos de ejecución pertinentes, se observa que:

a) Sobre la base de la información proporcionada por los Gobiernos pertinentes por intermedio de los organismos de ejecución, la cantidad total estimativa de CFC requeridos para la producción de inhaladores de dosis medidas en los países que operan al amparo del Artículo 5 en 2010 es de alrededor de 2 230 toneladas PAO. Varios países no han indicado los niveles de designaciones para usos esenciales después de 2010;

b) Los Gobiernos de Cuba, Indonesia, México, Uruguay y Venezuela no solicitarán usos esenciales de CFC para la fabricación de inhaladores de dosis medidas[2];

c) El Gobierno de Colombia no solicitará usos esenciales de CFC para la fabricación de inhaladores de dosis medidas para 2010. La decisión de presentar designaciones para usos esenciales para 2011 y 2012 dependerá de la situación de la ejecución del proyecto

[2] México y Venezuela satisfarán su demanda de CFC para la fabricación de inhaladores de dosis medidas en 2010 con las reservas disponibles en dichos países. Los proyectos para la conversión de las plantas de fabricación de inhaladores de dosis medidas que utilizan CFC en Cuba y Uruguay se completarán en 2009.

de inversión aprobado;

d) Los siguientes gobiernos han preparado y presentado la documentación para las solicitudes de designaciones para usos esenciales para la consideración del Comité de Opciones Técnicas sobre aplicaciones médicas:

i) Bangladesh por la cantidad de 156,7 toneladas PAO para 2010;

ii) China por la cantidad de 977,2 toneladas PAO para 2010. La información proporcionada en el proyecto para la eliminación de los CFC en la fabricación de inhaladores de dosis medidas indica que se podrían requerir 1 798,3 toneladas PAO de CFC adicionales para la producción de inhaladores de dosis medidas entre 2011 y 2013. El Gobierno de China ha confirmado que se espera que la planta productora de CFC que produce actualmente CFC para el sector de inhaladores de dosis medidas produzca CFC después de 2009 para satisfacer las necesidades del sector de inhaladores de dosis medidas en China y otros países que operan al amparo del Artículo 5;

iii) Egipto por la cantidad de 264 toneladas PAO para 2010;

iv) El Gobierno de la India ha presentado su solicitud de designación de uso esencial directamente al Comité de Opciones Técnicas sobre aplicaciones médicas. La información proporcionada en el proyecto para la conversión de las plantas de fabricación de inhaladores de dosis medidas en la India indica que se podrían requerir entre 240 y 340 toneladas PAO de CFC para la producción de inhaladores de dosis medidas en 2011 y 2012 (las cifras más precisas se conocerán sólo a mediados de 2009);

v) La República Islámica del Irán por la cantidad de 105 toneladas PAO para 2010;

vi) El Gobierno de Pakistán ha presentado su solicitud de designación de uso esencial directamente al Comité de Opciones Técnicas sobre aplicaciones médicas.

e) Al momento de preparar esta nota de estudio, el Gobierno de la Argentina estaba preparando la solicitud de designación de uso esencial para una cantidad de 178 toneladas PAO para 2010. La información proporcionada en el proyecto para la eliminación de los CFC en la fabricación de inhaladores de dosis medidas en la Argentina indica que se podrían requerir 1 088 toneladas PAO de CFC adicionales para la producción de inhaladores de dosis medidas entre 2011 y 2015. Sin embargo, el Gobierno revisará estas cifras en forma anual considerando los progresos logrados en la conversión de las líneas de fabricación de inhaladores de dosis medidas que utilizan CFC;

f) Los Gobiernos de Argelia y la República Árabe Siria solicitarán designaciones de usos esenciales por 85 toneladas PAO en total en 2010 y 2011.

**Recomendación**

8. El Comité Ejecutivo pudiera dar instrucciones a la Secretaría para que presente este informe sobre la situación de los acuerdos para convertir las instalaciones de fabricación de inhaladores de dosis medidas en los países que operan al amparo del Artículo 5 y la ejecución de los proyectos aprobados a la

29ª Reunión del Grupo de Trabajo de composición abierta, conforme a lo solicitado en el párrafo 2 de la decisión XX/4 de la 20ª Reunión de las Partes en el Protocolo de Montreal, en la inteligencia de que el documento debería ser actualizado en el caso de que las Partes que operan al amparo del Artículo 5 pertinentes presenten oficialmente otros datos sobre las solicitudes de designaciones para usos esenciales.

# Anexo I

## DECISION XX/4 : Producción unificada de CFC para inhaladores de dosis medidas

*Reconociendo* que el consumo y la producción de clorofluorocarbonos en las Partes que operan al amparo del párrafo 1 del artículo 5 cesarán a partir del 1º de enero de 2010, con posibles exenciones para usos esenciales,

*Reconociendo también* que muchas Partes que operan al amparo del párrafo 1 de artículo 5 importan inhaladores de dosis medidas sin clorofluocarbonos de Partes que no operan al amparo del párrafo 1 del artículo 5,

*Reconociendo* que la producción unificada ofrece posibles ventajas respecto de las propuestas anuales para usos esenciales para satisfacer las necesidades de clorofluorocarbonos de calidad farmacéutica conforme a lo dispuesto en la decisión IV/25,

*Observando* que en el párrafo 12 de la decisión XVIII/16 se pidió al Grupo de Evaluación Tecnológica y Económica que evaluara "la necesidad de una producción unificada y limitada de clorofluorocarbonos exclusivamente para inhaladores de dosis medidas tanto en las Partes que operan al amparo del párrafo 1 del artículo 5 como en las Partes que no operan al amparo del párrafo 1 de ese artículo",

*Observando también* que el Comité de Opciones Técnicas sobre aplicaciones médicas presentó conclusiones sobre las cantidades de clorofluorocarbonos que podrían necesitarse en 2008 para inhaladores de dosis medidas únicamente para Partes que operan al amparo del párrafo 1 del artículo 5,

*Reconociendo* que el Comité de Opciones Técnicas sobre aplicaciones médicas ha informado de la necesidad de contar con información complementaria en relación con la producción unificada final para las Partes que operan al amparo del artículo 5, con excepción de una importante Parte productora,

1. Pedir al Grupo de Evaluación Tecnológica y Económica que presente un informe a la 21ª Reunión de las Partes precedido de un informe preliminar a la 29ª reunión del Grupo de Trabajo de composición abierta, sobre:

   a) El posible calendario de la producción unificada final, teniendo en cuenta, entre otras cosas, la información presentada en las propuestas para 2010 y el hecho de que tal vez sea la primera vez que algunas Partes que operan al amparo del párrafo 1 del artículo 5 preparen propuestas para usos esenciales para presentarlas en la 21ª Reunión de las Partes;

   b) Opciones para el almacenamiento a largo plazo, la distribución y la gestión de las cantidades producidas de clorofluorocarbonos de calidad farmacéutica antes de que las Partes las necesiten, incluidos los métodos actuales utilizados por las Partes que no operan al amparo del párrafo 1 del artículo 5;

   c) Opciones para reducir al mínimo la posibilidad de que en el marco de la producción unificada final se fabrique una cantidad excesiva o insuficiente de clorofluorocarbonos;

   d) Disposiciones contractuales que podrían resultar necesarias, teniendo en cuenta los modelos que usan actualmente las Partes que no operan al amparo del párrafo 1 del

artículo 5 que presentan propuestas para usos esenciales de conformidad con la decisión IV/25;

e) Opciones para reducir la producción de clorofluorocarbonos de calidad no farmacéutica, conjuntamente con opciones para la eliminación final de dichos clorofluorocarbonos;

2. Pedir a la secretaría del Fondo Multilateral que informe a la 29ª reunión del Grupo de Trabajo de composición abierta sobre el estado de los acuerdos para la conversión de las fábricas de inhaladores de dosis medidas ubicadas en Partes que operan al amparo del párrafo 1 del artículo 5 y la ejecución de los proyectos aprobados.

**Annex II**

**SUMMARY REPORT ON CFC-MDI PHASE-OUT PROJECTS UNDER CURRENT IMPLEMENTATION IN ARTICLE 5 COUNTRIES**

1. Projects for the conversion of CFC-MDIs to alternative non-CFC propellants have been approved for the following 12 Article 5 countries: Argentina, Bangladesh, China, Colombia, Cuba, Egypt, India, Indonesia, Islamic Republic of Iran, Mexico, Pakistan, and Uruguay. A summary of these projects, based on the information contained in the documents that were prepared for consideration by the Executive Committee, is presented below.

## ARGENTINA[1]

2. CFC-MDIs are manufactured in Argentina by the following enterprises: Laboratorio Pablo Cassará (100 per cent local ownership), which consumes approximately 80 per cent of the pharma-grade CFCs imported into the country for the manufacturing of MDIs; 3M, a multinational enterprise that fills MDIs for a group of 15 laboratories, five of which are nationally owned; and Denver Farma, a local laboratory (100 per cent local ownership) that used to fill its MDIs through 3M but established its own CFC-MDI production line in 2007. The level of CFC consumption used for the manufacturing of MDIs in Argentina is shown in the table below.

| Description | ODP tonnes | | |
|---|---|---|---|
| | 2005 | 2006 | 2007 |
| Consumption for domestic use | 135.7 | 123.6 | 136.4 |
| Export to Article 5 countries | 51.3 | 49.5 | 59.5 |
| Total consumption | 187.0 | 173.1 | 195.9 |
| Consumption eligible for funding | | | |
| Pablo Cassará | 83.5 | 85.0 | 106.4 |
| Denver Farma(*) | 2.0 | 2.0 | 3.1 |
| Phoenix(*) | 10.9 | 10.9 | 4.4 |
| Dallas(*) | 0.1 | 0.1 | 0.1 |
| Raffo(*) | 2.7 | 3.1 | 3.6 |
| Roux(*) | 0.7 | 0.6 | 0.8 |
| Sub-total eligible enterprises | 99.9 | 101.7 | 118.4 |
| Consumption by multinational | | | |
| 3M(**) | 51.2 | 49.5 | 59.5 |
| IVAX(***) | 35.9 | 21.9 | 18.0 |
| Sub-total multinationals | 87.1 | 71.4 | 77.5 |

(*) CFC-MDIs filled through 3M. Denver Farma established its own CFC-MDI production line in 2007.
(**) Excluding CFC consumption used for filling CFC-MDIs for locally-owned enterprises.
(***) Stopped production of CFC-MDIs during 2007.

3. As of 2007, CFC-MDIs with the following seven different active ingredients were registered and sold in Argentina: salbutamol, budesonide, fenoterol, ipratropium, fluticasone, fluticasone/salmeterol, ipratropium/fenoterol, ipratropium/salbutamol and salmeterol/beclomethasone.

4. The objectives of the project are: replace the use of CFCs at Laboratorio Pablo Cassará for the production of salbutamol CFC-MDIs to isobutane; to replace the use of CFCs at Laboratorio Denver Farma for the production of salbutamol and budesonide CFC-MDIs to HFA technology; to provide technical support for development of HFA-MDI formulations for four locally-owned laboratories filling

[1] UNEP/OzL.Pro/ExCom/56/22.

their own MDIs through third parties; and to support the MDI transition strategy (information dissemination, awareness programmes and clinical symposiums and workshops).

**BANGLADESH**[2]

5. The first CFC-MDI in Bangladesh was developed and launched in 1997, with production reaching 507,000 units. The demand for MDIs in Bangladesh is satisfied primarily by the following three locally-owned manufacturing enterprises:

(a) Beximco Pharmaceutical: The company began manufacturing CFC-MDIs in 1997, with the production of 270,000 salbutamol and salmeterol MDIs. Currently, the company has a production capacity of 2.4 million MDIs per year with over ten different active ingredients. Since 2002, Beximco has manufactured salbutamol CFC-MDIs for GlaxoSmithKline (680,000 MDIs produced in 2006); and since 2006 for Eskayef (30,000 MDIs). In 2006, Beximco invested in the development of HFA salbutamol and beclomethasone MDIs through collaboration with Bespak, United Kingdom;

(b) Square Pharmaceutical: The company began manufacturing CFC-MDIs in 1997 with the production of 240,000 salbutamol, beclomethasone and salmeterol MDIs, and currently produces MDIs with over nine different active ingredients. The MDI formulation technology has been based on in-house research work. In 2002, Square began producing dry powder inhalers (DPIs) that were developed by the enterprise. Currently, the company manufactures single dose (capsule) DPIs of salbutamol, and salmeterol plus fluticasone;

(c) Acme Pharmaceutical: The company began manufacturing CFC-MDIs in 2004 with the production of 100,000 salbutamol, beclomethasone and salmeterol MDIs. In 2006, a total 250,000 MDIs were produced with four different active ingredients. Also in 2006, Acme produced 210,000 DPIs with four different active ingredients (salbutamol, salmeterol, salmeterol plus fluticasone and beclomethasone).

6. Production levels of CFC-MDIs in Bangladesh over the 2004-2006 period by active ingredient are shown in the table below:

| **Active ingredient** | **Beximco** | | | **Square Pharmaceutical** | | | **Acme** | | |
|---|---|---|---|---|---|---|---|---|---|
| | **2004** | **2005** | **2006** | **2004** | **2005** | **2006** | **2004** | **2005** | **2006** |
| Salbutamol | 1,225,437 | 1,167,517 | 1,300,000 | 276,000 | 325,000 | 388,500 | 57,082 | 92,197 | 181,188 |
| Salbutamol+ipratropium | | 30,724 | 25,000 | | 52,500 | 105,000 | | | |
| Levosalbutamol | | | 20,000 | | | 15,000 | | | |
| Beclomethasone | 101,128 | 104,462 | 95,000 | 125,000 | 160,000 | 199,500 | 22,463 | 13,411 | 20,842 |
| Salmeterol | 47,590 | 36,869 | 40,000 | 31,500 | 52,500 | 21,000 | 21,233 | 7,864 | 15,417 |
| Salmeterol+fluticasone | 41,641 | 47,930 | 85,000 | 10,000 | 32,000 | 32,000 | | 15,575 | 22,568 |
| Ciclesonide | | | 28,000 | 24,000 | | 33,000 | | | |
| Budesonide | 17,846 | | | 42,000 | 43,000 | 31,500 | | | |
| Ipratropium | | 6,145 | | | 33,000 | 10,500 | | | |
| Triotropium | | | 3,000 | | | | | | |
| **Total MDIs** | **1,433,642** | **1,393,647** | **1,596,000** | **508,500** | **698,000** | **836,000** | **100,778** | **129,047** | **240,015** |
| **CFC (ODP tonnes)*** | **49.5** | **44.2** | **52.9** | **10.3** | **14.3** | **17.3** | **2.5** | **3.3** | **6.1** |

* In 2006, 13.6 and 0.6 ODP tonnes of CFCs were used by Beximco for the production of MDIs for GlaxoSmithKline and Eskayef respectively.

7. Only some 127,900 HFA seretide MDIs and 26,427 seretide multi-dose dry powder inhalers (DPIs) are imported into the country.

[2] UNEP/OzL.Pro/ExCom/52/26.

8. MDIs containing salbutamol, beclomethasone, salbutamol plus ipratropium, and salmeterol plus fluticasone represent over 90 per cent of total current CFC-MDI production in Bangladesh. Therefore, the Government of Bangladesh, together with the three manufacturing companies, the Drug Regulatory Agency, the Lung Association and the medical community, decided to convert these MDIs to HFA technology. The Government of Bangladesh is proposing to implement a transition strategy with adequate awareness activities for enhancing MDI use and regulations aligned to the phase-out timing by the industry.

9. The project proposes that a third party company will provide technical assistance for the development of the formulation for each specific drug molecule and strength, and transfer the technology to each one of the three MDI manufacturing enterprises. These enterprises will then use their own staff to adapt to the new technology with the supervision of the service provider's technical expert. In the case of the salbutamol plus ipratropium, there is currently no suitable HFA-MDI approved. It is expected that the development of formulations for these MDIs will take approximately one year. During this time there will be a need for consultation with suitably experienced experts to advise the technical staff at the companies on the technical aspects of this project.

10. Due to non-availability of non-CFC formulations for ipratropium bromide, triotropium and salmeterol combination, these MDIs have not been considered for product development. The future need for these products was discussed with the Government of Bangladesh and the Lung Foundation. As a result, it has been decided to allow stockpiling of 45.4 ODP tonnes of CFCs for the continued production of MDIs for a three-year period starting in 2010. It is expected that the conversion process would be undertaken by the industry in Bangladesh as soon as feasible conversion options are available for these formulations.

**CHINA**[3]

11. There are 38 MDI manufacturing plants in China, with 104 production licenses. Sixteen manufacturing plants with 36 licenses have reported production in 2007[4] while 18 plants have not reported production for that year. The remaining five plants are owned by multinational corporations (one of which ceased production in 2005).

12. The MDI sector in China can be summarized as follows:

(a) CFC consumption for the production of MDIs increased from 152.1 ODP tonnes in 2004 to 340.5 ODP tonnes in 2007;

(b) Seven MDI manufacturing plants are also producing pharmaceutical aerosols in China[5];

(c) Three transnational corporations[6] have been producing MDIs over the last three years, as shown in the table below:

[3] UNEP/OzL.Pro/ExCom/56/24.
[4] The 16 enterprises hold an additional 22 licenses without production.
[5] The seven plants are: Beijing Haiderun Pharmaceutical; Guangzhou Dongkang Pharmaceutical; Guiyang Dechangxiang Pharmaceutical; Heilongjiang Tanglong Pharmaceutical; Penglai Nuokang Pharmaceutical; Shanghai Pharmaceutical Group; and Wuxi Shanhe Group.
[6] An additional multinational corporation, GlaxoSmithKlein, stopped producing CFC-based beclomethasone MDI from 2005.

| Company name | Active ingredient | CFC 2005 (kg) | CFC 2006 (kg) | CFC 2007 (kg) |
|---|---|---|---|---|
| AstraZeneca Pharmaceutical | Budesonide | 3,494.0 | 4,538.0 | |
| AstraZeneca Pharmaceutical | Terbutaline | 7,460.0 | 8,665.0 | |
| Beijing Shengdelaibao Pharmaceutical | Salbutamol | 745.9 | | 730.0 |
| Beijing Shengdelaibao Pharmaceutical | Beclometasone | 180.3 | | |
| Weifang Zhongshi Pharmacy | Beclometasone | - | - | 57.0 |
| Weifang Zhongshi Pharmacy | Salbutamol | 1,350.0 | 900.0 | 597.0 |
| Weifang Zhongshi Pharmacy | Salbutamol (suspension) | - | - | 70.7 |
| **Total** | | **13,230.2** | **14,103.0** | **1,454.7** |

(d) There are only 13 different active ingredients in MDIs that are currently produced in China, as shown in the table below. The total production of MDIs with beclomethasone, terbutaline, cromoglicate, salbutamol (both in solution and in suspension), and isoprenaline represents more than 97 per cent of total production in 2007:

| Active ingredient | CFC consumption (kg) | | | % CFC* |
|---|---|---|---|---|
| | 2005 | 2006 | 2007 | |
| Salmeterol xinafoate | | 10.0 | 10.0 | 0.00% |
| Dimethicone | 22.2 | 70.0 | 100.0 | 0.03% |
| Zhichuanling | 30.0 | 130.8 | 320.0 | 0.09% |
| Iprartropium bromide | - | 27.0 | 325.0 | 0.10% |
| Ketotifun fumarate | - | 1,271.0 | 1,271.0 | 0.37% |
| Ribavirin | 1,851.0 | 7,395.0 | 3,443.0 | 1.01% |
| Budesonide | 6,273.5 | 8,037.0 | 4,069.0 | 1.20% |
| Sodium cromoglicate | 6,902.0 | 7,541.5 | 13,591.0 | 3.99% |
| Terbutaline sulphate | 7,460.0 | 8,665.0 | 16,612.7 | 4.88% |
| Isoprenaline hydrochloride | 40,647.2 | 47,324.0 | 43,452.0 | 12.76% |
| Beclometasone dipropionate | 16,796.6 | 23,048.0 | 59,954.0 | 17.61% |
| Salbutamol (solution) | 69,905.3 | 91,650.0 | 85,378.0 | 25.07% |
| Salbutamol (suspension) | 93,793.1 | 85,396.2 | 111,968.7 | 32.88% |
| **Total** | **243,680.9** | **280,565.5** | **340,494.4** | **100.0%** |

(*) Percentage of the total CFC consumption in 2007.

13. At the time of the preparation of the project proposal, it was expected that CFC consumption will increase annually from 341 ODP tonnes in 2007 to a maximum level of 748.3 ODP tonnes in 2011 and then will decrease annually, achieving complete phase-out by 2014. The total cumulative CFC consumption between 2008 and 2014 amounts to 3,332.3 ODP tonnes[7]. According to the CFC production closure agreement between the Government of China and the Executive Committee, a total of 1,100 ODP tonnes of CFCs could be produced in 2008 and 2009[8]. Considering that reformulation to HFA-technology for beclomethasone and salbutamol MDIs is well known, it could be expected that conversion of at least these two MDIs, representing more than 75 per cent of total CFC consumption in China, could have been done at an earlier stage. If this is the case, the amount of CFCs that might be needed from 2010 could be substantially reduced. However, further reduction of the need for CFCs after 2010 phase-out cannot be proposed at this stage, although it will be pursued during the implementation process.

[7] According to information provided by UNIDO, the 2008 CFC consumption for manufacturing MDIs instead of 415 ODP tonnes that were estimated at the time of the preparation of the project.

[8] Under the agreement between the Government of China and the Executive Committee for the CFCs/CTC/halon accelerated phase-out plan, China could export 100 ODP tonnes of CFCs in 2008 and 50 ODP tonnes in 2009.

## COLOMBIA[9]

14. Laboratorios Chalver is the sole locally-owned enterprise producing CFC-MDIs. The MDI production line was established in 2001 with the first batch manufactured by the end of 2002. The enterprise has developed CFC-MDIs with seven different active ingredients, as shown in the table below:

| Active ingredient | MDI (units) CFC consumption (ODP tonnes) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 2003 | | 2004 | | 2005 | | 2006 | | 2007 | |
| | MDI | CFC | MDI | CFC | MDI | CFC | MDI | CFC | MDI | CFC |
| Beclomethasone | 63,000 | 1.1 | 69,000 | 1.2 | 3,000 | 0.1 | 9,000 | 0.2 | 45,366 | 0.8 |
| Ipratropium | 0 | - | 42,000 | 0.7 | 78,000 | 1.3 | 12,000 | 0.2 | 118,819 | 2.0 |
| Salbutamol | 144,000 | 2.4 | 300,000 | 5.0 | 0 | - | 72,000 | 1.2 | 239,501 | 4.0 |
| Salbutamol/beclomethasone | 6,000 | 0.1 | 3,000 | 0.1 | 36,000 | 0.6 | 15,000 | 0.3 | 32,750 | 0.5 |
| Salbutamol/ipratropium | 0 | - | 0 | - | 10,000 | 0.2 | 5,000 | 0.1 | 8,913 | 0.1 |
| Budesonide | 0 | - | 0 | - | 0 | - | 0 | - | 0 | - |
| Fluticasone | 0 | - | 0 | - | 0 | - | 0 | - | 0 | - |
| Total | 213,000 | 3.6 | 414,000 | 6.8 | 127,000 | 2.1 | 113,000 | 1.9 | 445,349 | 7.4 |

15. The National Institute of Food and Drug Surveillance is responsible for the registration of new drugs. In May 2004, the Drug Review Commission allowed the use of CFC-MDIs until 2010. In 2008, the Ministry of Health issued a ban on the registration of new CFC-MDIs and the renewal of existing registered CFC-MDIs, and established December 2009 as the deadline for the conversion of CFC-MDIs except for those active ingredients where conversion is not feasible.

16. The project is to assist Laboratorios Chalver to convert the CFC-MDI manufacturing line to HFA technology by 2012, including the development of HFA-MDIs for beclomethasone, ipratropium, salbutamol and salbutamol/beclomethasone.

## CUBA[10]

17. Laboratorio Farmacéutico Julio Trigo López consumes both CFC-11 and CFC-12 in the manufacture of salbutamol and beclomethasone CFC-MDI. The company has decided to stay with the MDI as the drug delivery system. For salbutamol, it is proposing to base the formulation on HFC-134a alone, and for beclomethasone, it is proposing dissolution in ethyl alcohol and the use of HFC-134a propellant. The implementation of the selected technologies require technology transfer from established enterprises.

18. The Government of Cuba is proposing to phase out the use of CFCs in MDIs through implementation of the national transition strategy and the conversion of the CFC-MDI manufacturer to HFC-134a MDIs. Once the project is completed, the Government of Cuba will prohibit the use of CFCs in all aerosol products, including MDIs.

## EGYPT[11]

19. Production of MDIs in Egypt began in 1984. There are two established domestic manufacturers of CFC-based MDIs in Egypt: the Arab Drug Company (ADCO) and the Egyptian International Pharmaceutical Industries Co., (EIPICO). Additionally, a number of multinational corporations offer several medications for asthma and CODP, including CFC-based salbutamol MDIs, salbutamol and fluticasone both as HFC-134a-based MDIs and as dry powder inhalers (DPI), and budesonide DPIs.

[9] UNEP/OzL.Pro/ExCom/56/25.
[10] UNEP/OzL.Pro/ExCom/41/33.
[11] UNEP/OzL.Pro/ExCom/50/29.

20. In 1991, ADCO began manufacturing two CFC-based MDIs under license from Chiesi Farmaceutici. Currently, these MDIs continue to be manufactured under the same brand name, although there is no longer a commercial license or limitation in place. ADCO has also introduced its own branded MDIs for: salbutamol; salbutamol with beclomethasone (produced from individual actives); beclomethasone; and, since 2002 salmeterol. Between 1991 and 1999, MDI production increased from about 294,000 MDIs to 2.1 million MDIs. In 1999, the company started to export MDIs to other Article 5 countries (some 590,000 MDIs). Since then, MDI production has increased continuously, reaching 6.6 million MDIs in 2005. The total current CFC consumption used for the production of MDIs is 145.9 ODP tonnes.

21. EIPICO began the production of CFC-based MDIs in 1984 as a licensee of 3M Riker (who is still the license holder for Aerolin salbutamol in Egypt). Between 1995 and 2005, the production of salbutamol CFC-MDIs increased from 600,000 to 1.05 million units. The total current CFC consumption used for the production of MDIs is 17.2 ODP tonnes.

22. The 2003-2005 levels of CFC consumption and MDI production in these two manufacturing plants is presented in the table below.

| Year | ODP tonnes | | | | MDI units |
|---|---|---|---|---|---|
| | CFC-11 | CFC-12 | CFC-114 | Total CFC | |
| **ADCO** | | | | | |
| 2003 | 37.4 | 100.6 | | 138.0 | 4,831,367 |
| 2004 | 43.2 | 107.7 | | 150.9 | 6,028,894 |
| 2005 | 42.5 | 106.1 | | 148.6 | 6,600,000 |
| **EIPICO** | | | | | |
| 2003 | 2.0 | 10.8 | 1.9 | 14.7 | 800,000 |
| 2004 | 2.5 | 13.6 | 2.4 | 18.4 | 1,000,000 |
| 2005 | 2.5 | 13.6 | 2.4 | 18.4 | 1,000,000 |
| **Total** | | | | | |
| 2003 | 39.4 | 111.4 | 1.9 | 152.7 | 5,631,367.0 |
| 2004 | 45.7 | 121.3 | 2.4 | 169.3 | 7,028,894.0 |
| 2005 | 45.0 | 119.7 | 2.4 | 167.0 | 7,600,000.0 |

23. The two companies have decided to convert their CFC-based MDIs to HFC-134a technology, which will require technology transfer from an established enterprise. The Government of Egypt has prepared a national strategy for the phase-out of CFC-based MDIs, aimed at meeting a timetable and criteria that has been agreed by all stakeholders. The strategy is based on patients' health as the first priority, ensuring that access to appropriate treatment is not interrupted, and on the development and implementation of an education programme with participation from major stakeholders.

**INDIA**[12]

24. There are currently five MDI manufacturers in India. Three of these manufacturers produce both CFC- and HFA-MDIs. The total production levels of MDIs in India in the 2003-2007 period are shown in the table below:

[12] UNEP/OzL.Pro/ExCom/56/34.

| Manufacturer | Total production (million MDIs) | | | | |
|---|---|---|---|---|---|
| | 2003 | 2004 | 2005 | 2006 | 2007 |
| **CFC-MDIs** | | | | | |
| Cadila Healthcare Ltd. | 0.15 | 0.30 | 0.42 | 0.69 | 0.71 |
| Cipla Ltd. | 26.27 | 33.04 | 28.18 | 35.44 | 27.39 |
| GlaxoSmithKline Pharmaceuticals Ltd. | 1.15 | 0.94 | 1.21 | 0.79 | 0.94 |
| Midas-Care Pharmaceuticals Ltd. | 0.97 | 1.02 | 1.65 | 1.85 | 1.76 |
| Sun Pharmaceutical Industries Ltd. | 0.29 | 0.39 | 0.31 | 0.39 | 0.39 |
| **Subtotal CFC-MDIs** | **28.83** | **35.69** | **31.77** | **39.16** | **31.19** |
| **HFA-MDIs** | | | | | |
| Cipla Ltd. | 0.47 | 1.21 | 4.03 | 11.01 | 24.06 |
| Midas-Care Pharmaceuticals Ltd. | 0.00 | 0.024 | 0.035 | 0.15 | 0.26 |
| Sun Pharmaceutical Industries Ltd. | 0.00 | 0.00 | 0.00 | 0.029 | 0.00 |
| **Subtotal HFA-MDIs** | **0.47** | **1.23** | **4.06** | **11.19** | **24.32** |
| **Total** | **29.30** | **36.92** | **35.84** | **50.35** | **55.51** |

25. The level of CFC consumption for the manufacturing of MDIs increased from 578.9 ODP tonnes in 2003 to 763.6 ODP tonnes in 2006. In 2007, CFC consumption decreased to 608.1 ODP tonnes, as shown in the table below:

| Manufacturer | CFC consumption (ODP tonnes) | | | | |
|---|---|---|---|---|---|
| | 2003 | 2004 | 2005 | 2006 | 2007 |
| Cadila | 2.9 | 5.9 | 7.5 | 11.6 | 8.5 |
| CIPLA | 526.6 | 687.6 | 670.9 | 698.2 | 537.7 |
| GSK | 24.6 | 20.1 | 25.9 | 16.9 | 20.1 |
| Midas-Care | 18.8 | 21.3 | 29.8 | 29.0 | 34.0 |
| Sun Pharma | 6.0 | 7.9 | 6.3 | 7.9 | 7.8 |
| **Total** | **578.9** | **742.8** | **740.4** | **763.6** | **608.1** |

26. The forecast of CFC and HFA demand for MDIs in India in 2008-2013 is shown in the table below:

| Propellant | CFC and HFA consumption (metric tonnes)* | | | | | |
|---|---|---|---|---|---|---|
| | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 |
| CFC | 604 | 484 | 338 | 203 | 71 | 0 |
| HFA | 566 | 760 | 983 | 1,205 | 1,405 | 1,556 |
| **Total** | 1,170 | 1,244 | 1,322 | 1,408 | 1,476 | 1,556 |

(*) Based on growth rates over the last five years, with the presumption of technical and financial assistance for the transition from CFC to HFA technologies, in the absence of which an additional three years will be needed for the complete phase-out of CFCs.

27. In 2003, CFC-MDIs with thirteen different active ingredients were manufactured in India, as shown in the table below. Several of the CFC-MDIs have been formulated in multiple strengths.

| Ingredient | CFC-MDIs manufactured by enterprise | | | | | | |
|---|---|---|---|---|---|---|---|
| | Cadila | Cipla | GSK | Midas-Care | SunPharma | Total MDI | %MDIs |
| Salbutamol | 30,010 | 16,905,000 | 1,044,505 | 611,800 | 56,600 | 18,647,915 | 64.6% |
| Beclomethasone | | 4,663,000 | 107,475 | 117,900 | | 4,888,375 | 16.9% |
| Beclomethasone/salbutamol | | 1,925,000 | | 27,400 | | 1,952,400 | 6.8% |
| Salmeterol/fluticasone | | 778,000 | | 10,000 | 163,771 | 951,771 | 3.3% |
| Ipratropium | 20,070 | 786,000 | | 43,000 | | 849,070 | 2.9% |
| Budesonide | 10,010 | 300,000 | | 15,200 | 51,738 | 376,948 | 1.3% |
| Ipratropium/dalbutamol | 20,070 | 293,000 | | 61,200 | | 374,270 | 1.3% |

| Ingredient | CFC-MDIs manufactured by enterprise | | | | | | |
|---|---|---|---|---|---|---|---|
| | Cadila | Cipla | GSK | Midas-Care | SunPharma | Total MDI | %MDIs |
| Budesonide/dormoterol | 69,293 | 191,000 | | 75,900 | 27,379 | 363,572 | 1.3% |
| Salmeterol | | 154,000 | | | | 154,000 | 0.5% |
| Fluticasone | | 134,000 | | | | 134,000 | 0.5% |
| Cromoglycate | | 66,000 | | | | 66,000 | 0.2% |
| Tiotropium | | 45,000 | | | | 45,000 | 0.2% |
| Formoterol | 1,910 | 31,000 | | 11,700 | | 44,610 | 0.2% |
| **Total MDIs** | **151,363** | **26,271,000** | **1,151,980** | **974,100** | **299,488** | **28,847,931** | **100.0%** |

28. With regard to the data presented in the above table and information presented in the MDI project, it is noted that:

(a) In 2003, almost 82 per cent of all CFC-MDIs contained salbutamol (64.6 per cent) or beclomethasone (16.9 per cent). An additional 10 per cent contained a combination of beclomethasone/salbutamol or salmeterol/fluticasone;

(b) One enterprise, Cipla, manufactures more than 91 per cent of all CFC-MDIs manufactured in India;

(c) GSK, the second largest manufacturer of CFC-MDIs, with 4 per cent of total production, is partially owned by a non-Article 5 company (50.67 per cent) foreign ownership.

29. It is estimated that the conversion to HFA technology will be completed by December 2013, i.e., four years after the mandatory date for the complete phase-out of CFCs. There are no CFC stockpiles available with MDI manufacturers to cover needs during the transition period. Stakeholders have been fully briefed by the Government on the essential use nomination process. Accordingly, the Government of India, with the assistance of the implementing agencies and MDI manufacturers, would be in a position to request essential uses by January 2009.

**INDONESIA**[13]

30. CFCs were used for the manufacturing of MDIs and other aerosol pharmaceutical products by several national (Otsuka, Daya Varia and Konimex) and multi-national (Astra Zeneca, Boehringer Ingelheim and GlaxoSmithKline) enterprises. In 2005, Konimex ceased production of MDIs in 2005 due to scarcity of pharmaceutical-grade CFCs on the local market, and high costs associated with the conversion to non-CFC propellant.

31. Of the four multinational enterprises currently providing MDIs in Indonesia, one company, PT. Boehringer Ingelheim Indonesia, is locally manufacturing CFC MDIs. The 2006-2009 production levels of CFC MDIs by active ingredient are shown in the table below. Boehringer has decided to completely stop manufacturing CFC MDIs by the end of 2009 (the Government of Indonesia will not request any essential uses of CFCs for the manufacturing of MDIs).

[13] UNEP/OzL.Pro/ExCom/56/35.

| Active ingredient | CFC MDIs (units) | | | |
|---|---|---|---|---|
| | 2006 | 2007 | 2008 | 2009 |
| Metaproterenol | 81,661 | 170,709 | 108,500 | 94,500 |
| Ipratropium | 21,366 | 21,687 | 37,500 | - |
| Ipratropium/fenoterol | 10,758 | 10,731 | 22,500 | 11,250 |
| Fenoterol (two different strengths) | 208,044 | 214,391 | 491,250 | 112,500 |
| Ipratropium/albuterol | 49,511 | 47,377 | 91,000 | 73,500 |
| Budesodine (four different strengths) | 23,716 | 127,630 | 198,000 | 150,800 |
| Total | 395,056 | 592,525 | 948,750 | 442,550 |
| **CFC consumption (ODP tonnes)** | **8.9** | **11.5** | **14.9** | **9.3** |

**ISLAMIC REPUBLIC OF IRAN**[14]

32. About 2 million MDIs and 85,000 dry powder inhalers (DPIs) are imported into the country annually by multinational enterprises. Approximately 10 per cent of the imported MDIs are HFA-based. Sina Darou Laboratories Co., is the only locally-owned manufacturer of MDIs in the Islamic Republic of Iran. Current production includes salbutamol, beclomethasone, salmeterol and cromolyn MDIs. Technology for the production of salbutamol was provided by Norton-Waterford Limited (Ireland). The three other CFC-MDIs were developed and formulated by the company. The production levels of these MDIs are shown in the table below:

| Active ingredient | 2003 | | 2004 | | 2005 | | 2006 | |
|---|---|---|---|---|---|---|---|---|
| | MDI units | CFC tonnes | MDI units | CFC tonnes | MDI units | CFC tonnes | MDI units | CFC tonnes |
| Salbutamol | 3,175,660 | 66.34 | 3,600,762 | 75.40 | 2,664,758 | 55.82 | 4,299,304 | 89.91 |
| Beclomethasone | 2,844 | 0.06 | 2,920 | 0.06 | 267,033 | 5.59 | | |
| Cromolyn | | | | | 5,353 | 0.11 | 95,450 | 2.00 |
| Salmeterol | | | 1,706 | 0.04 | 99,131 | 2.08 | 214,966 | 4.50 |
| Total | 3,178,504 | 66.40 | 3,605,388 | 75.50 | 3,036,275 | 63.60 | 4,609,720 | 96.40 |

33. The company has decided to convert three of their CFC-based MDIs (salbutamol, beclomethasone and salmeterol) to HFC-134a technology. This will require technology transfer from an established enterprise. CFC-MDIs with cromoglycate will not be converted to an HFA-MDI under this project.

**MEXICO**[15]

34. CFC-MDIs have been produced in Mexico by Laboratorios Salus since 1999, containing the following three active ingredients: salbutamol, beclomethasone and cromoglycate. Production of salbutamol and beclomethasone MDIs represents 99 per cent of the enterprise's total MDI production. About 70 per cent of MDIs produced by this company are for the Mexican Social Health system and other government medical health services. The remaining 30 per cent production is for the local market. The production levels of these MDIs are shown in the table below:

| Active ingredient | 2004 | | 2005 | | 2006 | |
|---|---|---|---|---|---|---|
| | MDIs | CFC (tonnes) | MDIs | CFC (tonnes) | MDIs | CFC (tonnes) |
| Salbutamol | 1,746,347 | 40.35 | 2,136,750 | 37.34 | 2,902,704 | 58.60 |
| Beclomethasone | 655,005 | 15.13 | 542,527 | 9.48 | 575,246 | 11.61 |
| Cromoglycate | 73,909 | 1.71 | 38,736 | 0.68 | 34,664 | 0.70 |
| Total | 2,475,261 | 57.19 | 2,718,013 | 47.50 | 3,512,614 | 70.91 |

[14] UNEP/OzL.Pro/ExCom/52/36.
[15] UNEP/OzL.Pro/ExCom/53/44.

35. Ipatropium CFC-MDIs are also produced in Mexico by one transnational corporation. In 2006, about 26 tonnes of CFCs were used by this company. In June of 2004, this company introduced tiotropium dry powder inhaler to provide significant and sustained improvements in lung function for patients with chronic obstructive pulmonary disease. Non-CFC-MDIs are also being imported into Mexico by three multinational companies with the following active ingredients: cromoglycate, budesonide, beclomethasone, fluticasone, salbutamol, combined salbutamol/beclomethasone and salmeterol. In 2006, over 2.4 million non-CFC MDIs were imported by these companies.

36. It is estimated that the conversion will be completed by February 2011. The Government of Mexico is intending to stockpile pharmaceutical aerosol-grade CFCs, which are already available in the country, to be used by the company during the conversion process to HFA technology.

## PAKISTAN[16]

37. The manufacturing of CFC-MDIs in Pakistan was started in 1981 by GlaxoSmithKline (GSK) Pakistan Limited, with a current annual production of 4 million MDIs. Since then, the following two additional MDI manufacturing enterprises have been established:

(a) Zafa Pharmaceutical Laboratories, that established and registered its products in 1998 (current production of 0.2 million MDIs/year); and

(b) Macter International, that purchased a used CFC-MDI production line in 2004, and where development and testing for two MDI products began in 2007 and the first three products were launched in 2008 (with current production of 10 million MDIs/year).

38. Currently, all MDIs manufactured in Pakistan are CFC-based, and there is no local capacity or capability to produce non-CFC-MDIs. In 2007, total CFCs used for the manufacturing of 4.21 million MDIs was 99.6 ODP tonnes. The active ingredients in MDIs are salbutamol (manufactured by the three enterprises), salbutamol/beclomethasone (manufactured by Macter and Zafa), and beclomethasone, salmetrol/fluticasone, ipratropium, salmeterol and triamcinolone acetonite (manufactured only by Macter).

39. The project proposes to assist the manufacturing enterprises to convert to HFA technologies with supporting public education and awareness activities. There is no capacity in the country to allow for stockpiling of CFCs. Therefore, the Government will utilize the essential use nominations procedure for requesting CFCs post 2009.

## URUGUAY[17]

40. Since 1980, Laboratorios Haymann S.A., (100 per cent locally owned), produces CFC-based MDIs both for the domestic market and for a limited amount of export. By 1994, the installed capacity was 1.5 million MDIs/year (similar to the current capacity), with a CFC consumption of about 10 ODP tonnes for the manufacturing of the following MDIs:

[16] UNEP/OzL.Pro/ExCom/56/42.
[17] UNEP/OzL.Pro/ExCom/43/44.

| Drug | Total units |
|---|---|
| Salbutamol | 209,300 |
| Salmeterol | 2,700 |
| Cromoglycate | 3,400 |
| Fluticasone | 1,800 |
| Beclomethasone | 17,600 |
| Salbutamol/beclomethasone | 177,300 |
| Fenoterol | 16,800 |
| Ipratropium | 5,900 |
| Budesonide | 1,100 |
| Salmeterol+fluticasone | 150 |
| **Total** | **436,050** |

41. Laboratorios Haymann, S.A., is proposing to reformulate the following drugs with HFA propellant: salbutamol (170,000 units), salmeterol/fluticasone (140,000 units), fenoterol (20,000 units), ipratropium (40,000 units), and fluticasone (50,000 units). Presently, there are no patents in Uruguay for HFA MDI formulations. The replacement formulations for HFA MDIs would be developed locally by the staff of Laboratorios Haymann. Therefore, a technology transfer or a license agreement would not be required for implementing the investment project.

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