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EXECUTIVE COMMITTEE OF
THE MULTILATERAL FUND FOR THE
IMPLEMENTATION OF THE MONTREAL PROTOCOL
Fifty-second Meeting
Montreal, 23-27 July 2007

PROJECT PROPOSAL: ISLAMIC REPUBLIC OF IRAN

This document consists of the comments and recommendation of the Fund Secretariat on the following project proposal:

Aerosol

• Phase-out of CFC consumption in the manufacture of aerosol metered-dose inhalers (MDIs)	UNIDO
• National transitional strategy for the phase-out of CFC propellants in metered-dose inhalers (MDIs)	UNEP

PROJECT EVALUATION SHEET – NON-MULTI-YEAR PROJECT
ISLAMIC REPUBLIC OF IRAN

PROJECT TITLE(S)	BILATERAL/IMPLEMENTING AGENCY
(a) Phase-out of CFC consumption in the manufacture of aerosol metered-dose inhalers (MDIs)	UNIDO
(b) National transitional strategy for the phase-out of CFC propellants in metered-dose inhalers (MDIs)	UNEP

NATIONAL CO-ORDINATING AGENCY	National Ozone Unit (NOU), Department for Environment

LATEST REPORTED CONSUMPTION DATA FOR ODS ADDRESSED IN PROJECT

A: ARTICLE-7 DATA (ODP TONNES, 2005, AS OF JUNE 2007)

CFC	2,221.0		

B: COUNTRY PROGRAMME SECTORAL DATA (ODP TONNES, 2005, AS OF JUNE 2007)

ODS	Subsector/quantity	Subsector/quantity	Subsector/quantity	Subsector/quantity
CFC-11	MDI/17.92			
CFC-12	MDI/45.20			

CFC consumption remaining eligible for funding (ODP tonnes)	

CURRENT YEAR BUSINESS PLAN ALLOCATIONS		Funding US $ million	Phase-out ODP tonnes
	(a)	1,075,000 (for 2007)	25
	(b)	0	n/a

PROJECT TITLE:	(a)	(b)
ODS use at enterprise (ODP tonnes):	965.6	
ODS to be phased out (ODP tonnes):	96.4	
ODS to be phased in (ODP tonnes):		
Project duration (months):	38	38
Initial amount requested (US $):	5,451,549	118,200
Final project costs (US $):		
Transition Strategy Cost:		
Incremental Capital Cost:		
Technology Transfer Cost:		
Incremental Operating Cost:		
Total Project Cost:		
Local ownership (%):	100%	
Export component (%):	0%	
Requested grant (US $):		
Cost-effectiveness (US $/kg):	57.77	
Implementing agency support cost (US $):		
Total cost of project to Multilateral Fund (US $):		
Status of counterpart funding (Y/N):	Y	n/a
Project monitoring milestones included (Y/N):	Y	Y

SECRETARIAT'S RECOMMENDATION	For individual consideration

PROJECT DESCRIPTION

1. On behalf of the Government of the Islamic Republic of Iran, UNIDO has submitted the national strategy for the phase-out of CFCs in metered-dose inhalers (MDIs) in the Islamic Republic of Iran together with an investment project proposal for the phase-out of 96.4 ODP tonnes of CFC-11 and CFC-12 used in the manufacture of MDIs for consideration by the Executive Committee at its 52nd Meeting. Upon a request by the Government of the Islamic Republic of Iran, the transition strategy will be implemented by UNEP.

Background

2. At its 47th Meeting, the Executive Committee considered a request submitted by UNIDO for the preparation of an (MDI) phase-out project in the Islamic Republic of Iran at the amount of US $70,000. During the review of this request, the Secretariat pointed out that the approved NPP for the Islamic Republic of Iran was for the complete phase-out of CFCs in the country and that the Islamic Republic of Iran had agreed, by its acceptance of the agreement and performance by the Executive Committee of its funding obligations, that the country was precluded from applying for or receiving further funding from the Fund in respect of the consumption of CFCs. The request was, therefore, not eligible for approval. On the basis of that information and after further discussion, the Executive Committee decided to approve funding for the preparation of an MDI investment project in the Islamic Republic of Iran "on the understanding that approval of funding of that project preparation was an exception and should in no way set a precedent for opening agreements between the Executive Committee and a country regarding limits on further funding" (decision 47/21).

Sector background

3. 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.

4. Sina Darou Laboratories Co. is the only locally-owned manufacturer of MDIs in the Islamic Republic of Iran. The company was established in 1962 and the MDI production department was set up in 1993. The first CFC-MDI locally produced was salbutamol. Current production includes three additional MDIs: beclomethasone, salmeterol and cromolyn sodium. 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 sodium					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

National strategy for the phase-out of CFC-based MDIs

5. The Government of the Islamic Republic of Iran has prepared a national strategy for the phase-out of CFC-based MDIs, aimed at meeting a timetable and criteria that have been agreed by all stakeholders. The strategy has taken into account sufficient time and resources for the education of health professionals and the patients and their families in the replacement of CFC-MDIs. The strategy is also based on the coordination and participation of the Ministry of Health and Medical Education and the Department of the Environment for Human Environment Affairs.

6. Through discussions with major stakeholders (Sina Darou, MDI importers and distributors, and health providers) and coordination by the Ministry of Health and Medical Education and the Division of Pharmaceutical and Narcotics Affairs, the legal framework will be modified to support the transition strategy. The entire transition to a non-CFC MDI process will be led by the Ozone Unit in close coordination with the Ministry of Health and Medical Education.

7. The estimated cost of the transition strategy is US $118,200, with the following breakdown:

Activity	Cost (US $)
Legal/medical advisors	18,000
Education and communication activities	48,600
Project technical support	24,600
Coordination by the Ozone Unit	27,000
Total	**118,200**

8. The Government of the Islamic Republic of Iran is proposing to launch a first batch of non-CFC-based MDIs 28 to 30 months after the national transition strategy and the MDI phase-out investment project have been approved by the Executive Committee.

Project description

9. MDI production at Sina Darou is based on the pressure filling manufacturing process using a Pamasol Micromat machine with an estimated maximum output of 45 canisters per minute. 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 that has experience in the formulation and manufacturing of non-CFC-MDIs and has the right to transfer the technology without infringement of any intellectual property related to either the drug molecule, the method of formulation, the design of the metering valve or actuator, or the filling process. The other CFC-MDI with sodium cromoglycate as the active ingredient, currently manufactured by the company, will not be converted to an HFA-MDI under this project.

10. The conversion to HFA propellant will entail additional manufacturing processes, (vacuum crimping and aspiration of the filling head) reducing the number of MDIs currently produced. To compensate for the reduction in the level of production, it is proposed to install two Macromat machines that will be fed from the existing single-can feeder and cleaner and will be discharged through the existing single check weigher and take-off table. The proposed filling equipment will be capable of both single- and two-stage filling, allowing both types of

formulations to be used. The total capital cost associated with the installation of the two production lines has been estimated at US $2,307,623, including costs associated with modifying the manufacturing area, retrofitting equipment, establishing a temporary HFA storage facility and contingencies.

11. The proposed modifications for the new HFC-134a-based MDIs, by active ingredient, are shown in the table below, with associated technology transfer costs (an additional US $50,000 is being requested for stability tests and travelling):

Active ingredient	Proposed modifications	Technology transfer cost (US $)
Salbutamol sulphate	Pressure filled, HFA/ethanol formulation with surfactant. Standard container.	800,000
Beclamethasone dipropionate	Pressure filled, HFA/ethanol formulation with active dissolved in ethanol. Standard container.	800,000
Salmeterol xinafoate	Pressure filled, HFA formulation with no surfactant. Container internally coated.	800,000
Total cost		**2,400,000**

12. Incremental operating costs, calculated on the basis of the difference in prices between CFCs and HFC-134a, and the increased costs of the canister, metering valve and actuator, have been estimated at US $693,926 for a two-year period.

Total cost of the project

13. The total cost of the phase-out of CFCs used in the manufacture of MDIs in the Islamic Republic of Iran has been estimated at US $5,569,749 with a cost-effectiveness of US $57.78/kg. The project cost breakdown is presented below:

MDI transition strategy	US $118,200
Capital costs	US $2,307,623
Technology transfer	US $2,450,000
Operating costs	US $693,926

SECRETARIAT'S COMMENTS AND RECOMMENDATION

COMMENTS

14. The Secretariat reviewed the national strategy for the phase-out of CFCs in MDIs in the Islamic Republic of Iran and the investment phase-out project in light of:

(a) The MDI policy papers considered by the Executive Committee at its 37th Meeting (UNEP/OzL.Pro/ExCom/37/58), 49th Meeting (UNEP/OzL.Pro/ExCom/49/39) and 51st Meeting (UNEP/OzL.Pro/ExCom/51/39);

(b) The MDI phase-out projects so far approved for Cuba (UNEP/OzL.Pro/ExCom/41/33 and paragraphs 4 to 17 of document

UNEP/OzL.Pro/ExCom/46/19), Uruguay (UNEP/OzL.Pro/ExCom/43/44) and Egypt (UNEP/OzL.Pro/ExCom/50/29);

(c) The national phase-out plan (NPP) for the Islamic Republic of Iran (UNEP/OzL.Pro/ExCom/41/38) approved by the Executive Committee at its 41st Meeting at a cost of US $11,250,000 plus agency support costs for Germany as the lead agency, and France, UNDP, UNEP and UNIDO as cooperating agencies (decision 41/20). The NPP also included an Agreement between the Government of the Islamic Republic of Iran and the Executive Committee.

Essential use exemptions for CFCs

15. The Secretariat pointed out that in its decision 51/34, the Executive Committee requested, *inter alia,* that countries with MDI manufacturing plants should be advised of the timing to begin considering the need for essential use exemptions beyond the 2010 phase-out date. According to the project proposal, it is estimated that the conversion will be completed by October 2010. However, neither the project proposal nor the transition strategy considers the need for essential use exemptions for CFCs in the Islamic Republic of Iran. UNIDO reported that, based on information provided by Sina Darou, it expects that the conversion to HFA salbutamol MDI will be completed by the end of 2010. At that time, about 30 ODP tonnes of CFCs per year may still be needed for manufacturing other MDIs until full conversion is accomplished. Once the actual amounts of CFCs are known, the Government would request essential use exemptions.

Selection of alternative technology

16. The multi-dose DPI was considered not to be a feasible alternative to CFC-MDI production in the Islamic Republic of Iran since it would require a suitable DPI device and new production manufacturing and packaging lines, and the operating costs would be significant. According to the 2006 Medical Technical Options Committee report, in some countries single-dose DPIs may have a role because they require simple manufacturing technology, and can provide the opportunity to purchase a small number of doses at an affordable cost. The low level of technology involved in manufacturing these DPIs and their potentially low cost make them cost-effective alternatives, particularly for products such as salmeterol, which are very difficult to convert to HFC-134a-based MDIs. Though there are concerns regarding the aggregation of particles in a hot and humid climate, they have been generally found to be effective.

17. On this issue UNIDO indicated that the question of DPIs as an alternative technology had been discussed with the enterprise and it was determined that it was not a viable replacement for CFC-MDIs for the following reasons:

(a) Although DPIs are preferred by some patients because of their ease of use, they do not represent a satisfactory therapeutic alternative to the pressurised MDI for all patients or for all active ingredients. For example, children five years old and under, patients with severe asthma, and elderly COPD patients may not always be able to achieve adequate breathing flow to ensure optimal medication delivery from DPIs;

(b) The price of a single-dose DPI device is comparable to the HFA-MDI pack; however, to manufacture the devices, significant investment would be required for

tooling, new assembly and packaging lines and associated clean room areas, and scale-up of the capsule manufacturing lines;

(c) Special machinery is required for filling and packaging the inhalation capsule since the capsule has to be protected from the effects of moisture. While conversion from CFC to HFA-MDI would not require clinical tests, the majority of DPI clinical tests will be required;

(d) In the case of MDIs, there is no need to address issues regarding the use of a new device or changes to the application techniques. However, since the DPI is a completely new device it will require new instructions on storage, handling, loading and delivery.

18. UNIDO also indicated that the single-dose DPI for cromolyn sodium sold in the Islamic Republic of Iran is imported from India and is more expensive than a CFC-MDI. This type of drug delivery system has not been well accepted by local doctors and patients.

Adjustment from the funding approved for the NPP for the Islamic Republic of Iran

19. In the context of the Executive Committee agreement on strategic planning (decision 33/54), the Committee agreed at its 35th Meeting that further funding must be predicated on a commitment by the country to achieve sustainable permanent aggregate reductions in consumption and production, as relevant. The Committee also acknowledged that some future years' reported consumption may go above or below the levels that result from the agreed calculation, but if consumption numbers go above the resulting levels, such increases in consumption would not be eligible for funding. The resulting numbers represent maximum residual ODS that the Fund will pay to reduce, and existing Fund guidance related to eligibility of projects would be maintained in all respects (decision 35/57).

20. The Government of the Islamic Republic of Iran selected Option 2 under decision 35/57 as the starting point for determining the sustained reduction in CFC consumption in the Islamic Republic of Iran. Accordingly, the NPP for the Islamic Republic of Iran was approved for the phase-out of 1,708.4 ODP tonnes, representing the total remaining CFC consumption eligible for funding. Since the remaining eligible consumption has already included the amount of CFCs that were used for manufacturing MDIs, the overall level of funding for the MDI project should be adjusted accordingly to avoid double-counting. For the calculation of this adjustment, the Secretariat pointed out that:

(a) The NPP for the Islamic Republic of Iran reported a CFC consumption of 93 tonnes of CFCs for the production of some 3.6 million MDIs containing salbutamol, bechlomethasone or salmeterol;

(b) The cost of the NPP for the Islamic Republic of Iran (as well as for the majority of the NPPs for non-LVC countries) was calculated on the basis of a cost-effectiveness value of US $5.00 per kg of CFC used in the refrigeration servicing sector (plus the cost-effectiveness threshold applied to each manufacturing sector where CFC was still used), plus additional funding for monitoring and reporting.

21. On this basis, the adjustment to the NPP for the Islamic Republic of Iran would be US $465,000, calculated on the basis of the CFC consumption of 93.0 ODP tonnes in 2003 for the production of MDIs, and a cost-effectiveness value of US $5.00/kg.

22. UNIDO advised that the NPP for the Islamic Republic of Iran addresses the phase-out of CFCs in the solvent (CFC-113) sector, foam manufacturing sector, refrigeration manufacturing sector and the refrigeration servicing sector, including MAC systems and excludes the MDI sub-sector. Assistance for the MDI enterprise will be requested when cost-effective alternatives would become available.

Scope and cost of the transition strategy

23. Several HFC-134a-based MDIs and DPIs have already been introduced and are currently being used in the Islamic Republic of Iran, the locally-owned MDI manufacturing enterprise has already selected the HFC-134a technology and detailed project proposals have been fully developed and submitted for approval by the Executive Committee. Also, the cost of the national strategy was agreed at US $70,000, which will allow for the implementation of the main activities proposed.

Technical and cost issues related to the production facility

24. The Secretariat and UNIDO discussed technical issues related to the feasibility of utilizing and/or retrofitting some baseline equipment items when replacing CFCs by HFC-134a, and whether or not the technological upgrade and increased capacity of the replacement equipment for Sino-Darou had been taken into account in the project proposal. The costs associated with the technology transfer were also discussed, and estimated at almost US $800,000 for each of the three active ingredients plus an additional US $50,000 for tests and travelling; and the incremental operating costs.

25. In reviewing the NPP for the Islamic Republic of Iran, the Secretariat noted that over 90 tonnes of CFCs were consumed by Sina Darou for the manufacturing of three different MDIs, namely salbutamol, beclomethasone and salmeterol. According to information presented in the project proposal, in 2003 Sino Darou was producing salbutamol and beclomethasone MDIs, and actual production of salmeterol MDIs started in 2004. In the case of salmeterol, the replacement of CFC-11 and CFC-12 with HFA propellant will require a more complex process since ethanol cannot be used in the new HFA formulation.

26. On the basis of the actual consumption of CFCs for the manufacturing of three different active ingredients for MDIs reported in the NPP for the Islamic Republic of Iran, and taking into consideration the relatively small production volumes of beclomethasone and salmeterol MDIs compared to salbutamol MDIs, UNIDO is assessing the technical feasibility and economical viability of retrofitting some equipment items of the current production line and using a 300-litre pressure vessel instead of a 500-litre vessel as originally requested. UNIDO is also considering the technology transfer costs in light of the comments from the Secretariat, and is calculating the operating costs on the basis of a one-year period.

27. The Secretariat also noted that UNIDO is currently negotiating an agreement with a technology developer for the development of HFA MDIs for salbutamol, beclomethasone and salmeterol in Egypt. Therefore it is assumed that the Multilateral Fund, as the provider of the

financial resources to UNIDO, will have the ownership of the full specifications (including all relevant documents) for the development of HFA-MDIs with those active ingredients. Taking into consideration that the production processes for the three active ingredient MDIs in the Islamic Republic of Iran will be similar to those produced in Egypt, the only incremental costs that would need to be paid are those associated with documentation and testing. These costs would be much lower than the US $800,000 being requested for the development of each drug. On this basis, the Secretariat asked UNIDO to further explore this approach, which will represent major savings to the Multilateral Fund without jeopardizing the conversion at Sina Darou or similar projects in the future.

28. Addressing this issue, UNIDO informed the Secretariat that although the Multilateral Fund has ownership of relevant specifications and documentation, regulations related to the development of the various MDIs could be different from country to country. MDI components such as valves and canisters used by one company may differ from components at another company. Also, stability requirements are country-related and depend, among other things, on the duration of the testing period (3 months, 6 months or 12 months) and climatic conditions (temperature and relative humidity). Therefore, the documentation developed for a MDI with a specific active ingredient could only be used when the production parameters, MDI components, chemical suppliers, and regulations are the same.

Revision to the agreement between the Government and the Executive Committee

29. The current agreement between the Government of the Islamic Republic of Iran and the Executive Committee addresses all the remaining CFC consumption eligible for funding, including 93.0 ODP tonnes of CFCs that were used for the manufacturing of MDIs at the time of the approval of the NPP. Therefore, in case the project for the phase-out of MDIs in the Islamic Republic of Iran is approved by the Executive Committee, the current agreement should be modified accordingly.

Agreed level of funding

30. The Secretariat and UNIDO are still discussing cost-related issues. Outcomes of the discussions will be communicated to the Executive Committee prior to the 52nd Meeting.

RECOMMENDATION

31. Pending.