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EXECUTIVE COMMITTEE OF
THE MULTILATERAL FUND FOR THE
IMPLEMENTATION OF THE MONTREAL PROTOCOL
Fifty-first Meeting
Montreal, 19-23 March 2007

Addendum

PROJECT PROPOSAL: PEOPLE'S REPUBLIC OF CHINA

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 pharmaceutical aerosol sector (2007-2008 biennial programme)	World Bank

PROJECT EVALUATION SHEET – MULTI-YEAR PROJECTS
PEOPLE'S REPUBLIC OF CHINA

PROJECT TITLE	BILATERAL/IMPLEMENTING AGENCY
Phase-out of CFC consumption in the pharmaceutical aerosol sector (2007-2008 biennial programme)	World Bank

NATIONAL CO-ORDINATING AGENCY:	State Environment Protection Administration

LATEST REPORTED CONSUMPTION DATA FOR ODS ADDRESSED IN PROJECT

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

CFC	13,321.7		

B: COUNTRY PROGRAMME SECTORAL DATA (ODP TONNES, 2006, AS OF SEPTEMBER 2006)

ODS	Aerosol	Foam	Ref.	ODS	Solvents	Process agent	Fumigant
CFC-11	112.725						
CFC-12	372.366						

CFC consumption remaining eligible for funding (ODP tonnes)	

CURRENT YEAR BUSINESS PLAN: Total funding: US $13.63 million: Total phase-out: 386.0 ODP tonnes

PROJECT DATA		2006	2007	2008	2009	2010	Total
CFC (ODP tonnes)	Montreal Protocol limit	4,471.5	**4,471.5**	4,471.5	4,471.5	Tbd	
	Annual consumption limit	8,385.57	**8,385.57**	8,385.57	8,385.57	Tbd	
	Annual phase-out from ongoing projects	485.1	**485.1**	0	0	0	485.1
	Annual phase-out newly addressed						
	Annual unfunded phase-out						
TOTAL ODS CONSUMPTION TO BE PHASED OUT		485.1	**485.1**	0	0	0	485.1
Total ODS consumption to be phased-in (HCFCs)							
Final project costs (US $):							
Funding for Lead IA: World Bank		0	**8,793,520**	0	3,509,474	0	12,302,994
Total project funding		0	**8,793,520**	0	3,509,474	0	12,302,994
Final support costs (US $):							
Support cost for Lead IA: World Bank		0	**659,514**	0	236,211	0	922,725
Total support costs		0	**659,514**	0	236,211	0	922,725
TOTAL COST TO MULTILATERAL FUND (US $)		0	**9,453,034**	0	3,772,685	0	13,225,719
Final project cost effectiveness (US $/kg)							

FUNDING REQUEST: Approval of funding for the first tranche (2007) as indicated above.

SECRETARIAT'S RECOMMENDATION	Pending

PROJECT DESCRIPTION

1. On behalf of the Government of People's Republic of China (China), the World Bank has re-submitted a sector plan for phase-out of CFC consumption in China's pharmaceutical aerosol sector (Pharmaceutical Aerosol Plan), at a total cost to the Multilateral Fund of US $12,302,994, plus agency support costs of US $922,725, for consideration by the Executive Committee at its 51st Meeting.

Background

2. At its 50th Meeting, the Executive Committee considered for the first time the Pharmaceutical Aerosol Plan (UNEP/OzL.Pro/ExCom/50/28, paragraphs 1 to 35). The cost of the Plan as submitted was US $15,926,838 plus agency support costs of US $1,194,513 for the World Bank.

3. In introducing the project proposal to the Executive Committee, the Secretariat pointed out the main issues requiring consideration namely: assistance for some enterprises that were established after the cut-off date of 25 July 1995; funding for other enterprises that had not reported CFC baseline consumption; the selection of HFC-134a over hydrocarbon (HC) grade aerosol as a replacement for CFC propellant; and the overall cost-effectiveness of the project which, at US $32.83/kg, was more than seven times the threshold for the aerosol sector (US $4.40/kg). The Secretariat also informed the Executive Committee that the World Bank maintained that the 1995 cut-off date should not be applied, as the replacement technology was not available in China at that time, and further maintained that the cost-effectiveness threshold for the aerosol sector should not be applied.

4. Subsequently, the World Bank indicated that the Plan required additional work and requested that the project be withdrawn and re-submitted to the 51st Meeting of the Executive Committee.

Project summary

5. The revised Pharmaceutical Aerosol Plan is based on the replacement of CFC propellant by HFC-134a used in 41 pharmaceutical aerosol products (28 skin aerosol products and 13 cavity aerosol products), manufactured by 23 eligible enterprises.

6. The total cost of the Pharmaceutical Aerosol Plan is based on the following costs:

Cost Item	Unitary Cost (US $)	Units	Total Cost (US $)
Technical assistance	1,100,000	1	1,100,000
Screening substitutes	43,750	41	1,793,750
Technical dossier for skin aerosols	75,000	28	2,100,000
Technical dossier for cavity aerosols	93,750	13	1,218,750
Plant modifications (skin aerosol line)	63,750	13	828,750
Plant modifications (cavity aerosol line)	38,750	7	271,250
Production validation (per production line)	37,500	20	750,000
Training programme (per production line)	17,500	20	350,000
Operating cost	3,509,474	1	3,509,474
Contingency	841,250	1	841,250
Adjustment (foreign ownership)	(460,223)	1	(460,223)
Total			12,303,001

7. A copy of the revised project proposal is attached to the present document.

SECRETARIAT'S COMMENTS AND RECOMMENDATION

COMMENTS

8. The project proposal has included additional information on the eligibility of enterprises with zero or low CFC consumption. It covers the proprietorship of traditional medicinal herbs; the ingredients of chemical-based medicines; procedures required when changing the propellant in a registered drug; the use of alternative delivery mechanisms or alternative propellants; and a detailed description of the production process (including equipment baseline) in 17 enterprises.

9. The Pharmaceutical Aerosol Plan is based on the same technology and the same cost items as the Plan submitted to the 50th Meeting. It has only excluded eleven enterprises with zero or low CFC consumption levels which were unable to submit production plans for 2007, reducing the funding request by US $3,002,350. Therefore, the issues identified in the proposal submitted to the 50th Meeting still remain. These issues and the responses received from the World Bank are presented below.

Funding eligibility

Decision 17/7

10. Funding of US $704,000 is requested for the conversion of two enterprises that were established after the cut-off date of 25 July 1995 (Table 1). On the basis of decision 17/7 (i.e., "in the light of technological advances, not to consider any projects to convert any ODS-based capacity installed after 25 July 1995"), these enterprises are ineligible for funding:

Table 1

Enterprises established after 25 July 1995

Enterprise name	Lines	CFC (kg)	Product No.
17. Shandong Bencao Pharmaceutical	1	428	A26, A38
26. Huayi Pharmaceutical	1	380	A41
Total	**2**	**808**	

11. On the issue of the cut-off date for funding, the World Bank responded as follows:

(a) Decision 17/7 should apply only to the foam, refrigeration and general aerosol sectors, not the pharmaceutical aerosol sector. For this reason, the Executive Committee had not approved a single pharmaceutical aerosol project before 1995;

(b) Under the Drug Administration Law of China it is mandatory to submit any alteration to an approved drug to the regulatory agency before it can be produced. Obtaining approval from the regulatory agency usually takes three to four years; therefore, the research and development of pharmaceutical aerosol applications approved in July 1999 must have started at least in 1995;

(c) Substitute technologies were not available in the pharmaceutical sector in China in 1995. In fact, pharmaceutical aerosols were specifically excluded from the CFC ban in China's 1997 ODS regulation.

12. The Secretariat wishes to note, however, that:

(a) CFC alternative technologies for pharmaceutical aerosols were available prior to 1995. For example, because of the bans imposed by the Government of the United States on the use of CFCs in aerosols from 31 March 1978, the aerosol industry (including pharmaceutical aerosols) converted to HC technology. There were no issues associated with the use of HC propellants, and formulators of pharmaceutical products made an easy transition to their use. At the time of the transition to HC, HFC-134a was not commercially available;

(b) The Executive Committee has approved five investment projects for the phase-out of CFCs used in the production of pharmaceutical aerosols in three countries. The issue of availability of substitute technologies prior to 1995 was not raised in any project;

(c) The industry expert who assisted the Secretariat in reviewing the proposal has developed several pharmaceutical aerosols based on HC propellants for fillers in a number of countries (i.e., Argentina, Colombia, and Israel). Similar products are being filled in several other countries (such as Algeria, Australia, Brazil, Mexico, South Africa, and Tunisia).

Enterprises with no CFC consumption

13. Two other enterprises included in the Pharmaceutical Aerosol Plan, established prior to 25 July 1995, had no reported CFC baseline or CFC consumption, as shown in Table 2 below. Therefore, funding for these enterprises is not eligible.

Table 2

Enterprises with no CFC baseline or CFC consumption*

Enterprise name	Product No.
2. Beijing Haiderun Pharmaceutical	A25, A28, A30
8. Xinyi Pharmaceutical General Factory (Shanghai Pharmaceutical Group)	A06, A24, A35

(*) As presented in Table 2-3 in the project proposal.

14. The World Bank reported that even though the two companies have no reported CFC baseline, it does not mean that they have given up their aerosol business, as production is subject to market demand as well as production arrangements. Based on the latest review of the proposal, the two enterprises had reported a small amount of production in 2006. In order to maintain their production rights, the Government of China is requesting funding associated with screening and registration.

Conclusion

15. On the basis of the above analysis, the Secretariat concludes that the 17 enterprises listed in Table 3 below are eligible for funding since they were established prior to 25 July 1995, have CFC baseline consumption and are currently using CFCs.

Table 3

List of enterprises eligible for funding

Enterprise name	Lines	CFC (kg)*	Skin product	Cavity product
1. Wuxi Shanhe Group No.1 Pharmaceutical	2	823	A10, A23	
5. Guiyang Dechangxiang Pharmaceutical	1	13		A07
7. Beijing Tongrentang Technology Development	1	14	A35	A21, A34
9. Fujian Nanshaolin Pharmaceutical	1	10,684	A22, A33	
11. Penglai Nuokang Pharmaceutical	1	3,491	A23	
13. Hubei Nanyang Pharmaceutical	1	34,575	A29	
14. Shenyang Jingcheng Pharmaceutical	1	28,859	A17	
16. Pharmaceutical Factory of Hunan Bencao pharmacy	1	1,300	A16	
18. Shandong Jewim Pharmaceutical BlueBox	1	12,080	A23	A38, A39
19. Suizhou Pharmaceutical (Wuhan Jianmin Group)	1	13	A14, A19	
20. Guizhou Antai Pharmaceutical	1	20,827	A02, A08	
21. Guizhou Xinyi Pharmaceutical Corporation	1	229	A13	
23. Xinjiang Biochemistry Pharmaceutical	1	2,592		A05
24. Yunnan Baiyao Group Corporation	1	273,333	A45	
27. Zhanjiang Xintongde Pharmaceutical	1	29,397	A11, A22, A23, A27, A32	A38, A40
29. Guizhou Hongyu Pharmaceutical	1	1,231	A36	A01
32. Shanghai Yishengyuan Pharmaceutical	1	112	A11, A23	
Total	**17**	**419,573**		

***** Total eligible CFC consumption after deducting 30 and 50 per cent of foreign ownership of enterprises 13 and 14 respectively

16. The World Bank considers that the following four enterprises are also eligible for funding: Beijing Haiderun Pharmaceutical (No. 2) Xinyi Pharmaceutical General Plant, Shanghai Pharmaceutical Group (No. 8), Shandong Bencao Pharmaceutical (No. 17) and Huayi Pharmaceutical (No.26).

Selection of alternative propellant

17. Based on an analysis of the properties of dimethyl ether (DME), HC and HFC-134a as alternative propellants, and a review of technical literature, the Pharmaceutical Aerosol Plan tentatively concluded that:

(a) HFC-134a, HFA-227, DME, HC and compressed gas (such as carbon dioxide) are all considered potential alternative propellants. Each propellant has its unique physicochemical properties; each aerosol application has a different production process and different formulation. Therefore, the substitute screening test is arranged to choose the optimal alternative propellant from a medical perspective;

(b) The price of propellants is not the only factor that determines the selection of a substitute. The selection of the alternative propellant must also take into consideration the drug, its effect on the safety and efficacy of the drug, its compatibility with all the ingredients, changes in production technique, equipment and raw materials, safety and efficacy;

(c) Conversion to either DME or HC propellant is technically more difficult than converting to HFC-134a, which has properties similar to those of CFCs. It will require substantial investment at the enterprise level, and in some cases relocation of the production line, to meet safety requirements. Conversion to HFA-134a will require minor modifications to existing production lines, and therefore will be cheaper and faster to implement. Moreover, HFC-134a is widely used as an aerosol propellant in other countries;

(d) Although DME and HC are cheaper than HFC-134a, savings associated with their use will be small due to the smaller amount of propellant used in pharmaceutical aerosols compared to other aerosol products;

(e) There is no international experience for the conversion of CFC-based traditional Chinese medicine aerosols. Some enterprises had reported that, based on preliminary testing, HC was not compatible with their aerosol products;

(f) Therefore, the Pharmaceutical Aerosol Plan proposes the conversion of all enterprises to HFC-134a propellant, as the least costly option maintaining product quality.

18. In regard to the selection of HFC-134a as the replacement propellant, the Secretariat notes as follows:

(a) Although HFC-134a has been selected as the replacement propellant for pharmaceutical aerosols, the proposal states that "presently, due to lack of testing data, Chinese pharmaceutical manufacturers are not able to decide which substitute is the best one for their aerosol products, particularly for those producing Traditional Chinese Medicine aerosol products". It is further indicated that "funding is requested to allow those enterprises to screen potential substitutes. The objective of the screening is to identify the best substitute or alternative delivery system for their pharmaceutical aerosol products";

(b) Expert advice available to the Secretariat indicates that all the pharmaceutical aerosol products could be converted to HC propellants. This conclusion, which was questioned by the World Bank, is based on documented evidence of HC propellant use in pharmaceutical aerosol skin and cavity products available worldwide,[1] and on the Secretariat's experience with projects for the conversion of pharmaceutical aerosols funded by the Multilateral Fund in at least three Article 5 countries, where several pharmaceutical aerosols are currently being produced with HC propellants;[2]

[1] A few examples of these products are nitrate vasodilator for acute relief of angina pectoris due to coronary artery disease sprayed on or under the tongue; hydrocortisone acetate and pramoxine hydrochloride topical aerosol foam for anal use; topical corticosteroids used as anti-inflammatory and antipruritic agents; several anti-fungi aerosols for treatment of tinea pedis (athlete's foot), tinea cruris (jock itch) and tina corporis due to T. rubrum, T. mentagrophytes and E. flocossum, exclusive of nails and hair area; betamethasone valerate for the treatment of corticosteroid-responsive scalp dermatoses; first aid antiseptic liquid bandage spray; aerosol formulation containing beclomethasone dipropionate; and topical anaesthetic spray containing benzocaine as active ingredient).

[2] These products include: pain relief and muscle relaxant which uses methyl salicylate and allied chemicals; local anaesthetic with a chemical like lidocaine; pharmaceutical products for skin burn relief and remedy including

(c) HCs are better propellants than CFCs or HFC-134a, mainly due to their lower molecular weights. For example, the same aerosol product using 8 per cent (in weight) of CFCs, would use only 4 per cent HCs or 9 per cent HFC-134a. Also, water-based pharmaceutical aerosol products cannot be reformulated to use HFC-134a propellant, since the internal pressure in the can will be too high and, due to its density (1.2 g/ml), the propellant will sink to the bottom of the can so damaging the product;

(d) Furthermore, there is no compelling evidence to suggest that the Chinese traditional medicine drugs are compatible with CFC but not HC propellants. Aerosol-grade HCs have never been cited as undergoing chemical reactions with thousands of aerosol ingredients currently produced, including chemical drugs; herbal medicines; animal, fish and marine plant extracts; other pharmaceutically active compounds; and aerosol food products;

(e) Except for metered dose inhalers (MDIs), the use of HFC-134a as a propellant has already been banned in the majority of aerosol applications in Canada, several European countries and the United States.[3]

Production line modifications

19. The capital cost for the replacement of CFC propellant in 20 production lines (13 for skin aerosols and 7 for cavity aerosols) is based on the following assumptions:

(a) US $63,750 for each automatic production line for skin aerosol products converted to HFC-134a propellant;

(b) US $38,750 for each semi-automatic production line for cavity aerosol products converted to HFC-134a propellant;

(c) US $360,000 for each production line irrespective of the type of aerosol produced (i.e., skin or cavity) converted to HC. This cost includes US $190,000 for replacement of the existing production line.

20. Based on the above assumptions, a total capital cost of US $1,100,000 has been estimated for the conversion to HFC-134a propellant and US $7,200,000 for the conversion to HC propellant. An additional US $3,509,474 has been estimated as operating costs associated with the use of HFC-134a propellant over a two-year period (if a four-year period had been considered, the operating costs would have been about US $6.63 million).

21. The Secretariat notes as follows:

(a) The cost analysis fails to acknowledge that there is no need to replace the entire

antiseptics and anaesthetics; povidone iodine (broad spectrum antiseptic and antifungal); antisceptic air freshener containing BKC; medicinal body deodorant; and wound dressing aerosol which contains cetrimide; dental products containing lidocaine and other chemicals to stop bleeding; and rubbing alcohol spray for massage containing isopropyl alcohol.

[3] In the United States, HFC-134a propellants are allowed in applications where flammability is a concern and not-in-kind alternatives are not available or applicable.

production line when replacing CFC with HC propellant.[4] The only equipment items that might need to be provided are a gasser unit, pumps, gas sensors, crimper tools and ventilation equipment. The total cost of the equipment required for the conversion, including shipping cost, installation, training (at the plant level) and contingency costs (at 10 per cent), has been estimated at US $2,460,000;

(b) The replacement of the entire production line at a cost of US $190,000 as proposed in the project would imply an increase in production capacity for all the existing production lines. For example, the current price in the United States of a new aerosol production line (40 cans/min) consisting of a rotary index machine with two product fillers, a vacuum crimper, propellant charger and conveyor would be US $100,000. This machine would be capable of producing 5 million aerosols/year on the basis of the standardized production period of 2,080 hours/year;

(c) The annual amount of HC that would be required by five enterprises is very small (between 8 and 143 kg per year). For five other enterprises, the annual amount of HC could be stored in two or three one-tonne cylinders (i.e., portable horizontal tanks about 800 mm in diameter and 2.4 m long, holding about 375 kg of HP blends that will need to be refilled once or twice a year). For the remaining six enterprises, their current CFC-bulk tank could be used for HCs.[5] To avoid an increase in the size of the CFC tanks to compensate for the lower density of HCs, the tanks would need to be refilled at shorter intervals (i.e., every four months instead of the current six months);

(d) Moreover, the use of HC propellants would yield operating savings of US $710,000 for a two-year period or almost US $1,3 million if 4 years were to be considered (this analysis is based on propellant prices of US $2.20/kg for CFCs and US $1.56 for HC, and considering a 37.5 per cent reduction by weight in the amount of HCs as compared to CFCs). In comparison, the use of HFC-134a would yield operating costs of US $3,536,824 over a two-year period;

(e) Furthermore, there are two plants in China with hydrogenation purification equipment allowing for the production of aerosol-grade HCs.

22. The Secretariat also noted that if HFC-134a were to be selected as a propellant, there would be no need to replace any of the equipment in existing production lines using CFC propellant. Some equipment suppliers suggest the use of certain types of rubber gaskets on the gasser, as recommended by the producers of HFC-134a, but this capital cost would not amount to the US $63,750 requested for each production line for skin aerosol products and US $38,750 for each production line for cavity aerosol products converted to HFC-134a propellant.

23. In response, the World Bank pointed out that:

[4] There is no need to replace the product filler, crimper or gasser when switching from CFC to HC propellants. The replacement of the gasser (and the crimper for relatively large production outputs) could be justified in the interest of reduction in leakage of HC propellant, and to reduce production down-time, and enhance injection accuracy.

[5] CFC-11 bulk tanks would require sandblasting and filling with iso-butane or nitrogen, after which the tank manhole can be resealed and the tank filled with HCs.

(a) There are many differences in equipment types and models in the pharmaceutical aerosol production lines in China. Given the advances in pharmaceutical manufacturing machines, it would be impractical to purchase the low-level equipment needed to replace the current combination of automatic and semi-automatic production lines, particularly since the principle of the programme is to maintain the original scale and level of production without enlarging or reducing the production capacity;

(b) The modification costs should be based on the production lines, rather than on baseline production, because production is subject to market demand and might increase in the future. Existing production lines vary from 500-5,000 can/hour;

(c) With regard to the cost savings represented by HC technology, the quantity of HC used in each aerosol must be determined according to the result from the substitute-screening test.

Issues related to technical assistance

24. In reviewing the unitary costs proposed in the Pharmaceutical Aerosol Plan, the Secretariat noted that:

(a) US $1.1 million has been requested for technical assistance activities, which include workshops, training programmes, public awareness activities, consultants, study tours and other unidentified activities. An additional US $6,212,250 has been requested for the following activities: US $1,793,500 for screening substitutes, US $3,318,750 for the preparation for technical dossiers for registration; US $750,000 for production validation; and US $350,000 for staff training. In many cases, this would constitute double counting since similar activities are requested more than once (i.e., toxicological evaluations and tests, studies on quality, training for sales staff);

(b) The funding levels being sought for screening substitutes, for the preparation of technical dossiers and for production validation have not taken into consideration the production levels of each product. For example, the total cost associated with these items for the enterprise with a production output of 100 cans per year is US $312,500 while the total cost for the enterprise producing over 5 million cans per year is US $156,250. If the two enterprises manufactured similar aerosols, the cost per can for these elements alone would be US $3,125.00 and US $0.03, respectively;

(c) There are only 21 different types of pharmaceutical aerosols that are produced in China (i.e., some products are manufactured by more than one enterprise). However, funding for screening substitutes and for preparation of technical dossiers are requested for 41 aerosol products. This would constitute double counting;

(d) Pharmaceutical enterprises manufacturing the same type of product could share data development (i.e., formulation data, packaging data, methodology of compounding the concentrates, drug assay methods and results, product stability

data) avoiding duplication in a number of cost and time-intensive areas. The shared data could then be used to satisfy many of the requirements of the product registration form;

(e) A senior chemist with extensive experience in the development of pharmaceutical aerosol formulations would be able to develop quantitative formulations for replacing CFC propellants in all the aerosols included in the Pharmaceutical Aerosol Plan; the method of compounding the concentrate; stability data limited to physical tests of formula and dispenser compatibility (such as the absence of can corrosion or the continued satisfactory operation of the aerosol valve); the specifications of the can and valve, and packaging notes;

(f) Technical assistance can be obtained from the Spray and Aerosol Research Centre located in Shanghai, China. The Director of the centre has lectured hundreds of times at national and international seminars and symposia and published several books in Chinese and English (i.e., Aerosol Technology, Aerosol Propellant Handbook; Aerosol Valve and Spray Pump Handbook; Design of Aerosols and its Formulation Technology).

25. In response to the above issues, the World Bank stated that:

(a) The training under the technical assistance programme includes protection of the ozone layer; the implementing procedures and requirements for the Fund-supported ODS phase-out programme; instruction for purchasing, financing and reporting; auditing requirements; and policy. However, the training conducted for each enterprise consists of the introduction of substitutes or substituting techniques at the production lines;

(b) There are only five products which are being produced by more than one enterprise. When one application is produced by several enterprises, the production process is often different, and thus the technical dossier must be finished independently. In addition, business confidentiality issues may arise from the conversion, so data sharing is therefore not considered;

(c) Since the substitute screening and tests for registration are required by law, the necessary procedures for the CFC conversion programme are independent of the numbers of an aerosol being manufactured; and

(d) Due to the specificity of drugs, the cost of technical activities carried out to meet legal requirements is very high, and there is no direct relation with the level of production of pharmaceutical aerosols or CFC consumption.

Industrial rationalization and cost-effectiveness

26. In reviewing the Pharmaceutical Aerosol Plan, the Secretariat developed an indicative table associating each unitary cost proposed in the Plan to each of the 17 eligible enterprises (Table 4 attached). In this analysis, the total requests for technical assistance and operating costs were divided by the total amount of CFCs to be phased out (i.e., 465.355 ODP tonnes) and pro-rated among the 17 enterprises eligible for funding on the basis of their total CFC consumption.

27. Based on this analysis, the Secretariat came to the following conclusions:

(a) CFC consumption in five enterprises is very small, ranging from 13 to 229 ODP kg per year. The total CFC consumption of one enterprise (273.3 ODP tonnes) represents 65.1 per cent of total eligible consumption in the sector;

(b) The overall cost-effectiveness (CE) of the project is US $27.23/kg (on the basis of the 17 eligible enterprises), which is more than 6 times the CE threshold for the aerosol sector established by the Executive Committee at its 16th Meeting (i.e., US $4.40/kg);

(c) The most cost-effective enterprise is the largest producer of pharmaceutical aerosols in China (plant No. 24), with a CE of US $12.15/kg. Of the total cost requested for the conversion of that enterprise (i.e., US $3,321,869), US $2,065,780 is in operating costs associated with the use of HFC-134a propellant;

(d) The five "least cost-effective" enterprises have CE values between US $1,152.03/kg and US $40,279.05/kg;

(e) Contrary to the practice in formulating several of the national sectoral phase-out plans approved for China and all other Article 5 countries, industrial rationalization has not been considered in the Pharmaceutical Aerosol Plan.

28. The Secretariat further notes that the five pharmaceutical aerosol projects that have been funded by the Multilateral Fund had a CE equal to or below the CE threshold of US $4.40/kg for the aerosol sector.

29. In response to the Secretariat's analysis, the World Bank said that:

(a) Small production levels for some of the companies did not reflect the importance of the product. The small CFC consumption in the manufacture of 12 pharmaceutical aerosols was due to market and clinical demands and frequency of use and price that made production output vary considerably. Furthermore, the data presented in the proposal was based on actual production by the enterprises, which could be expanded at any time once the legally prescriptive conditions and capacity for production were achieved;

(b) The CE of the project is poor. However, as this is a new sector, the Bank disagreed that the threshold of US $4.40/kg for general aerosols could be applied, particularly since cost elements not relevant to general aerosols are necessary for

pharmaceutical aerosols. The Executive Committee has not yet discussed, nor decided on polices and guidelines for the pharmaceutical aerosol sector;

(c) The CFC consumption per unit in pharmaceutical aerosols is significantly lower than in general aerosols (i.e., 10 to 20 per cent of what is contained in general aerosols). Therefore, the cost of converting pharmaceutical aerosols per kg of CFC phased out would be significantly higher than for general aerosols;

(d) Although substitute screening and tests for registration are the key points to ensure the phase-out of CFCs, they belong to the scope of technical activity. By subtracting these two costs, and the cost of the use of a substitute (at US $5,593,869), the overall CE value is between US $6.45 US $6.71 per kg;

(e) Except for one enterprise, the remaining 20 enterprises use only one production line to manufacture several products. Products of one enterprise are, in most cases, different from those of other enterprises. In addition, business confidentiality and potential property rights would arise from the conversion, so industrial rationalization is not considered in the pharmaceutical sector.

Level of funding proposed

30. Based on the calculations by the Secretariat, the total capital cost for the conversion of all the eligible enterprises to HC propellant would be US $2,460,000; the operating savings (calculated over a two-year period instead of the four-year period used in all aerosol projects) would be US $710,000 (compared to US $5,340,501 for the use of HFC-134a propellant), with a net incremental cost of US $1,750,000, resulting in a CE value of US $4.17/kg. The Secretariat is recommending, however, to apply the CE threshold for the aerosol sector on the eligible consumption of CFCs plus an additional 20 per cent for technical assistance for the entire pharmaceutical aerosol sector (excluding the MDI sub-sector). On this basis, the level of funding would be US $2,221,500. This amount has not included the costs associated with screening, registration of drugs and technical dossiers for which the World Bank is requesting US $5,862,250; the Secretariat cannot indicate a funding level for these costs, since similar costs were not requested in any of the pharmaceutical projects that have been approved by the Executive Committee.

31. The World Bank responded that, while the project is not as cost-effective as the Secretariat might want, all of the costs are incremental and eligible and should be considered as such. It reiterated that the pharmaceutical aerosol sector includes components that are not relevant to the general aerosol sector, hence the CE for that sector should not be applied. Finally, the 1995 cut-off date should not be applied, since the technology was not available in China at that time.

RECOMMENDATION

32. The Executive Committee may wish to consider the Pharmaceutical Aerosol Plan in light of the above comments and observations.

Table 4

Analysis by the Fund Secretariat of the submitted cost of the Pharmaceutical Aerosol Plan for all eligible enterprises

Enterprise name	CFC eligible	TAS	Screen	Dossier	Plant mod.	Validate	Training	Operating Cost	Contingency	Total Cost	CE
1. Wuxi Shanhe Group No.1 Pharmaceutical Co., Ltd	823	2,158	87,500	150,000	127,500	75,000	35,000	6,220	48,338	531,715	646.07
5. Guiyang Dechangxiang Pharmaceutical Co., Ltd	13	34	43,750	93,750	38,750	37,500	17,500	98	23,138	254,521	19,578.51
7. Beijing Tongrentang Technology Development Co.	14	37	131,250	262,500	63,750	37,500	17,500	106	51,264	563,907	40,279.05
9. Fujian Nanshaolin Pharmaceutical Co., Ltd	10,684	28,010	87,500	150,000	63,750	37,500	17,500	80,747	46,501	511,508	47.88
11. Penglai Nuokang Pharmaceutical Co., Ltd	3,491	9,152	43,750	75,000	63,750	37,500	17,500	26,384	27,304	300,340	86.03
13. Hubei Nanyang Pharmaceutical Co., Ltd	34,575	90,646	43,750	52,500	63,750	37,500	17,500	261,310	56,696	623,651	18.04
14. Shenyang Jingcheng Pharmaceutical Co., Ltd	28,859	75,659	43,750	37,500	63,750	37,500	17,500	218,105	49,376	543,140	18.82
16. Pharmaceutical Factory of Hunan Bencao pharmacy Co. Ltd	1,300	3,408	43,750	75,000	63,750	37,500	17,500	9,825	25,073	275,807	212.16
18. Shandong Jewim Pharmaceutical Co., Ltd BlueBox	12,080	31,670	131,250	262,500	63,750	37,500	17,500	91,297	63,547	699,015	57.87
19. Suizhou Pharmaceutical Co. Ltd of Wuhan Jianmin Group	13	34	87,500	150,000	63,750	37,500	17,500	98	35,638	392,021	30,155.43
20. Guizhou Antai Pharmaceutical Co., Ltd	20,827	54,602	87,500	150,000	63,750	37,500	17,500	157,405	56,826	625,083	30.01
21. Guizhou Xinyi Pharmaceutical Co.	229	600	43,750	75,000	63,750	37,500	17,500	1,731	23,983	263,814	1,152.03
23. Xinjiang Biochemistry Pharmaceutical Co., Ltd	2,592	6,795	43,750	93,750	38,750	37,500	17,500	19,590	25,764	283,399	109.34
24. Yunnan Baiyao Group Corporation	273,333	716,602	43,750	75,000	63,750	37,500	17,500	2,065,780	301,988	3,321,869	12.15
27. Zhanjiang Xintongde Pharmaceutical Co., Ltd	29,397	77,071	306,250	562,500	63,750	37,500	17,500	222,175	128,675	1,415,420	48.15
29. Guizhou Hongyu Pharmaceutical Co., Ltd	1,231	3,227	87,500	168,750	63,750	37,500	17,500	9,304	38,753	426,284	346.29
32. Shanghai Yishengyuan Pharmaceutical Co., Ltd	112	294	87,500	150,000	63,750	37,500	17,500	846	35,739	393,129	3,510.08
	419,573	1,100,000	1,443,750	2,583,750	1,097,500	675,000	315,000	3,171,020	1,038,602	11,424,623	27.23

Sector Plan for Phaseout of CFCs Consumption in China Pharmaceutical Aerosol Sector

State Environmental Protection Administration

State Food and Drug Administration

and

National Institute for the Control of Pharmaceutical and Biological Products

January 20, 2007

TABLE OF CONTENTS

Summary

This sector plan aims to assist China to phase out CFCs consumption in its pharmaceutical aerosol sector excluding MDIs applications. The funding request targets the consumption of 485.089 ODP MT CFCs. The sector plan was prepared on the basis of a detailed analysis of eligible aerosol applications in China. It proposes conversion to non-ODS substitute aerosol where mature substitutes are available. Before new non-CFCs production starts, manufacturers are allowed to use stockpiled CFCs to maintain production to meet clinical demand. The sector plan will be implemented through two biennial programs starting in 2007. The sector plan includes policy actions to ensure that the phase-out proceeds on schedule. An action plan indicating annual CFC phase-out targets is included in the proposal and the first biennial program for 2007-2008 is submitted along with this sector plan.

Pharmaceutical Aerosol Manufacturers:	**39**
Eligible Manufacturers:	**32**
Applications by Eligible Manufacturers:	**24** Skin Aerosol Applications **16** Cavity Aerosol Applications
CFCs Baseline Consumption(Average of 2003-2005):	**485.089 ODP MT**
ow. CFCs Consumption Requested for MLF Grant:	**464.355 ODP MT**
Project Duration:	**4 years**
Project Incremental Cost:	**US$12.303 million**
Requested MLF Funding:	**US$ 12.303 million**
IA Support Cost	**US$ 922,725**
Total cost to the MLF	**US$ 13.226 million**
Cost Effectiveness:	**US$ 25.36/kg ODP**
National Coordinating Agency:	**SFDA and SEPA**

PROJECT COVER SHEET – MULTI-YEAR PROJECTS

COUNTRY: China, Peoples Republic of

PROJECT TITLE	**BILATERAL/IMPLEMENTING AGENCY**
Phaseout of CFC consumption in the Pharmaceutical Aerosol Sector	WORLD BANK

NATIONAL CO-ORDINATING AGENCY: STATE ENVIRONMENT PRTOCTION ADMINISTRATION

LATEST REPORTED CONSUMPTION DATA FOR ODS ADDRESSED IN PROJECT

A: ARTICLE-7 DATA (ODP TONNES, 2005, SUBMITTED SEPT 2006

Annex A, Group 1 productions (CFCs)		Annex A, Group 1 consumption (CFCs)	

B: COUNTRY PROGRAMME SECTORAL DATA (ODP TONNES, 2006 AS OF SEPT 2006

ODS	Pharmaceitical aerosol	ODS			
CFC-11	112.723				
CFC-12	372.366				

CFC consumption remaining eligible for funding (ODP tonnes)	Not Applicable

CURRENT YEAR BUSINESS PLAN: Total funding $10 million: total phase-out ODP tonnes.

PROJECT DATA		2006	2007	2008	2009	2010	Total
CFC (ODP tonnes)	Montreal Protocol Production Limits	4,471.5	4,471.5	4,471.5	4,471.5	Tbd	
	Montreal Protocol Consumption Limits	8,385.57	8,385.57	8,385.57	8,385.57	Tbd	
	Max CFC consumption (Note 2: CFC-11 and CFC-12)	485.1	485.1	0	0	0	485.1
	Stockpiled CFC used during a transitional period from Aug. 2007	-	Note 1	Note 1	Note 1	Note 1	
TOTAL ODS CONSUMPTION TO BE PHASED OUT		485.1	485.1	0	0	0	485.1
Total ODS consumption to be phased-in (HCFCs)		NA	NA	NA	NA	NA	NA
Project Funding for P.R. China : (US $ in thousands)			8,793,520	0	3,509,474	0	12,302,994
Funding for lead agency [*WB*], (US $ in thousands):			8,793,520	0	3,509,474	0	12,302,994
Total project funding			8,793,520	0	3,509,474	0	**12,302,994**
Support costs (US $ (US $ in thousands):))			659,514	0	263,211	0	922,725
Support cost for lead agency WB (US $ in thousands):]			659,514	0	263,211	0	922,725
Total support costs			659,514	0	263,211	0	**922,725**
TOTAL COST TO MULTILATERAL FUND (US $)			**9,453,034**	**0**	**3,772,685**	**0**	**13,225,719**

Project cost effectiveness (US $/kg)

Note 1: CFC from stockpile established before July 2007 may be used based on special permission from SFDA

Note 2: 112.723 ODP tons of CFC-11 and 372.366 ODP tons of CFC-12

FUNDING REQUEST: FOR THE BI-ENNIAL PROGRAM FOR 2007-2008 US$ 12,680,000 and support cost of US$ 951,000

Prepared by: SEPA and SFDA **Date: January 2007**

Reviewed by: World Bank **Date: January 2007**

CHAPTER 1 Introduction

1. Background

1. The Government of China ratified the Montreal Protocol on Substances that Deplete the Ozone Layer in 1991 and finalized China Country Program for Ozone Depleting Substances Phase-out in January 1993. This Country Program was submitted to the 9th Executive Committee (ExCom) of the Multilateral Fund of the Montreal Protocol in March 1993 and was updated by China in November 1999. From 1997 to 2006, several phase-out sector plans have been developed and implemented, reaffirming China's commitment to meeting its obligations for phase-out of ODS consumption with the support of MLF.

2. Funding of US$ 135,000 was approved at the 43rd ExCom meeting in July 2004 to prepare *the Sector Plan for Phase-out of CFCs Consumption in China Pharmaceutical Aerosol Sector (non-MDIs)*. As the leading agency for the implementation of Montreal Protocol, the State Environmental Protection Administration of China (SEPA), in cooperation with the State Food and Drug Administration (SFDA), selected National Institute for the Control of Pharmaceutical and Biological Products (NICPBP) to prepare this sector plan.

2. Objectives

3. The main objectives of this sector plan include the following:

   a Identify all CFCs-based pharmaceutical aerosol manufacturers, their aerosol applications and CFCs consumption;

   b Design a technical scheme for phaseout of CFCs consumption in China pharmaceutical aerosol sector based on available non-ODS substitutes;

   c Develop a CFCs Phaseout Action Plan to meet the requirement of *China Accelerated Phase-out Plan(APP);*

   d Request MLF funding consistent with the MLF policies and guidelines to phase out CFCs in the sector[1];

   e Develop new CFCs phase-out policies for pharmaceutical aerosol sector; and

   f Develop a monitoring and management system to ensure successful implementation of the CFC phase-out in the pharmaceutical aerosol sector and rational utilization of MLF funds.

[1] As substitute technology was not available in 1990s, it is proposed that the cutting off date should be July 1, 1999 after which Article 5 Parties had the obligation to freeze CFCs production and consumption (see paragraph 45).

CHAPTER 2 Sector Profile

1. Background

4. China pharmaceutical aerosol industry started fairly late. In 1964, Shanghai Institute of Pharmaceutical Industry, in cooperation with Shanghai Sine Pharmaceutics Factory, Wuxi First Pharmaceutics Factory and Chongqing Seventh Pharmaceutics Factory, developed and produced Pingchuan (Anti-asthmatic), the first aerosol product in China. The period from 1964 to the 1980s saw comparatively slow development of China pharmaceutical aerosol sector due to the bottleneck of development of containers, valves and metered-dosed charging equipment. However, after those problems were solved, great progress has been achieved in the sector.

2. Sector Survey

5. NICPBP was selected to carry out the sector survey and to prepare the sector plan for China pharmaceutical aerosol sector. The survey covered both non-MDIs and MDIs pharmaceutical aerosol manufacturers. To collect data, an investigation questionnaire was jointly prepared by SFDA, SEPA and NICPBP.

6. In June 2004, SFDA sent the questionnaire to pharmaceutical aerosol manufacturers in China. By November 2004, SFDA had received feedback from 57 enterprises.

7. In August 2004, SEPA, NICPBP and SFDA verified three aerosol manufacturers by site visit, namely, S&P Pharmaceutical Industry Co. Ltd., Xinjiang Biochemical Pharmaceutical Co. and Xinjiang Pharmaceutical Factory.

8. In September 2005, SFDA and NICPBP visited 40 pharmaceutical aerosol manufacturers to collect data.

9. In March 2006, SFDA requested again that its provincial Food and Drug Administration Bureaus confirm the list of aerosol manufacturers and their aerosol products.

10. In April 2006, pharmaceutical manufacturers were invited to attend a meeting in Beijing to learn the CFCs phaseout for the sector. At the meeting, they confirmed their data of aerosol products. The meeting also provided information on the process for phasing out CFC and the requirements for new registrations of aerosol products.

11. In April 2006, NICPBP visited eight pharmaceutical manufacturers. Therefore, total 51 manufacturers have been investigated by site visit. For the other 11 manufacturers without aerosol production, NICPBP had collected by sending questionnaires their relevant information including product approval numbers. So total 62 pharmaceutical aerosol manufacturers were investigated. It is confirmed by NICPBP that the survey covered all the CFCs-based non-MDIs pharmaceutical aerosol manufacturers.

12. The sector survey indicates that Chinese pharmaceutical aerosol manufacturers only have conceptual ideas on the CFCs substitutes and conversion technology.

3. Sector Profile

13. The *UNEP 2002 Report of the Aerosol S, Sterilants, Miscellaneous Uses and Carbon Tetrachloride Technical Options Committee 2002 Assessment* clearly states that "the reformulation of medical aerosol products (other than MDIs) and industrial/technical aerosols may require technical and financial assistance. In the case of medical aerosols, approval by national health and drug authorities will be required, after pharmacological and toxicity tests and clinical trials."

14. In evaluating the cost effectiveness of projects in the pharmaceutical sector, a) the amount of CFC used per can is much smaller than for general aerosol products, hence the CFC consumption for the same amount of cans produced would be significant smaller than for general aerosol and cost effectiveness in terms of USD/kg ODP would be significant higher and b) cost of registration and certification does not apply to general aerosol products. In reviewing the pharmaceutical aerosol in orther countries, it was found that HFC-134a indeed is used as propellant.

15. To ensure any changes to the medicinal products do not give rise to public health concerns, re-registration of medicine is required in many countries. When these changes are taken place, such as changes of specifications of excipident, or change to different excipident, or change to different type of drugs, respective requirement and procedures of re-registrations are specified by medicinal administrations of many countries.

16. Pharmaceutical aerosol product comprises the propellant compatible with the drug, a container capable of withstanding vapor pressure of propellant and a valve system. Propellants used in China pharmaceutical aerosol sector are mainly CFCs including CFC-11 and CFC-12. CFC-11 is used as a dispersant while CFC-12 as a propellant. Containers are made of glass, aluminum, stainless steel and plastic, but glass and aluminum containers are more often seen. Valves are often made of plastic, rubber, aluminum and stainless steel. Valves have to be inert with formulations in the canisters.

17. Pharmaceutical aerosols can be grouped by dispersing system into three types, namely, solution type, suspension type and emulsion type. China pharmaceutical aerosols can also be divided by medical usage into three groups – i) aerosol absorbed through skin (Skin Aerosol hereinafter), which is also called as external-use aerosol in China. ii) aerosol absorbed through cavity and mucosa, e.g. oral, nasal and vaginal cavity (Cavity Aerosol hereinafter) and iii) aerosol inhaled through respiratory tract (MDIs). The first two groups are referred to as non-MDIs aerosols, which are addressed in this sector plan. China will submit another sector plan for MDIs sector separately at a later stage. Table 2-1 is the survey summary of the non-MDIs sector.

Table 2-1 Summary of China Pharmaceutical Aerosol Sector

	Eligible for MLF Grant*	Not Eligible for MLF Grant	Total
CFCs Baseline Consumption (MT)	464.355	20.733	485.089
Number of Manufacturers	32	7	39
Number of Production Lines	35	6	41
Number of Production Lines with	22	5	27

Baseline Consumption			
Number of Skin Aerosol Applications	24	3	-
Number of Cavity Aerosol Applications	16	4	-
Number of Skin Aerosol Products	42	3	45
Number of Cavity Aerosol Products	21	4	25

* Aerosol manufacturers with production lines established before cutting-off date (July 1, 1999).

3.1 Aerosol Applications

18. **Skin Aerosol Applications.** Skin Aerosols are used for wound surface protection, cleaning, sterilization, topical anesthesia and homeostasis etc. They are requested to have no stimulation effect. The surface coverage (thin film) provided by those aerosols should have good permeability. SFDA has issued 51 drug production approval numbers (i.e. drug specifications), relating to 25 applications (see table 2-3). Out of the 25 applications, 10 are chemicals applications which are as same as those in foreign countries; 15 are Traditional Chinese Medicine (TCM) Applications, of which 12 are proprietary applications owned by Chinese manufacturers. There are total 30 manufacturers with registration numbers for Skin Aerosol products.

19. **Cavity Aerosol Applications.** SFDA has issued 24 registration approval numbers for Cavity Aerosols, relating to 19 applications (see Table 2-3), among which 8 are chemicals applications and 11 TCM applications. There are four nasal aerosol applications, mainly peptides and protein drugs, which exert general action, obviate gastrointestinal and hepatic first-pass action and improve bioavailability. There are two vaginal aerosol applications, mainly with tropical therapy for virginities and with contraception purpose. There are 13 oral aerosol applications, mainly with local action for the treatment of pharyngitis. Total 18 pharmaceutical manufacturers have registration numbers for cavity aerosol products.

Table 2-2 Information on Pharmaceutical Applications

Application ID	Application Name	Approval Number	TCM*/ Chemical Application	Effective Elements	Function and Indications
A01	Baofukang Foam	GUOYAOZHUNZI. Z10980092	TCM, proprietary product.	Oleum curcumae wenchowensis,Borneol	Bactericidal effect to Candida albicans and bacteriostatic action to Bacillus coli.
A02	Ice Cape Jasmine Distress Aerosol	GUOYAOZHUNZI. Z20025399	TCM, proprietary product.	Rhubarb,Cape Jasmine Fruit,Zhongjiefeng,Nux Vomica,Rehmannia Root-facient,Rosewood,tuber onion	Depriving the heat, activating blood circulation, odynolysis. Be used for low-grade empyrosis, soft tissue injury with blood stasis, boss, and soreness.

Application ID	Application Name	Approval Number	TCM*/ Chemical Application	Effective Elements	Function and Indications
				root,Borneol,Peach Seed,Chinese pine node,Camphor,et al	
A05	Cangxin Aerosol/ Xanthiun and Magnolia Flower Aerosol	GUOYAOZHUNZI. Z20027431	TCM	Siberian Cocklebur Fruit,Biond Magnolia Flower,pedicellus melo,et al	Be used for allergic coryza, acute coryza and chronic coryza.
A06	Fluconazol Aerosol	GUOYAOZHUNZI. H20010549	Pharmaceutical chemicals	Fluconazol	
A07	Fudekang Foam	GUOYAOZHUNZI. Z52020422	TCM, proprietary product.	Matrine	Clearing away heat and wetness, antibiosis. Be used for chronic cervicitis, cervical erosion, and coleitis.
A08	Compound Salicylic Acid and Clortrimazol Aerosol	GUOYAOZHUNZI. H52020529	Pharmaceutical chemicals,	Salicylic Acid,Clotrimazole,Phenol,Camphor,betula oil et al	Anti-eumycete, relieving itching, des-tinea.Be used for onychomycosis,neurodermatitis,the athlete's foot.
A10	Compound Chlorobutanol Aerosol	GUOYAOZHUNZI. H50021909, H32026527	Pharmaceutical chemicals	Chlorobutanol, Benzocaine, Chlorhexidine acetate	Preservation, hypothermy, sterilization. Be used for empyrosis.Chlorobutanol is used to antisepticize andrelieve pain □ Benzocaine is used to obstruct sensory nerve; Chlorhexidine acetate is used to sterilize.
A11	Compound Methyle Salicylater and Diphenhydramine Aerosol	GUOYAOZHUNZI. H44022736	Pharmaceutical chemicals	Methyle Salicylater and Diphenhydramine	Anti-bacterial and Pain relief
A13	Compound Cape Jasmine Aerosol	GUOYAOZHUNZI. Z20025744	TCM, proprietary product.	Lightyellow Sophora Root,Cape Jasmine Fruit,Arnebia Root,Garden Burnet Root,Pricklyash peel,Borneol,Rhubarb,Golden Thread,et al	Clearing away heat and toxic materials, haemostasis, detumescence, odynolysis.Be uesed for incised wound, furuncle.

Application ID	Application Name	Approval Number	TCM*/ Chemical Application	Effective Elements	Function and Indications
A14	Compound Arnebia Root Aerosol □Arnebia Root Oil Aerosol□	GUOYAOZHUNZI. Z20044383	TCM	Arnebia Root,et al	Clearing heat-evil, odynolysis. Be used for low-grade empyrosis.
A16	Haobai Damp Impairement Aerosol	GUOYAOZHUNZI. Z20027459 Z20027460	TCM	Shortstalk monkshood root,Dahurian Angelica Root,Paniculate swallowwort Root,Menthol,Extractum Belladonnae Liquidum,Tinospora Root,Zedoray Rhizome,et al	Activating blood circulation, odynolysis, dispelling wind-evil and wetness-evil. Be used for imperfecta, contusion, beriberoid disease, lumbodorsal pain.
A17	Hongyao Aerosol	GUOYAOZHUNZI. Z21021527	TCM, proprietary product.	Sanchi,Safflower ,Szechwan Lovage Rhizome,Chinese Angelica,Dahurian Angelica Root ,Himalayan Teasel Root,Ground Beetle	Many active constitutent,such as RADIX NOTOGINSENG Amoxcillin,Sanchi Glycoside,were found in Sanchi.RADIX NOTOGINSENG Amoxcillin has the effective of haemostasis and promoting blood flow at mean time,which wae said two-ways regulation,and dilating micrangium,anticogulation,improving microcirculation and oxygen delivery capacity.Sanchi Glycoside has the effective of antiinflammatory and enhancing immunologic function.
A19	Compound Lithospermi Aerosol	GUOYAOZHUNZI. Z20044009	TCM	Chinese Angelica,Szechwan Lovage Rhizome,Safflower,Clore,Fresh Ginger,Camphor,Turpentine Oil,et al	Activating blood circulation to dissipate blood stasis,detumescence,odynolysis.Be used for acute soft tissue injury
A21	Kuanxiong Aerosol	GUOYAOZHUNZI. Z11020961	TCM		Regulating vital energy and odynolysis. Be used for anesis of angina.

Application ID	Application Name	Approval Number	TCM*/ Chemical Application	Effective Elements	Function and Indications
A22	Dolicaine and Chlorhexidine Aerosol	GUOYAOZHUNZI. H35021400 H44024772	Pharmaceutical chemicals,	Lidocaine,Chlorhexidine acetate,Benzalkonii bromidum	Be used for incised wound, abrasion, soft tissue injury□the effectiveness is odynolysis, relieving itching, dephlogisticate.The effectiveness of lidocaine is local anesthesia and odynolysis; The effectiveness of chlorhexidine acetate and benzalkonii bromidum is dephlogisticate and disinfection.
A23	Dolicaine and Chlorhexidine Aerosol	GUOYAOZHUNZI. H20043850 H37023231 H37023255 H32026054 H44024771	Pharmaceutical chemicals,	Lidocaine,Chlorhexidine acetate,Benzalkonii bromidum	Be used for incised wound, abrasion, soft tissue injury, the effectiveness is odynolysis, relieving itching, dephlogisticate. The effectiveness of lidocaine is local anesthesia and odynolysis; The effectiveness of chlorhexidine acetate and benzalkonii bromidum is dephlogisticate and disinfection.
A24	Lidocaine Aerosol	GUOYAOZHUNZI. H10920107,	Pharmaceutical chemicals	Lidocaine hydrochloride	Local anesthetic.Be used for splanchnoscopy.Lidocaine hydrochloride belongs to trichostachine.After absorption, there would be periaqueductal gray stimulation and depressant effect to systema nervosum centrale.When the blood drug level is low□there will be analgesic effect and lethargy.
A25	Molsidomine Aerosol	GUOYAOZHUNZI. H23022579 H11022311 H23022943 H31022548	Pharmaceutical chemicals	Molsidomine	anti-anginal drug
A26	Qiweiqingyan Aerosol	GUOYAOZHUNZI. Z10980067	TCM, proprietary product.	Muscone,Vietnamese Sophora Root,Dwarf Lilyturf Tuber,Figwort Root,Blackberrylily Rhizome,Toad Venom,Borneol	Clearing heat-evil of lung and chylostomach, detumescence. Be used for Hoarseness, sore throat, diphtheria.

Application ID	Application Name	Approval Number	TCM*/ Chemical Application	Effective Elements	Function and Indications
A27	Ruxiang Rheumatism Aerosol	GUOYAOZHUNZI. Z20027458	TCM	Methyl Salicylate,Ole Menthal,Myrrh,Frankincense,Ocimum Oil,Cassia Bark Oil,Dragon's blood,Muscone,Eucalyptus oil,et al	Activating blood circulation to dissipate blood stasis, detumescence, odynolysis. Be used for rheumatalgia, arthralgia,lumbodynia.
A28	Shangle Aerosol	GUOYAOZHUNZI. Z10910038	TCM, proprietary product.	Szechwan Lovage Rhizome,Chinese Angelica,Danshen Root,Dahurian Angelica Root,Amur Cork-tree,et al	Activating blood circulation, dredging the meridian passage, detumescence.Be used for soft tissue injury, with manifestations of engorgement and stagnated blood
A29	Huoxinagquton g Aerosol	GUOYAOZHUNZI. Z20043551 Z42021342	TCM	Musk,Sanchi, Safflower, Dragon's blood,Rehmannia Root,Doubleteeth Pubesscent Angelica Root ,Camphor,Borneol,Menthol,et al	Activating blood circulation to dissipate blood stasis,dredging the meridian passage, detumescence, odynolysis
A30	Shiyang Aerosol	GUOYAOZHUNZI. Z10910039	TCM, proprietary product.	Golden Thread,Amur Cork-tree, Chinese Angelica, et al	Depriving the heat and wetness, detoxicating and relieving itching. Be used for acute eczema, with erythema, effusion, pruritus.
A32	Diclofenac Sodium Aerosol	GUOYAOZHUNZI. H19991425 H19991426	Pharmaceutical chemicals	Diclofenac Sodium	Be used for acute luxatio, contund and yosalgia.Also can be used for arthralgia.
A33	Methyl Salicylate Aerosol	GUOYAOZHUNZI. H35021187	Pharmaceutical chemicals	Methyl Salicylate	detumescence, odynolysis.Be used for acute soft tissue injury such as luxatio and myosalgia.
A34	Suxiaojiuxin Aerosol	GUOYAOZHUNZI. Z11020374	TCM, proprietary product.	Tree peony Bark,Szechwan Lovage Rhizome,Borneol	Depriving the heat, activating blood circulation, odynolysis.Be used for angina, with feverish dysphoria.
A35	Suxiaozhitong Aerosol	GUOYAOZHUNZI. Z11020364	TCM, proprietary product.	Dragon's blood,Safflower,Camphor, Frankincense(stir-frying with vinegar),Borneol,Musk	Detumescence, odynolysis, activating blood circulation to dissipate blood stasis, dephlogisticate, dredging the meridian passage. Be used for sprain, contusion, luxatio imperfecta,fracture, et al.

Application ID	Application Name	Approval Number	TCM*/ Chemical Application	Effective Elements	Function and Indications
A36	Wanjinxiang Aerosol	GUOYAOZHUNZI. Z20026302	TCM, proprietary product.	smartweed Herba,pungent litse fruit,Blume conspicua Hayata oil	Deintoxication, relieving itching, detumescence. Be uesed for baraquet, calefy, cephalalgia, flare of Sting
A38	Nitroglycerin Aerosol	GUOYAOZHUNZI. H20003570 H37021173 H44024858	Pharmaceutical chemicals	Nitroglycerin	Emergency medical treatment drug for angina.
A39	Isosorbide Dinitrate Aerosol	GUOYAOZHUNZI. H37022650	Pharmaceutical chemicals, proprietary product.	Isosorbide Dinitrate	Emergency medical treatment drug for angina.
A40	Econazole nitrate Aerosol	GUOYAOZHUNZI. H20043832 H44024735	Pharmaceutical chemicals	Econazole nitrate	Antimycotic drug. Bacteriostatic action to Dermatophyte, mould, Blastocystis, such as Candida albicans.
A41	Yansukang Aerosol (Rapid Recovery of throat)	GUOYAOZHUNZI. Z10960052	TCM,	Artificial bezoar,Pearl,Realgar,Toad Venom,Borneol,Musk,et al	Clearing heat-evil, detumescence, odynolysis. Be used for pharyngalgia, diphtheria, pneumonia. Anti-inflammatory effect, bacteriostatic action and analgesic effect.
A45	Yunnan Baiyao Aerosol □50g,100g□	GUOYAOZHUNZI. Z53021102 Z53021106 Z53021107 Z53021105 Z53021103 Z53021104	TCM, proprietary product.	Yunnan white powder	Activating blood circulation to dissipate blood stasis, detumescence, odynolysis.

Table 2-3 China Pharmaceutical Aerosol Applications

Application ID	Application Name	CFCs Baseline (kg)	Number of Manufacturers	Manufacturer Name(#ID)
1) Skin Aerosol Application (total 25 applications)				
A02	Ice Cape Jasmine Distress Aerosol	19,053	1	Guizhou Antai Pharmaceutical Co., Ltd (#20)
A08	Compound Salicylic Acid and Clortrimazol Aerosol	1,773	1	Guizhou Antai Pharmaceutical Co., Ltd (#20)
A09	Compound ethyl chloride aerosol	0	1	Guangzhou Baiyunshan Hejigong Pharmaceutical Co., Ltd (#03)
A10	Compound Chlorobutanol Aerosol	717	2	Wuxi Shanhe Group No.1 Pharmaceutical Co., Ltd. (#01); Chongqing Kerui Pharmaceutical Co., ltd. (#25)
A11	Compound Methyl Salicylate and Diphenhydramine Aerosol	0	2	Zhanjiang Xintongde Pharmaceutical Co., Ltd. (#27), Nantong Zhongbao Pharmaceutical Co., Ltd.(#37)
A13	Compound Cape jasmine Aerosol	229	1	Guizhou Xinyi Pharmaceutical Corporation (#21)
A14	Compound lithospermi aerosol	6	1	Suizhou Pharmaceutical Co. Ltd of Wuhan Jianmin Group (#19)
A16	Haobai Damp Impairment Aerosol	1,412	2	Hunan Bencao Pharmaceutical Co., Ltd. (#16); Shanghai Yishengyuan Pharmaceutical Co., Ltd. (#32)
A17	Hongyao Aerosol	57,717	1	Shenyang Jingcheng Pharmaceutical Co., Ltd. (#14)
A19	Keshangtong Aerosol	7	1	Suizhou Pharmaceutical Co. Ltd of Wuhan Jianmin Group (#19)
A22	Dolicaine chlorhexidine aerosol	833	2	South shaolin Pharmaceutical Co., Ltd in Fujian. (#09); Zhanjiang Xintongde Pharmaceutical Co., Ltd. (#27)

Application ID	Application Name	CFCs Baseline (kg)	Number of Manufacturers	Manufacturer Name(#ID)
A23	Dolicaine chlorhexidine aerosol	35,616	10	Wuxi Shanhe Group No.1 Pharmaceutical Co., Ltd. (#01); Guangdong Baiyunshan Hejigong Pharmaceutical Co., Ltd. (#03); Guangdong Baiyunshan Externally Applied Agent Factory (#04); Penglai Nuokang Pharmaceutical Co., Ltd. (#11); Shandong Jingwei Pharmaceutical Co., Ltd. (#18); Hangzhou Sino-US huadong Pharmaceutical Co., Ltd. (#22); Zhanjiang Xingtongde Pharmaceutical Co., Ltd. (#27); Heilongjiang Tianlong Pharmaceutical Co., Ltd. (#28); Nantong Zhongbao Pharmaceutical Co., Ltd. (#37); Anshan No.1 Pharmaceutical Factory (#39);
A24	Lidocaine aerosol	0	1	Sine Pharmaceutical Factory of Shanghai Pharmaceutical Group Co., Ltd. (#08)
A25	Molsidomine Aerosol	0	6	Beijing Haiderun Pharmaceutical Co., Ltd. (#02); Beijing Double-Crane Modern Pharmaceutical Technology Co., Ltd. (#06); Sine Pharmaceutical Factory of Shanghai Pharmaceutical Group Co., Ltd. (#08); Harbin Hengcang Pharmaceutical Co., Ltd. (#15); Heilongjiang Tianlong Pharmaceutical Co., Ltd. (#28), Harbin Guangji Pharmaceutical Factory. (#36);
A27	Ruxiang Rheumatism Aerosol	0	1	Zhanjiang Xingtongde Pharmaceutical Co., Ltd. (#27)
A28	Shangle Aerosol	0	1	Beijing Haiderun Pharmaceutical Co., Ltd. (#02)
A29	Huoxianqutong Aerosol	49,530	3	Hubei Nanyang Pharmaceutical Co., Ltd. (#13), Heilongjiang Tianlong Pharmaceutical Co., Ltd. (#28), Hubei Lishizhen Medical Group Co., Ltd. (#34)

Application ID	Application Name	CFCs Baseline (kg)	Number of Manufacturers	Manufacturer Name(#ID)
A30	Shiyang Aerosol	0	1	Beijing Haiderun Pharmaceutical Co., Ltd. (#02)
A32	Diclofenac Sodium Aerosol	5,583	1	Zhanjiang Xingtongde Pharmaceutical Co., Ltd. (#27)
A33	Methyl Salicylate aerosol	9,851	1	Fujian Nanshaolin Pharmaceutical Co., Ltd. (#09)
A35	Sunshangsuxiaozhitong Aerosol	0	1	Beijing Tongrentang Technology Development Corporation. (#07)
A36	Wanjinxiang Aerosol	38	1	Guizhou Hongyu Pharmaceutical Co., Ltd. (#29)
A37	Xiangbingqutong Aerosol	13	1	S & P Pharmaceutical Industry Co., Ltd.(#30)
A42	Lidocaine Hydrochloride Aerosol	0	1	Shanghai Fuxingzhaohui Pharmaceutical Co., Ltd. (#10)
A45	Yunnan Baiyao Aerosol	273,334	1	Yunnan Baiyao Group Corporation. (#24);
	Subtotal	**455,712**		
2) Cavity Aerosols Application (total 19 applications)				
A01	Bao Fu Kang foam	1,193	1	Guizhou Hongyu Pharmaceutical Co., Ltd.(#29)
A03	Beclometasone Tubinaire (Beconase)	20,390	1	Glaxo SmithKline (Tianjin) Pharmaceutical Co., Ltd.(#12)
A04	Beclometasone Aerosol	0	1	Guangzhou Dongkang Pharmaceutical Co., Ltd.(#31)
A05	Xanthiun and Magnolia flower Aerosol	2,592	1	Xinjiang Biochemistry Pharmaceutical Co., Ltd.(#23)
A06	Fluconazol Aerosol	0	1	Sine Pharmaceutical Factory of Shanghai Pharmaceutical Group Co., Ltd.(#08)
A07	Fudekang foam	13	1	Guiyang Dechangxiang Pharmaceutical Co., Ltd.(#05)
A12	Compound Chlorobutanol Aerosol	0	1	Chongqing Kerui Pharmaceutical Co., ltd.(#25)
A15	Isoconeazole Nitrate Aerosol	0	1	Heilongjiang Tianlong Pharmaceutical Co., Ltd. (#28)
A18	Jinlan aerosol	0	1	Anshan No.1 Pharmaceutical Factory. (#39)
A20	Stomatitis spraying agent	48	1	Shannxi Fengwuchendayaotang Pharmaceutical Factory Co., Ltd. (#35)
A21	Huanxiong Aerosol	0	2	Beijing Tongrentang Technology Development Corporation. (07); Anshan No.1 Pharmaceutical Factory. (#39)
A26	Qiweiqingyan Aerosol	293	1	Shandong Bencao Pharmaceutical Co., Ltd. (#17)

Application ID	Application Name	CFCs Baseline (kg)	Number of Manufacturers	Manufacturer Name(#ID)
A31	Shuanghuanglian Aerosol	145	1	Sanjing Pharmaceutical Co., Ltd of Harbin Pharmaceutical Group. (#33)
A34	Suxiaojiuxin Aerosol	14	1	Beijing Tongrentang Technology Development Corporation.(#07)
A38	Nitroglycerin Aerosol	528	4	Shandong Jewim Pharmaceutical Co., Ltd. (#18); Zhanjiang Xintongde Pharmaceutical Co., Ltd. (#27); Xian Lisheng Pharmaceutical Co., Ltd.(#38); Shandong Bencao Pharmaceutical Co., Ltd.(#17)
A39	Isosorbide Dinitrate Aerosol	3	1	Shandong Jewim Pharmaceutical Co., Ltd.(#18)
A40	econazole nitrate aerosol	3,780	3	Guangzhou Baiyunshan Hejigong Pharmaceutical Co., Ltd.(#03), Zhanjiang Xingtongde Pharmaceutical Co., Ltd. (#27); Heilongjiang Tianlong Pharmaceutical Co., Ltd. (#28)
A41	Rapid recovery of throat aerosol	380	1	Huayi Pharmaceutical Co., Ltd. (#26)
A44	Yinhuangpingchuan Aerosol	0	1	Anshan No.1 Pharmaceutical Factory (#39)
	Subtotal	**29,377**		
	Total	**485,089**		

Table 2-3 Overviews of Pharmaceutical Aerosol Manufacturers

Enterprise ID	Name of Enterprise	Chinese Share (%)	Lines	Date of Line.	Cap. (can/hour)	CFCs Baseline (kg)	Baseline CFCs for SA[1] (kg)	Baseline CFCs for CA[1] (kg)	Total Prodt. Quantity[2] (can)	SA Prodt. Quantity (can)	CA Prodt. Quantity (can)	SA App. ID	CA App. ID
01	Wuxi Shanhe Group No.1 Pharmaceutical Co., Ltd	100%	2	1965	2000	823	823	0	26,667	26,667	0	A10, A23	-
02	Beijing Haiderun Pharmaceutical Co., Ltd	100%	2	1978	-	0	0	0	0	0	0	A25, A28, A30	-
03	Guangzhou Baiyunshan Hejigong Pharmaceutical Co., Ltd	100%	1	1983	-	0	0	0	0	0	0	A09 A23	A40
04	Externally Applied Agent Factory of Guangzhou Baiyunshan Pharmaceutical Co., Ltd	100%	1	1959	-	0	0	0	0	0	0	A23	-
05	Guiyang Dechangxiang Pharmaceutical Co., Ltd	100%	1	1979	600	13	0	13	100	0	100	-	A07
06	Beijing Double-Crane Modern Pharmaceutical Technology Co., Ltd	100%	1	1980	-	0	0	0	0	0	0	A25	-
07	Beijing Tongrentang Technology Development Corporation	100%	1	1981	1800-3600	14	0	14	1,267	0	1,267	A35	A21,A34
08	Xinyi Pharmaceutical General Factory of Shanghai Pharmaceutical Group Co., Ltd	100%	1	1969	0	0	0	0	0	0	0	A24,A25	A06
09	Fujian Nanshaolin Pharmaceutical Co., Ltd	100%	1	1985	3000	10,684	10,684	0	48,571	48,571	0	A22, A33	-
10	Shanghai Fuxingzhaohui	100%	1	1988	-	0	0	0	0	0	0	A42	-

Enterprise ID	Name of Enterprise	Chinese Share (%)	Lines	Date of Line.	Cap. (can/hour)	CFCs Baseline (kg)	Baseline CFCs for SA[1] (kg)	Baseline CFCs for CA[1] (kg)	Total Prodt. Quantity[2] (can)	SA Prodt. Quantity (can)	CA Prodt. Quantity (can)	SA App. ID	CA App. ID
	Pharmaceutical Co., Ltd												
11	Penglai Nuokang Pharmaceutical Co., Ltd	100%	1	1986	2000	3,491	3,491	0	100,600	100,600	0	A23	-
13	Hubei Nanyang Pharmaceutical Co., Ltd	70%	1	1991	1000	49,393	49,393	0	1,171,333	1,171,333	0	A29	-
14	Shenyang Jingcheng Pharmaceutical Co., Ltd	50%	1	1992	2000	57,717	57,717	0	968,533	968,533	0	A17	-
15	Harbin Hengcang Pharmaceutical Co., Ltd	100%	1	1992	-	0	0	0	0	0	0	A25	-
16	Pharmaceutical Factory of Hunan Bencao pharmacy Co., Ltd	100%	1	1993	800-1000	1,300	1,300	0	58,333	58,333	0	A16	-
17	Shandong Bencao Pharmaceutical Co., Ltd	100%	1	1997	1500	428	0	428	56,720	0	56,720	-	A26,A38
18	Shandong Jewim Pharmaceutical Co., Ltd BlueBox	100%	1	1993	500-600	12,080	11,685	395	318,281	276,314	41,967	A23	A38,A39
19	Suizhou Pharmaceutical Co. Ltd of Wuhan Jianmin Group	100%	1	1993	2000	13	13	0	700	700	0	A14, A19	-
20	Guizhou Antai Pharmaceutical Co., Ltd	100%	1	1983	500-600	20,827	20,827	0	580,000	580,000	0	A02, A08	-
21	Guizhou Xinyi Pharmaceutical Corporation	100%	1	1993	500-600	229	229	0	8,333	8,333	0	A13	-
22	Hangzhou Sino-US Huadong Pharmaceutical Co., Ltd	75%	1	1993	-	0	0	0	0	0	0	A23	-

Enterprise ID	Name of Enterprise	Chinese Share (%)	Lines	Date of Line.	Cap. (can/hour)	CFCs Baseline (kg)	Baseline CFCs for SA[1] (kg)	Baseline CFCs for CA[1] (kg)	Total Prodt. Quantity[2] (can)	SA Prodt. Quantity (can)	CA Prodt. Quantity (can)	SA App. ID	CA App. ID
23	Xinjiang Biochemistry Pharmaceutical Co., Ltd	100%	1	1994	2500	2,592	0	2592	50,000	0	50,000	-	A05
24	Yunnan Baiyao Group Corporation	100%	1	1995	5000	273,333	273,333	0	5,306,667	5,306,667	0	A45	
25	Chongqing Kerui Pharmaceutical Co., ltd	100%	1	1975	-	0	0	0	0	0	0	A10	A12
26	Huayi Pharmaceutical Co., Ltd	100%	1	1996	500	380	0	380	70,000	0	70,000	-	A41
27	Zhanjiang Xintongde Pharmaceutical Co., Ltd	100%	1	1987	3600	29,397	25,917	3,480	1,240,000	1,036,667	203,333	A11, A22, A23,A27, A32,	A38, A40
28	Heilongjiang Tianlong Pharmaceutical Co., Ltd	100%	2	1996	1500-2000	300	0	300	33,333	0	33,333	A23, A25, A29	A15,A40
29	Guizhou Hongyu Pharmaceutical Co., Ltd	100%	1	1998	1500	1,230	38	1,193	76,933	2,800	74,133	A36	A01
31	Guangzhou Dongkang Pharmaceutical Co., Ltd.	100%	1	1987	-	0	0	0	0	0	0	-	A04
32	Shanghai Yishengyuan Pharmaceutical Co., Ltd	100%	1	1983	600-800	112	112	0	4,845	4,845	0	A16	-
37	Nantong Zhongbao Pharmaceutical Co., Ltd	100%	1	1990	-	0	0	0	0	0	0	A11, A23	-
39	Anshan No.1 Pharmaceutical Factory	100%	1	1990	-	0	0	0	0	0	0	A23	A18, A21, A44
30	Sanpu Pharmaceutical Co., Ltd	100%	0	2002	-	13	13	0	1,700	1,700	0	A37	-
33	Sanjing Pharmaceutical Co., Ltd of	100%	1	2003	1200	145	0	145	15,210	0	15,210	-	A31

Enterprise ID	Name of Enterprise	Chinese Share (%)	Lines	Date of Line.	Cap. (can/hour)	CFCs Baseline (kg)	Baseline CFCs for SA[1] (kg)	Baseline CFCs for CA[1] (kg)	Total Prodt. Quantity[2] (can)	SA Prodt. Quantity (can)	CA Prodt. Quantity (can)	SA App. ID	CA App. ID
	Harbin Pharmaceutical Group												
34	Hubei Lishizhen Medical Group Co., Ltd	100%	1	2004	100	137	137	0	86,667	86,667	0	A29	-
35	Shannxi Fengwuchendayaotang Pharmaceutical Factory Co., Ltd	100%	1	2003	1800	48	0	48	6,000	0	6,000	-	A20
36	Harbin Guangji Pharmaceutical Factory	100%	1	NA	-	0	0	0	0	0	0	A25	-
38	Xian Lisheng Pharmaceutical Co., Ltd	100%	1	NA	-	0	0	0	0	0	0	-	A38
12	Glaxo SmithKline (Tianjin) Pharmaceutical Co., Ltd	0%	1	1991	1300-2000	20,390	0	20,390	1,216,000	0	1,216,000	-	A03
	Total		41			485,089	455,712	29,377	11,446,793	9,678,730	1,768,063		
	Eligible for MLF Fund		**35**			**464,355**	**455,561**	**8,794**	**10,121,216**	**9,590,363**	**530,853**		
	Not Eligible for MLF Fund		6			20,733	150	20,583	1,325,577	88,367	1,237,210		

1: SA: Skin Aerosol, CA: Cavity Aerosol; 2: Production quantity of baseline year.(average of 2003-2005).

3.2. CFCs Historical Consumption and Forecast for Future CFCs Consumption.

3.2.1. CFCs Consumption for Skin Aerosol

20. Table 2-4 shows the annual CFCs consumption data from 1996 to 2005 for Skin Aerosol. Baseline consumption is based on the average CFCs consumption of 2003 to 2005.

Table 2-4 CFCs Consumption for Skin Aerosol (1996-2005)

Year	CFC-11 Consumption (kg)	CFC-12 Consumption (kg)	Total (kg)
1996	30,519	117,596	148,116
1997	32,274	145,891	178,166
1998	33,834	133,219	167,054
1999	31,884	148,851	180,736
2000	43,007	165,436	208,443
2001	90,215	236,591	326,807
2002	124,551	296,296	420,847
2003	127,041	342,803	469,844
2004	97,120	347,122	444,242
2005	97,940	355,109	453,049
Baseline Level Average of 03-05	107,367	348,345	455,712

Chart 2-1 Annual CFC-11 Consumption for Skin Aerosol (1996-2005)

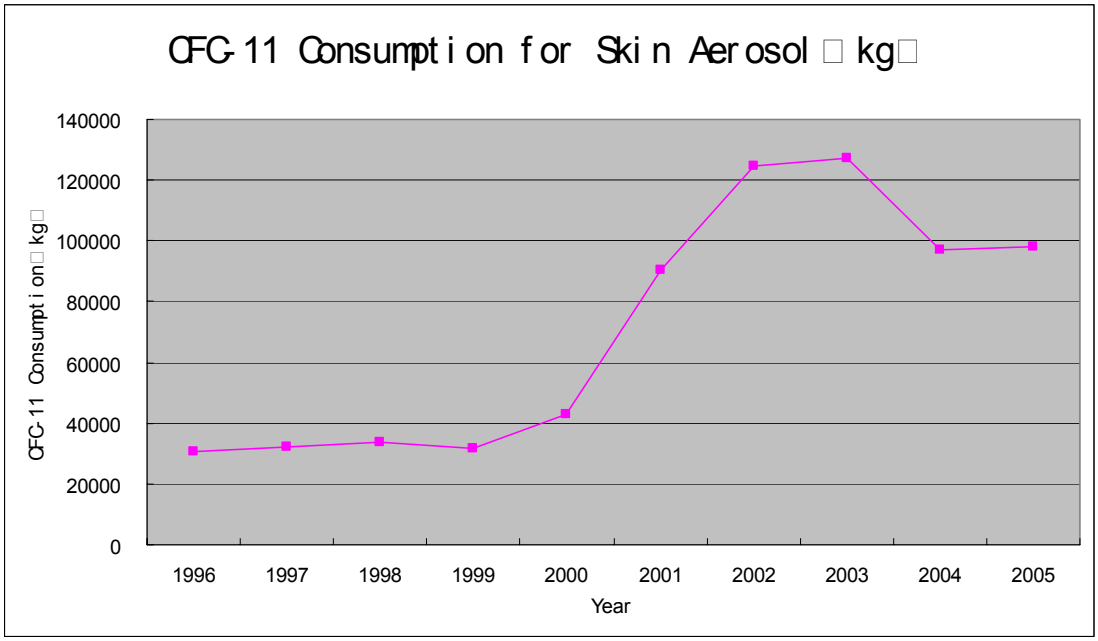


Chart 2-2 Annual CFC-12 Consumption for Skin Aerosol (1996-2005)

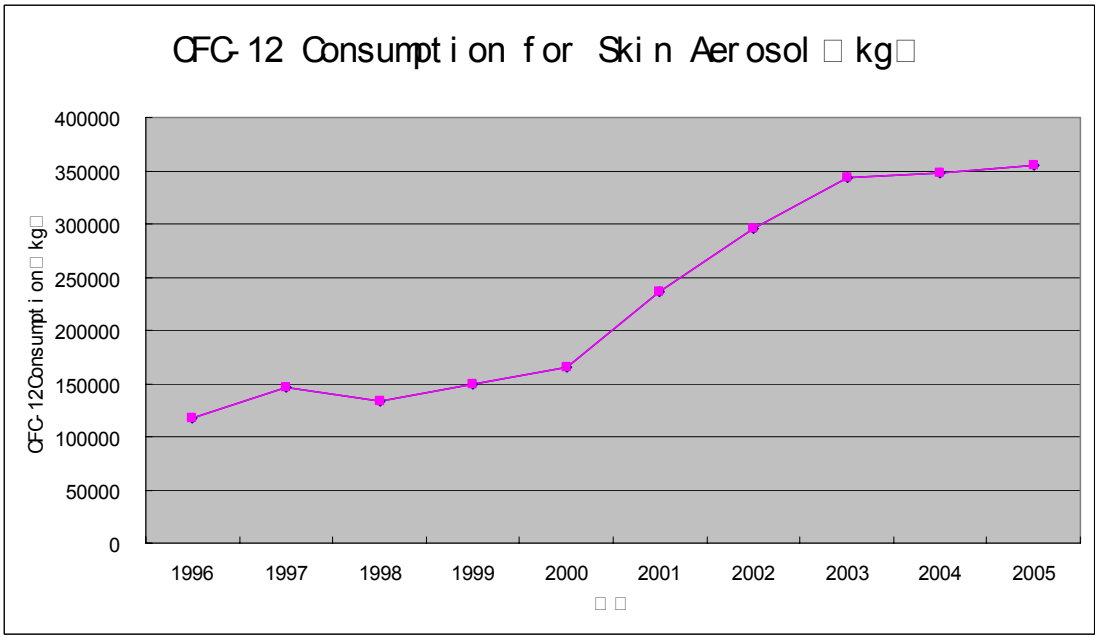
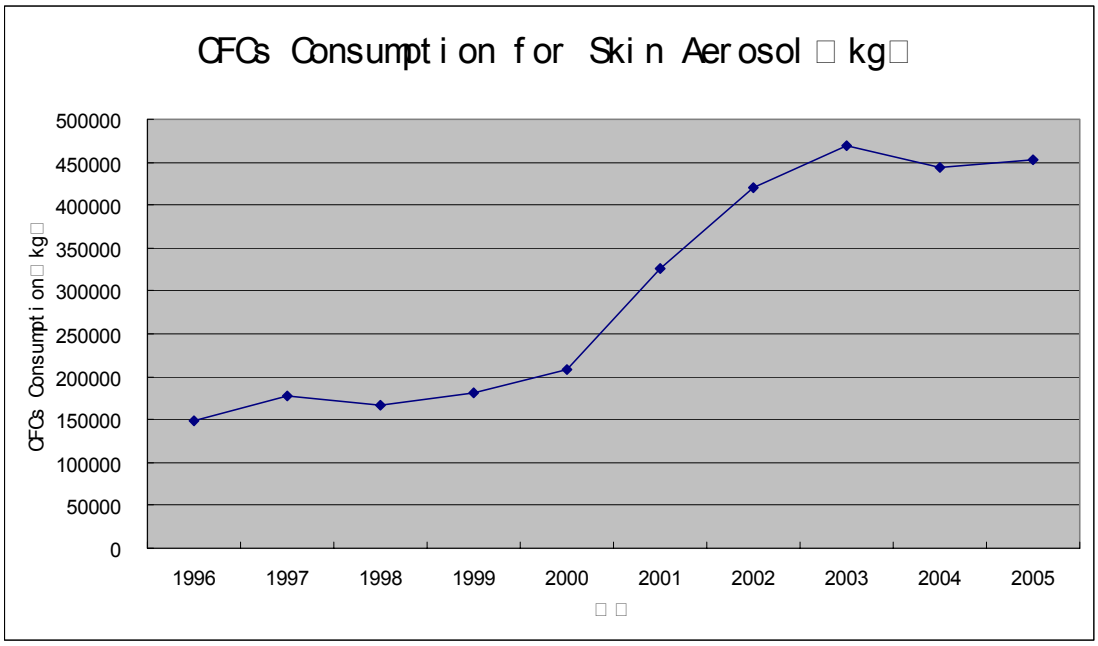


Chart 2-3 Aggregated Annual CFCs Consumption for Skin Aerosol (1996-2005)



3.2.2. CFCs Consumption for Cavity Aerosol

21. Table 2-5 shows annual CFCs consumption for Cavity Aerosol from 1996 to 2005. Baseline Consumption is based on the average CFCs consumption of 2003- 2005.

Table 2-5 CFCs Consumption for Cavity Skin Aerosol (1996-2005)

Year	CFC-11 Consumption (kg)	CFC-12 Consumption (kg)	Total (kg)
1996	1,137	2,924	4,061
1997	550	1,445	1,995
1998	1,614	6,125	7,739
1999	2,285	9,926	12,211
2000	2,058	9,881	11,939
2001	2,909	13,210	16,119
2002	1,867	10,425	12,292
2003	3,826	20,437	24,263
2004	8,228	32,471	40,699
2005	4,015	19,155	23,170
Baseline Level (average of 03-05)	**5,356**	**24,021**	**29,377**

Chart 2-4 CFC-11 Consumption for Cavity Aerosol (1996-2005)

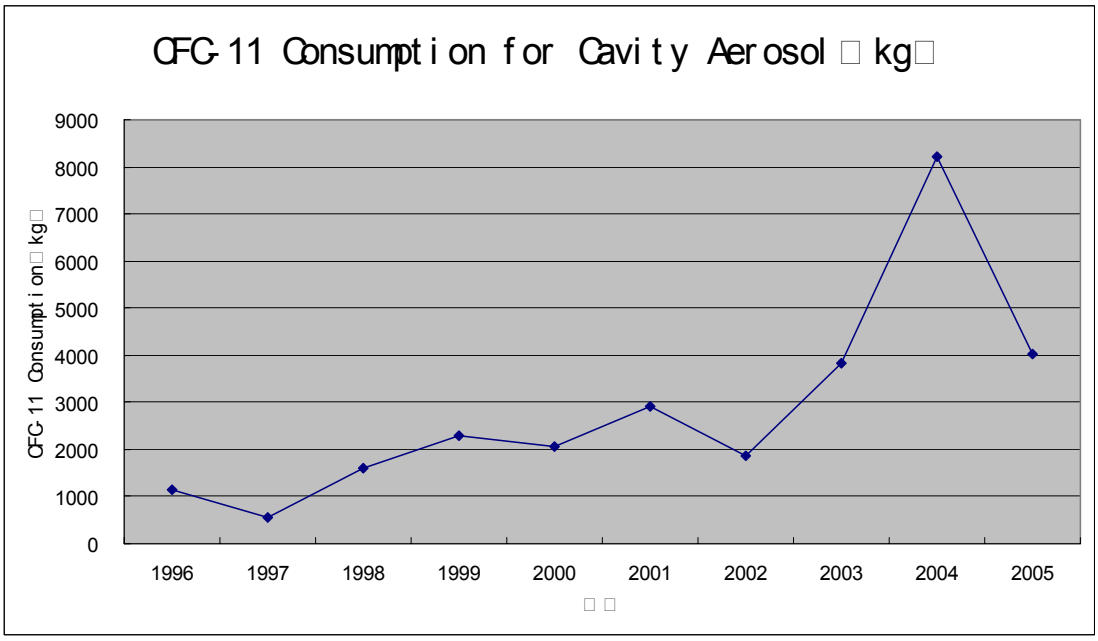


Chart 2-5 CFC-12 Consumption for Cavity Aerosol (1996-2005)

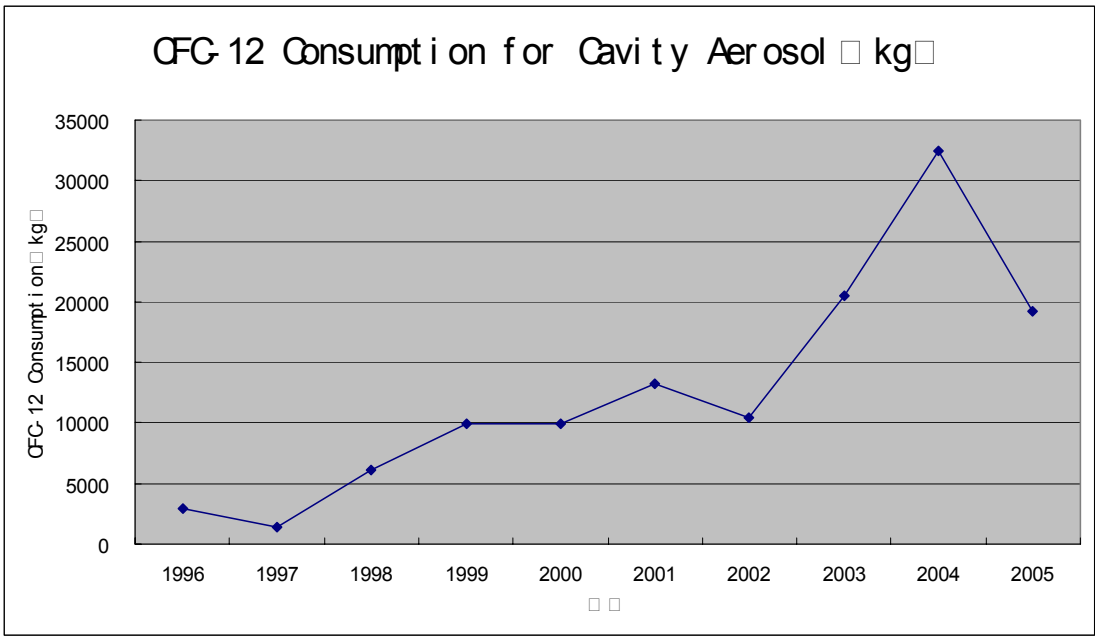
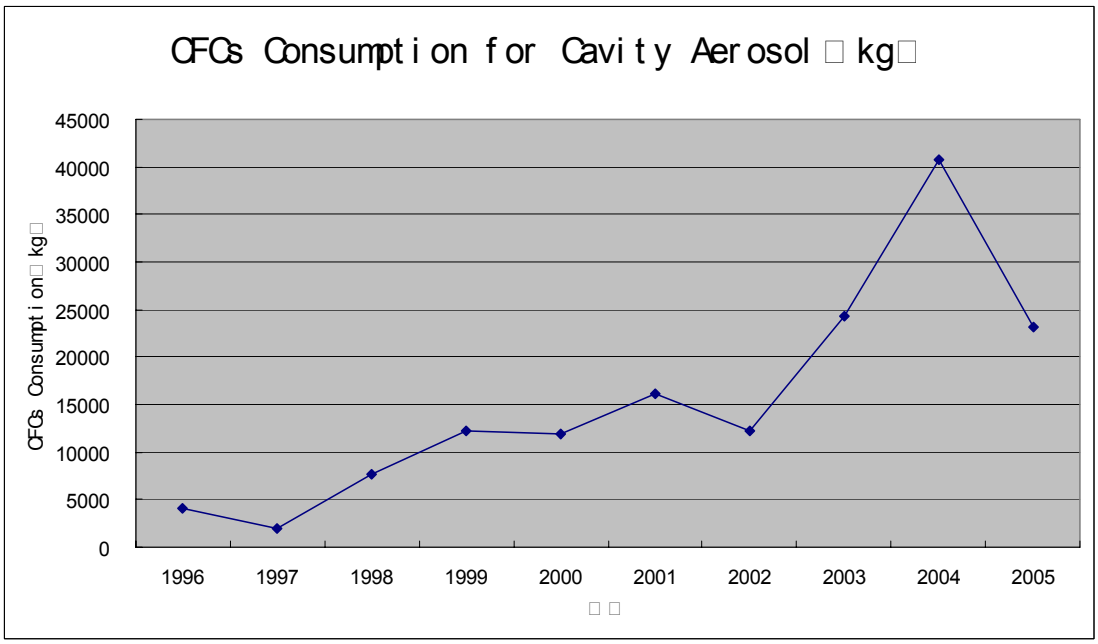


Chart 2-6 Aggregated Annual CFCs Consumption for Cavity Aerosol (1996-2005)



3.2.3. Forecast for CFCs Demand.

a) CFCs Demand Prediction for Skin Aerosol

22. CFCs consumption for Skin Aerosol increased from 1996 to 2005. Predicted by the tendency linear equation below, CFCs consumption for Skin Aerosol would reach at 700 tons in 2010.

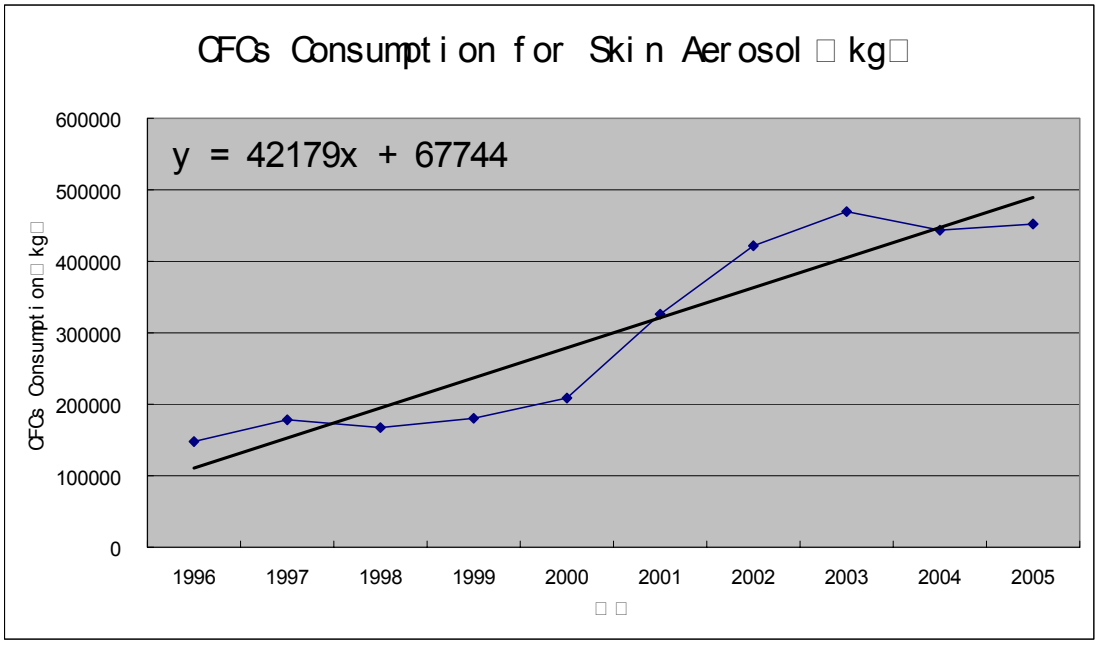
Y=42179X+67744

Where

X: The certain year minus 1995

Y: Annual CFCs consumption at a certain year;

Chart 2-7 Tendency Linear Equation for CFCs Demand Prediction for Skin Aerosol



b) CFCs Demand Prediction for Cavity Aerosol

23. CFCs consumption for Cavity Aerosol increased from 1996 to 2005. Predicted by the tendency linearity equation below, CFCs consumption for Cavity Aerosol would be about 37 tons in 2010.

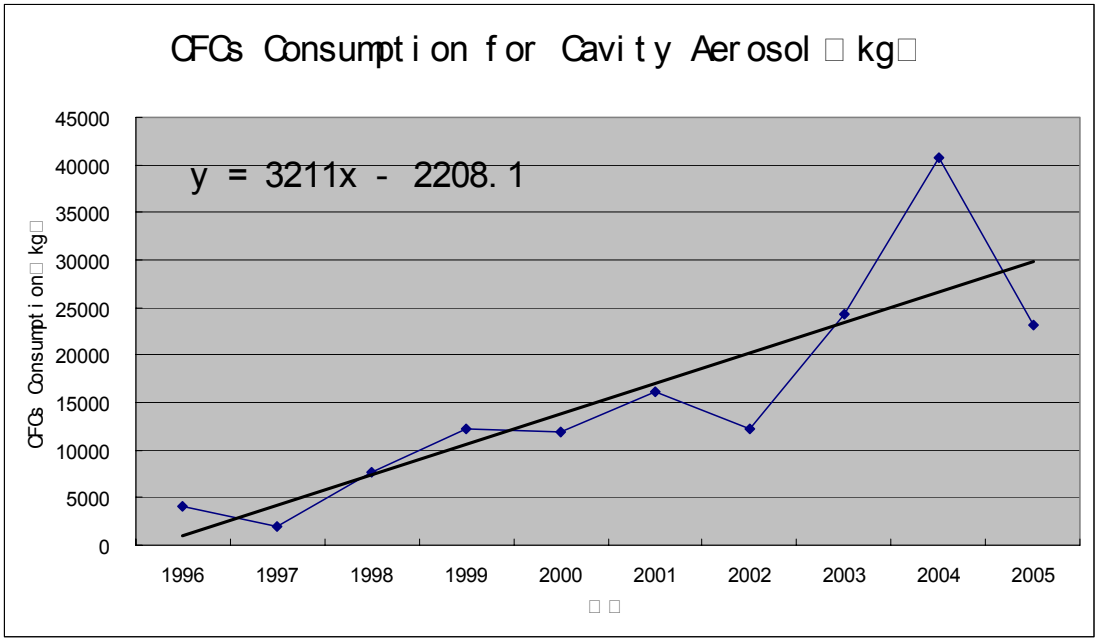
Y=3211X-2208.1

Where

X: The certain year minus 1995

Y: Annual CFCs consumption at a certain year;

Chart 2-8 Tendency Linear Equation for CFCs Demand Prediction for Cavity Aerosol



CHAPTER 3 Sector Polices

24. **Existing Policies** CFCs are used as excipients for pharmaceutical aerosol products. Replacement of CFCs with non-CFCs excipients or with different dosage form is subject to Chinese relevant laws, regulations and policies which mainly include the following:

1. Drug Administration Law of the People's Republic of China (effective since December 1, 2001)

25. This Law is enacted to strengthen drug administration, to ensure drug quality and safety for human beings, to protect the health of people and their legitimate rights and interests in the use of drugs. Article 2 of this law stipulates that all institutions and individuals engaged in research, production, distribution, use, or drug administration in the People's Republic of China shall abide by this Law. Some clauses related to the pharmaceutical aerosol sector plan include, but not limited to:

26. **Control over Manufacturers.** Article 9 states that "drug manufacturers shall conduct production according to the Good Manufacturing Practice for Pharmaceutical Products (GMP) formulated by the drug regulatory department under the State Council on the basis of this Law. The drug regulatory department shall inspect a drug manufacturer as to its compliance with the GMP requirements and issue a certificate to the manufacturer passing the inspection. The specific measures and schedule for implementing the GMP shall be formulated by the drug regulatory department under the State Council."

27. **Control over Drugs**. Article 29 stats that the dossier on a new drug research and development including the manufacturing process, quality specifications, results of pharmacological and toxicological study, and the related data and the samples shall, in accordance with the regulations of the drug regulatory department under the State Council, be truthfully submitted to the said department for approval, before clinical trial is conducted. Measures for verifying the qualifications of clinical study institutions for drugs shall be formulated jointly by the drug regulatory department and the administrative department for health under the State Council. When a new drug has gone through clinical trials and passed the evaluation, a New Drug Certificate shall be issued upon approval by the drug regulatory department under the State Council.

28. Article 31 states that "A drug manufacturer may produce the drug only after an approval number is granted to it."

2. Provisions on Drug Registration issued by SFDA (No. 17, effective since May 1, 2005)

29. Article 8 states that "a new drug application means a registration application for a drug that has not been marketed in China. A drug that has been marketed in China for which an application is made for a

change in dosage form, or route of administration of medicaments, add new indication shall be treated as a new drug application."

30. "Application for a drug already with national standards means application for production of a drug for which SFDA has already issued formal standards. Supplemental application means an application for the change, addition, or cancellation of any item or contents in the existing registration approval of a new drug, drug already with national standards, or import drug."

3. Notice of Stopping Using Chlorofluorocarbons (CFCs) as Excipients for Pharmaceutical Aerosol

issued by SFDA on June 22, 2006. In order to cooperate with China Accelerated Phaseout Plan - to stop CFCs production by June 30, 2007 - SFDA issued the following policy. As per this notice,

31. (i) China is to stop using CFCs as excipients for external-use aerosol production since July 1, 2007. CFCs-based external-use aerosols products in storage are allowed to be circulated and used until the expiration of their validity periods. China is to stop using CFCs as excipients for MDIs aerosol production since January 1, 2010. CFCs-based MDIs aerosols products in storage are allowed to be circulated and used until the expiration of their validity periods. SFDA will introduce special provisions for the transitional period from July 2007 to December 2009(see Chapter 5).

32. (ii) China is to stop importing CFCs-based external-use aerosols since July 1, 2007. CFCs-based external use aerosol products imported before this date are allowed to be circulated and used until the expiration of their validity periods. China is to stop importing CFCs-based MDIs aerosol since January 1, 2010. CFCs-based MDIs aerosol products imported before this date are allowed to be circulated and used until the expiration of their validity periods.

33. (iii) China is to stop approval of registration for external-use aerosols with CFCs as excipients from July 1, 2007 (including application for the imported CFC-based external use aerosol products). China is to stop approval of registration for MDIs aerosol products with CFCs as excipients (including application for the imported CFC-based MDIs aerosol products) since January 1, 2010.

34. (iv) Should any pharmaceutical manufacturer change excipients or dosage form of aerosols, it shall submit such applications in accordance with Provisions on Drug Registration.

CHAPTER 4 Technical Analysis

35. As CFCs propellants are degrading the ozone layer, researchers are studying on CFCs-free pharmaceutical aerosol. There are mainly two approaches to replace CFCs: i) to identify CFCs substitutes; ii) to use alternative delivery system, such as compressed-air spray, ultrasonic spray, two-phase system, self-pressurized system and dry powder inhaler. Presently, there are four commonly used CFCs substitutes: Hydrofluoroalkane (tetrafluoroethane HFA 134a and heptafluoropropane HFA 227), Dimethyl ether (DME), Hydrocarbon (isobutane) and compressed gas (e.g carbon dioxide). Substitute propellants being used in foreign countries comprise tetrafluoroethane HFA-134a, heptafluoropropane HFA-227 and DME.

1. Potential Substitutes

1) Hydrofluroalkane

36. Compared with CFCs, Hydrofluoroalkane has similar properties, poorer chemical stability and less polarity. Table 4-1 indicates the physical and chemical properties of Hydrofluoroalkane and its impact on the atmosphere in comparison to CFCs.

Table 4-1 Properties of Hydrofluoroalkane and CFCs

Item	Trichlorofluoromethane (CFC-11)	Dichlorodifluoromethane (CFC-12)	Dichlorotetrafluoroethane (CFC-114)	Tetrafluoroethane (HFA-134a)	Heptafluoroethane (HFA-227)
Molecular Formula	$CFCl_3$	CF_2Cl_2	CF_2ClCF_2Cl	CF_3CFH_2	F_3CHFCF_3
Vapor Pressure (Psig/20□)	-1.8	67.6	11.9	4.71	3.99
Boiling Point (□)	-24	-30	4	-26.5	-17.3
Density (g/ml)	1.49	1.33	1.47	1.22	1.41
ODP*	1	1	0.7	0	0
GWP*	1	3	3.9	0.22	0.7
Atmospheric Life Cycle (year)	75	111	7200	15.5	33

*Ozone Depleting Potential/ Global Warming Potential relative to CFC-11

2). Dimethyl Ether (DME)

37. Table 4-2 shows the properties of DME (CH3OCH3). DME is flammable and has low acute and

chronic toxicity. It is mainly used as CFCs substitute for external-use aerosols. One of DME's advantages is that it can be dissolved homogeneously with water at a certain proportion.

Table 4-2 Properties of DME

Molecular formula	CH_3OCH_3
Molecular weight	46.07
Boiling point	-24.9□
Vapor pressure	6kg/cm^2
Density	0.66g/ml
Water solubility	35.5%
Flammability Limits in Air, Vol %	3.4~26.7%
Damage on ozone layer	-

3). Hydrocarbon

38. Table 4-3 lists the physical properties of Hydrocarbon (mainly including isobutane, propane, and n-butane). Despite with good stability and low density, Hydrocarbon is toxic, inflammable and explosive, thus entailing high safety standard for production. Hydrocarbon is commonly blended with Hydrofluoroalkane as propellant.

Table 4-3 Physical Properties of Hydrocarbon

Chemical Name	Formula	Molecular Weight	Flashing Point (□)	Boiling Point (□)	Vapor Pressure (gauge pressure, kPa, 21.1□)	Liquid Density [21.1□ (g/cm^2)]	Flammability Limit in Air [% (ml/ml)]	
							Min.	Max.
Propane	CH3(CH2)CH3	44.1	-104.4	-42.1	744.8	0.50	2.2	9.5
Isobutane	CH(CH3)3	58.1	-32.8	-11.7	214.3	0.56	1.8	8.4
N-butane	CH3(CH2)2CH3	58.1	-73.9	-0.5	116.4	0.58	1.9	3.5

4). Compressed Gas.

39. Table 4-4 lists the physical properties of compressed gas (mainly including carbon dioxide, nitrogen and nitrogen monoxide). In comparison with DME and HFA, Compressed Gas is more chemically stable and inflammable but has lower boiling point after liquefaction and higher vapor pressure at normal atmospheric temperature, thus requiring that packaging containers should withstand higher pressure (e.g. small steel cylinder as the packaging container). If un-liquefied compressed gas is filled

in the container, pressure within the container falls rapidly and continuous injection cannot be maintained. Presently, compressed gas is basically not used for aerosol products, but for spray products.

Table 4-4 Physical Properties of Compressed Gas

Chemical name	Molecular Formula	Molecular Weight	Boiling Point (□)	Vapor Pressure (gauge pressure, kPa, 21.1□)	Inflammability
Carbon dioxide	CO_2	44.0	-78.3[1]	5767	No
Nitrogen monoxide	N_2O	44.0	-88.3	4961	No
Nitrogen	N_2	28.0	-195.6	3287[2]	No

1: Sublimation; 2: Critical temperature: -147.2□

40. During past few years, Boeheringer, Fisons, 3M, Glaxo and Riker have obtained relevant formulation patents which cover propellant system including components, co-solvent, hydrocarbon surfactant and fluoro-surfactant. It is reported that a few issues have to be solved for Hydrofluoroalkane being employed as propellants for pharmaceutical aerosol sector.

    i) **Co-solvent with Low Boiling Point.** Both tetrafluoroethane and heptafluoropropane have higher vapor pressure and are in gaseous state under normal atmospheric temperature. Presently, no Hydrofluoroalkane has the same high boiling point as CFC-11 does. Therefore, it brings challenges to design formulation and production process. One of solutions is to seek proper solvent without toxicity or irritation but with certain volatility and good compatibility with Hydrofluoroalkane. Commonly used co-solvents include low-molecular-weight alkane (e.g propane and butane) and low-molecular-weight alcohols (e.g ethanol and isopropanol).

    ii) **Surfactant Selection.** Surfactant is to disperse medicament particles and lubricate the valve. As Hydrofluoroalkane has smaller polarity than CFCs, it can not dissolve majority of surfactants. One solution is to identify surfactants with good solubility and compatibility with medicaments. Another solution is to add co-solvent which can dissolve surfactant.

    iii) **Drug Characteristics.** Some medicaments easily form solvate in new propellant system, thus increasing the tendency of crystal growth. Some poly-crystalline drugs (such as steroid hormone) are easier to have crystalline transformation and promote crystal growth. Thus, drug characteristics should be taken into account in formulation design, particularly in the design for the suspended aerosol.

    iv) **Valve Selection.** As Hydrofluoroalkane is less chemically stable than CFCs, valve components (e.g airproof rubber and its additive should be compatible with propellants. Similarly, valve components should not cause HFA to decompose. At present, several major valve companies such as Bespak, 3M and Valois conduct research on the valve system for

Hydrofluoroalkane.

v) **Alternative Actuator.** In case medicament can not be formulated into suspended aerosol, it is generally made into solution aerosol. In general, solution aerosol has poorer atomization effect. Decreasing vapor pressure of the canister results in bigger atomized particles sizes. Though increasing the pressure can reduce the particle sizes, it also causes majority of particulate medicaments to be accumulated at throat due to the bumping of particles arising from the increase of initial speed. Thus, it is needed to design new actuators which can both crash the particles and reduce the initial speed.

2. Preliminary Analysis

Table 4-5 Comparison of CFCs Substitutes

	Advantage	Disadvantage	Remarks
DME	- Very soluble in water. - In aqueous solutions, the propellant is hydrolytically stable over a wide pH range. - Zero ODP.	- Acute and chronic toxicity. - May cause anesthetic effects. May irritate eyes, skin, and mucous membranes. - Flammable.	- DME is a flammable chemical. If using it as the CFCs substitute, Chinese pharmaceutical manufacturers have to renovate their workshops substantially or may have to relocate to other places. The incremental cost is likely to be astronomical.
Hydrocarbon	- Low cost of Hydrocarbon; - Zero ODP; - Negligible greenhouse effect; - Excellent solvent. - Low GWP.	- Highly flammable; - Aftertaste; - Unknown toxicity following inhalation; - Low level density. - Potential reaction and interaction with TCM. - High conversion cost.	- Hydrocarbon is a flammable chemical. If using it as the CFCs substitute, Chinese pharmaceutical manufacturers have to renovate their workshops substantially or may have to relocate to other places. The incremental cost is likely to be astronomical.
HFA	- Low inhalation toxicity; - High chemical stability; - High purity; - Zero ODP;	- Poor solvents; - GWP lower than CFC's; - High cost of HFA. - Low conversion cost.	- HFA is known to be used by foreign manufacturers as CFCs substitutes.

Compressed Gas	- Low inhalation toxicity; - High chemical stability ; - High purity; - Inexpensive; - Zero ODP.	- Require use of a non-volatile co-solvent; - Produce course droplet spray; - Pressure falls during use;	- Use of compressed gas propellant is typically restricted to applications where spray characteristics are not critical;

3. Conclusion

41. Based on the above technical analysis, it is tentatively concluded that

    a. Ideal CFCs substitutes should possess properties such as similar physical properties, insignificant damage to the atmosphere, similar toxicity, good thermodynamic property, non-inflammability and economical feasibility.

    b. Based on international literature, HFC-134a, HFA-227, DME, hydrocarbons (isobutane) and compressed gas are all potential substitutes for CFCs in pharmaceutical aerosol products. To choose the suitable substitute, Chinese pharmaceutical aerosol manufacturers have to take into account a number of factors including drug efficacy, compatibility between the substitute and drug substance, price of the substitute, different requirmenets for re-registration, safety standards, and incremental cost associated with the conversion. The manufacturers will choose a substitute that maintaine the effectiveness of their products and meet health and safety requirements at least cost. Investigation shows that majority of Chinese manufacturers are likely to use the HFA as CFCs substitute. The Sector Plan proposal is accordingly based on HFC-134a as the least cost option maintaining the product quality.

    c. The properties of DME and Hydrocarbon are not similar to those of CFCs. Exploring the conversion to DME or Hydrocarbon is technically more difficult, though the two chemicals are cheaper than HFA. Especially for Traditional Chinese Medicine Applications, there is no international experience for Chinese manufacturers. Some TCM enterprises reported that based on preliminary test, hyrdocaron is not compatible with their aerosol products.

    d. In comparison with DME and Hydrocarbon, the properties of HFA are similar to those of CFCs. Besides, international experience shows that HFA is the substitute being widely used in foreign countries.

    e. Conversion to DME or Hydrocarbon will require substantial investment in workshops modification and in some cases relocation to meet safety requirements. Due to the smaller amount of propellant used in pharmaceutical aerosols compared to general aerosol, there would not be the savings per unit from using the less costly hydrocarbon and DME. Converting to HFA-134a will require minor modification on existing equipment and associated facilities, is less costly and can be done quicker.

f. Compressed gas is often used for spray products but not for aerosol products.

CHAPTER 5 Phaseout Strategy

1. Principle.

42. The phaseout of CFCs in China pharmaceutical aerosol sector should not impose any significant negative impact on the clinic demand for aerosol products. In other words, the principle of the strategy is to phase out CFCs rather than the pharmaceutical aerosol products.

2. Two priority Issues.

43. **a. Substitute Selection**. Out of 44 aerosol applications, Chinese manufacturers have 26 Traditional Chinese Medicinal Aerosols, for which no experience can be borrowed from the abroad. Thus selection of suitable substitutes for those TCM aerosols will be challenging. Based on international experience, HFA-134a, HFA-227, DME, hydrocarbon (isobutane) and compressed gas (carbon dioxide) are deemed as potential CFCs substitutes. However, each CFCs substitute has different chemical and physical properties. Each aerosol application is different in terms of production process and formulation. Therefore, selection of suitable CFCs substitute or conversion technology (such as alternative delivery system) is the key issue for CFCs phase-out in China pharmaceutical aerosol sector. The pharmaceutical aerosol manufacturers will have to screen CFCs substitutes or conversion technology first, then determine conversion plan which covers new formulations and production process.

44. **b. Preparation for Technical Dossier for Registration**. In accordance with relevant laws and regulations, replacement of CFCs with alternative excipients is subject to the approval of the government agencies. Manufacturers have to prepare technical dossier stipulated by the regulations so as to have their CFCs-free products registered at SFDA. The preparation for registration should be immediately initiated after the completion of the substitute selection

3. New Policies Proposed.

45. **a. Policies over Transition Period (July 1, 2007~December 31, 2009).** China will stop using CFCs as excipients for external-use aerosols since July 1, 2007. Given the limited timeframe, pharmaceutical aerosol manufacturers have to use CFCs in storage before they can obtain from SFDA the approval numbers for their new products. However, using of CFC in storage would be under stringent supervision of the government. SFDA will make transitional arrangement within the framework of Country Program. When receiving the application form the manufacturers for using CFCs in storage during the transition period, SFDA and SEPA will review and approve the applications. SEPA plans to establish a license system to control CFCs consumption for those aerosol manufacturers.

46. **b. Supervision after 2010.** After 2010, SFDA will monitor non-CFCs aerosol products so as to guarantee its safety and efficacy of clinical application.

4. Phaseout Schedule.

47. China plans to implement the CFCs phaseout for pharmaceutical aerosol sector in three stages.

    a. The first stage is to develop sector policies and to screen substitutes (January-December, 2007);

    b. the second stage is to complete registration for new aerosol products (January 2007-June 2009);

    c. In parallel, the third stage is to start new production after the completion of facility modification, production validation and staff training (July, 2007-December 2009).

CHAPTER 6 Cost Analysis

1. Basis for Cost Calculation

48. **Cutting-off Date.** The cutting-off date of July 25, 1995 should not be applied to the pharmaceutical sector as substitute aerosol technology in 1990s was not available. It is proposed that the cutting off date should be July 1, 1999 after which Article 5 Parties had the obligation to freeze CFCs production and consumption. China will not request MLF fund for seven manufacturers with production lines established after the cutting-off date. Those enterprises have to use their own funding to phase out CFCs consumption.

49. **Eligible Incremental Cost.** Cost calculation covers Technical Assistance (TA), preparation for technical dossier for registration of new aerosol products, modification on the existing facilities, production validation, staff training and two years (and not four years as used as default until the ExCom establishes guidelines for new sectors and sub-sectors)) of Incremental Operation Cost. For eligible manufacturers with baseline consumption, both Incremental Capital(IC) and Incremental Operation Cost (IOC) are considered as eligible Incremental Cost. A few eligible manufacturers have not been in production for years. However, as long as they have aerosol product approval numbers issued by SFDA, they have legal rights to resume production depending on the market demand. Therefore, for those manufacturers without the baseline consumption, only cost for substitute screening and cost for preparation for technical dossier for registration purpose are considered as eligible incremental cost.

50. **Reasons to Use HFC-134a for Cost Calculation.** Cost analysis is based on the sector survey and the literature review on international experience. It is estimated that from technical perspective, majority of Chinese pharmaceutical aerosol manufacturers may use HFA (e.g. HFA-134a, HFA-227) as CFCs substitute after screening a variety of substitutes. Besides, conversion to HFA is more financially feasible in China because in case of conversion to DME or Hydrocarbon, Chinese manufacturers have to renovate their workshops substantially or relocate to other places to meet safety standards. As CFCs has high chemical stability, it is not mandatory that the existing workshops meet national anti-explosive standards or safety standards. If converted to hydrocarbon and DME production, the existing facilities and the workshops would have to be replaced to meet the area hazard classification as per Chinese regulations. Storage vessels, pipe system and valves would have to be installed according to Chinese safety regulations, which might not in all cases be possible without relocation of workshops. As the filling takes place in special enclosed clean rooms, use of hydrocarbon as propellant would require changes to the ventilation system and enclosure as well. Consequently, the conversion cost to Hydrocarbon or DME would be very prohibitive.

51. In Chinese market, HFA-227 is slightly more expensive than HFA-134a. Besides, only limited experience on the conversion to HFA-134a is available when the sector plan is under preparation.

Therefore, the Incremental Cost calculation is based on the conversion to HFA-134a. In case any Chinese pharmaceutical aerosol manufacturer selects other substitutes (e.g. DME, Hydrocarbon or others) in the future, it is the manufacturer which has to raise sufficient counterpart funding for the renovation or the relocation of its workshops.

52. After the 50th ExCom meeting, a review of China Pharmaceutical Aerosol enterprises with zero/small CFCs baseline has been undertaken. Based on the review, China will not request funding for the following eleven enterprises which had neither pharmaceutical aerosol production in 2006 nor plans to resume such production in 2007.

Table 6-1 Enterprises without Funding Request

Enterprise ID	Name of Enterprise	CFCs Baseline (kg)	Skin Aerosol Application ID	Cavity Aerosols Application ID
28	Heilongjiang Tianlong Pharmaceutical Co., Ltd	300	A23, A25, A29	A15,A40
03	Guangzhou Baiyunshan Hejigong Pharmaceutical Co., Ltd	0	A09 A23	A40
04	Externally Applied Agent Factory of Guangzhou Baiyunshan Pharmaceutical Co., Ltd	0	A23	
06	Beijing Double-Crane Modern Pharmaceutical Technology Co., Ltd	0	A25	
10	Shanghai Fuxingzhaohui Pharmaceutical Co., Ltd	0	A42	
15	Harbin Hengcang Pharmaceutical Co., Ltd	0	A25	
22	Hangzhou Sino-US Huadong Pharmaceutical Co., Ltd	0	A23	
25	Chongqing Kerui Pharmaceutical Co., ltd	0	A10	A12
31	Guangzhou Dongkang Pharmaceutical Co., Ltd.	0		A04
37	Nantong Zhongbao Pharmaceutical Co., Ltd	0	A11, A23	
39	Anshan No.1 Pharmaceutical Plant	0	A23	A18, A21, A44
	Total	**300**		

2. Technical Assistance (TA)

53. In order to implement the sector plan smoothly, it is necessary to undertake TA activities Total Fund requested for Technical Assistance is 1.1 million US dollars covering the following activities:

    a. Workshops for aerosol manufacturers, equipment manufacturers and technical experts during the

implementation of the sector plan.

b. Training for government agencies such as local Food and Drug Administration Bureaus and Environmental Protection Bureaus on the implementation of the phaseout policies;

c. Public awareness promotion including training activities;

d. Recruitment of individual consultants to provide technical support for phaseout activities. Recruitment of consultant firms to provide technical support such as review test data and appraise feasibility study reports etc.;

e. Development of a MIS system.

f. Auditing for CFCs consumption annually for pharmaceutical aerosol manufacturers

g. Study tours to learn international experience.

h. Other TAs as necessary.

3. Incremental Cost for Manufacturers.

3.1. Substitute Screening

54. Presently, due to lack of testing data, Chinese pharmaceutical manufacturers are not able to decide which substitute is the best one for their aerosol products, particularly for those producing Traditional Chinese Medicine aerosol products. MLF Funding is requested to allow those enterprises to screen potential substitutes as mentioned in Chapter 4. The objective of the screening is to identify the best substitute or alternative delivery system for their pharmaceutical aerosol products. Due to business confidentiality and potential property rights which may arise from the conversion, manufacturers should screen substitutes by themselves. In case some manufacturers do not have such capacity, they may have to engage qualified institutions to do the screening. After the screening, manufacturers should submit feasibility study reports for the conversion to non-CFCs production, which consists of screening on formulations and production processes, preliminary evaluation on drug quality and stability, pharmacology comparison test, preliminary evaluation on toxicology and preliminary analysis on the manufacturing equipment. Those study reports will furnish technical basis to develop phase-out policies and to make arrangement for the transitional period. These reports may also provide technical reference for those non-eligible manufacturers so as to facilitate CFCs phase-out in the whole sector.

55. If suitable CFCs alternatives can not be identified for an application, it would be necessary to use alternative delivery system, such as compressed air spray, ultrasonic spray, two-phase system, self-pressurized system and dry powder inhaler. Such alternative delivery system would have to follow the same screening procedures as that for aerosol products.

56. In case some manufacturers are not able at all to identify suitable substitute or alternative delivery system, their study reports may also be used as technical basis for exemption applications for essential

use after January 1, 2010.

57. The cost for each item of the tests is shown in table 6-2. There are 41 aerosol products, so the total cost adds up to USD 1,793,750.

Table 6-2 Cost for Screening Substitutes

Item	Activity	Cost (USD)
Screening for Formulations and Production Process	Test for Formulation and Production Process	12,500
Evaluation on Quality and Stability	Evaluation on Quality-related Factors	6,250
	Preliminary Stability Test	6,250
Pharmacodynamics Comparative Test		6,250
Preliminary Toxicology Evaluation		6,250
Pre-analysis on Major Equipment		6,250
Subtotal		43,750
Number of Products		41
Total Cost (US$)		**1,793,750**

3.2. Preparation of Technical Dossier for CFCs-Free Aerosol Registration Application

58. As any change in excipients or delivery system may have consequence for the safety and efficacy, *China Drug Administration Law* and *Provisions of Drug Registration* require that pharmaceutical aerosol manufacturers apply for new registration. For the registration purpose, manufacturers have to prepare technical dossier in accordance with relevant national regulations, Table 6-3 lists the dossier for application for change of excipients already with National Standards; Table 6-4 lists the dossier for Drug Registration Application with New Excipients; Table 6-5 lists the dossier for Drug Registration Application for Change in Dosage Form.

Table 6-3 Dossier for Application for Change of Excipients with National Standards

No.	Document Name
1	photocopy of drug approval certificate and appendix
2	supporting documents
3	Sample of revised *Package Insert* enclosed with detailed revision illustrations
4	Sample of revised package/ label enclosed with detailed revision illustrations
5	Documents of pharmacological research
6	Sample of drug

23	Research documents & literature of genital toxicity research
24	Research documents & literature of carcinogenesis research
25	Domestic and foreign relevant overview of clinical trial documents
26	Plan & scheme of clinical trial
27	Clinical researcher manual
28	Sample of Informed Consent, and approval document of Ethics Committee.
29	Clinical Trial Report

Table 6-4 Dossier for Drug Registration Application with New Excipients

No	Document Name
1	Name & naming basis of medicinal adjuvant
2	Certification documents
3	Objective & basis of topic establishment
4	Summary & assessment of main research results
5	Sample of *Package Insert*, drafting illustrations, and latest reference
6	Design sample of package & label
7	Overview of pharmacological research documents
8	Research documents & literature of production process
9	Research documents & literature verifying chemical structure or compositions
10	Research documents & literature of quality research work
11	Research documents & literature of drug-related compatibility
12	Standard draft and drafting illustrations, with standard product or control product
13	Inspection Report on 3 continuous batches of samples
14	Research documents & literature of stability research
15	Selection basis & quality standard of packing materials and containers in direct contact with medicinal adjuvant
16	Overview of pharmacological & toxicological research documents
17	Research documents & literature of pharmacodynamics influence on to-be-applied drug
18	Research documents & literature of general pharmacological research
19	Research documents & literature of acute toxicological research
20	Research documents & literature of long-term toxicological research
21	Research documents & literature of main local/systemic-administration-related special safety test, such as allergy (local, systemic, and light), hemolysis, and local irritability (blood vessel, mucosa, muscle)
22	Research documents & literature of mutagenesis research
23	Research documents & literature of genital toxicity research
24	Research documents & literature of carcinogenesis research
25	Domestic and foreign relevant overview of clinical trial documents
26	Plan & scheme of clinical trial

27	Clinical researcher manual
28	Sample of Informed Consent, and approval document of Ethics Committee.
29	Clinical Trial Report

Table 6-5 Dossier for Drug Registration Application for Change in Dosage Form.

No.	Document Name
1	Drug name
2	Certification documents
3	Objective & basis of topic establishment
4	Summary & assessment of main research results
5	*Package Insert*, drafting illustrations, and relevant reference
6	Design sample of package & label
7	Overview of pharmacological research documents
8	Research documents & literature of production process for raw drugs, and research documents & literature of prescription and process for preparation
9	Research documents & literature verifying chemical structure or compositions
10	. Research documents & literature of quality research work
11	Drug standard and drafting illustrations, with standard product or control product
12	Inspection Report on samples
13	Origin, quality standard, and Inspection report of raw drugs and adjuvant
14	Research documents & literature of drug stability research
15	Selection basis & quality standard of packing materials and containers in direct contact with drug
16	Overview of pharmacological & toxicological research documents
17	Research documents & literature of special safety test, such as allergy (local, systemic, and light), hemolysis, and local irritability (blood vessel, mucosa, muscle)
18	Research documents & literature other than clinical pharmacokinetics research
19	Domestic and foreign relevant overview of clinical trial documents
20	Plan & scheme of clinical trial
21	Clinical researcher manual
22	Sample of Informed Consent, and approval document of Ethics Committee.
23	Clinical Trial Report

59. Cost for preparation for the technical dossier will depend on applications, selected propellants and production process. It can not be accurately calculated at the currant stage. Therefore, Table 6-6 is the best estimation based on the past experience. Six key items are included for the estimation, though there are other items not included. Compared with the Skin Aerosol, cost for dossier preparation for Cavity Aerosol is more costly because the requirement for the latter is more stringent.

60. In accordance with relevant regulations, each manufacturer has to make registration for their aerosol products based on its formulation and production process, though some products may also be produced by multiple manufacturers. Therefore, enterprises have to make registration application for total 28 Skin Aerosol products and 13 Cavity Aerosol products.

Table 6-6 Cost for Preparation for Technical Dossier for Registration

No.	Name of the data	Cost for Skin Aerosol Product (USD$)	Cost for Cavity Aerosol Product (USD$)
1	Study on Pharmacy	6,250	6,250
2	Study on Production Process	12,500	12,500
3	Study on Quality	6,250	6,250
4	Pharmacological Study	18,750	25,000
5	Toxicological Study	18,750	25,000
6	Special Safety Test	125,00	18,750
	Subtotal	75,000	93,750
	Number of Products	28	13
	Subtotal	**2,100,000**	**1,218,750**
	Total	**3,318,750**	

3.3. Modification on Existing Facilities

61. The requested incremental cost for modification on existing facilities is based on the assumption that these manufacturers will convert to a non-flammable propellant such as HFA-134a. As HFC-134a is not compatible with hermetic materials of the existing facilities, it is needed to modify or replace existing pumps, pipes, hermetic components for pipes, valves and filling&charging equipment and associated instruments.

62. Based on the sector survey, existing production lines can be divided into two groups, one is automatic (Type A), while the other is semi-automatic (Type B). Modification cost is showed in Table 6-7.

Table 6-7 Modification Cost for Existing Facilities

Items	**Type A**	**Type B**
	(USD)	**(USD)**
1.1 Storage Vessel for Propellant	15,000	15,000
1.2 Pipes and Hermetic Components(for pipes, valves, filling& charging equipment)	10,000	10,000

1.3 Pumps	12,500	12,500
1.4 Detecting Leakage Equipment	25,000	N.A
1. 5 Labor Cost	1,250	1,250
Total Cost for One Line with Baseline Consumption	63,750	38,750
Number of Lines with Baseline Consumption	13	7
Subtotal	828,750	271,250
Total	**1,100,000**	

63. In the case of conversion to Hydrocarbon, estimated modification cost based on initial assessment for enterprises would be as follows:

Table 6-8 Modification Cost for One Production Line Converted to Hydrocarbon*

Item	Cost (USD)
1.1. Replacement of Existing Filing Line	150,000
1.2 Piping and Valves	40,000
1.3. Hydrocarbon Storage Tank	30,000
1.4. Replacement of Electrical Installation and Grounding of Filling Line:	20,000
1.5. Aerosol Lid Control	5,000
1.6. Clean Room Modification and Ventilation System:	20,000
1.7. Gas Detection System:	15,000
1.8. Fireproof Facility	30,000
1.9. Installation	20,000
1.10: Safety Certification:	30,000
Subtotal	**360,000**
Number of Lines with Baseline Consumption	20
Total	**7,200,000**

* Cost for workshop relocation is not taken into accounted.

3.4. Production Validation

64. *Provisions on Quality Management for Pharmaceutical Production* (SFDA #9, effective August 1, 1998) was issued by SFDA in 1998. Article 57 stipulates that validation for pharmaceutical production shall consist of validation for workshop, validation for installation of facilities and equipment, validation for facility operation and performance and validation for products. Article 58 states that re-validation shall be carried out in case of change of main quality related factors such as production process, quality control method, main excipients and production facility,

65. In accordance with *Guidance of Validation for Pharmaceutical Production* (2004), Drug production validation includes prospective validation, concurrent validation, retrospective validation and revalidation. Due to the replacement of propellant or change of dosage form, new production equipment, new production technology and new product application may be introduced. Therefore, it is necessary to carry out prospective validation before commercial production. The purpose of prospective validation is to evaluate and confirm the reproducibility and reliability of production process. Concurrent validation is to obtain data from the actual process operation, so as to prove that it fulfills the expected requirements. Retrospective validation is to collect statistics data and make trend analysis after normal production for a certain period of time, thus discovering the worst conditions for the process operation and indicating the risk of potential malfunction. Revalidation includes compulsive validation, alterant validation and regular validation.

A. Validation for Changing Excipient (Alternative Propellant)

66. Changing of excipients has to conduct prospective validation, concurrent validation, retrospective validation and revalidation. The validation include i) validation of workshop; ii) validation of public utilities; iii) validation of computer system; iv) validation of production equipment; v) validation of production process; vi) validation of personnel; vii) validation of other relevant items

a) Validation for Workshop, Public Utility System and Computer System

67. Validation of workshop is to confirm that 1) reconstructed workshops shall be in compliance with design standards; 2) the flow of people and materials shall be reasonable;3) workshop cleanliness shall be up to the level of 300,000. Validation of public utilities consists of six items, namely, heating, ventilation, air conditioning, discharging system, cooling system and propellant supply system. Validation of computer system consist of four items, namely, batch record/SOP management system, material management system, lab system and the management system for production/engineering spare parts.

b) Validation for Production Equipment

68. Validation of production equipment comprises six items, namely, weighing scales, containers, valve cleansing equipment, and compound vessel system, filling equipment, weight inspection system and spray inspection system.

c) Validation for Production Process

(i) Validation items for dispensing preparation includes: temperature of liquid product in compound vessels, particle sizes and homogenization of the drug liquid.

(ii) Validation of cleaning effect of containers: various impurities placed into the container shall be totally removed after cleaning.

(iii) Validation items for filling process include appearance, filling weight and leakage. At least three batches shall be inspected. Samples shall be taken from different places to check the appearance, filling weight, active ingredient and leakage.

(iv) Validation items for weighting equipment include weighing accuracy and elimination of under-weighed and over-weighed samples.

(v) Validation items for the product inspection time include leakage and shot weight per actuation. Different inspection times shall be selected to test the leakage and the shot per actuation so as to find out the best inspection time.

(vi) Validation item for spray inspection include the performance of spray and elimination of samples that don't spray or don't spray constantly.

(vii) Against product quality standard, validation items for metered aerosols comprise appearance, active ingredient per actuation, times of actuation per canister, shot weight per actuation, spray distribution, microbes, etc. Validation for non-metered aerosol includes appearance, spray speed, shot weight per actuation and microbes, etc. At least three batches of samples shall be inspected with validated sampling and analysis methods to ensure that finished products are produced steadily in compliance with product delivery standards.

(viii) Validation items for cleanliness include the cleanliness of compound vessels and filling lines. There shall be no cross-contamination between different batches. After filling of cleaning, the contents of raw medicinal material, water and solvent shall be measured, to make sure that no active medicinal material or solvent remains.

d) Validation for Personnel and Other Relevant Items

69. Validation for personnel consists of establishment of filing system for each person engaged in aerosol production, including records for training, health and safety and personnel performance, etc. Validation for other relevant items includes document record, instrument calibration, preventative maintenance, production areas, and area for changing clothes, and waste cleansing and sterilization.

B. Validation for Change in Dosage Form

70. For change in dosage form, it is required to conduct prospective validation, concurrent validation, retrospective validation and revalidation. The validations are basically the same as those for Part A, except that there are some differences in validation items for finished product, which are part of production process validation. Validation for metered aerosol includes appearance, total times of actuation per canister shot weight per actuation, active ingredient per actuation, spray distribution, variation of filling amount (filling amount) and microbes, etc. Validation items for non-metered aerosol includes appearance, spray speed, shot weight per actuation and microbes, etc. At least three batches of samples shall be inspected with validated sampling and analysis methods to ensure that finished products are produced steadily in compliance with product delivery standards.

71. Validation is needed for 20 production lines befor commercial production. Cost for production validation is detailed in Table 6-9.

Table 6-9 Cost for Production Validation

No.	Validation	Contents	Cost (US$)
1	Equipment	Scales, Containers, Valve Cleansing Equipment; Compound Vessel System; Filling &Charging Equipment; Weight Checking System; Spray Checking System	12,500
2	Production Process	Liquid Drug Processing, Cleaning effectiveness for Containers; Filling Process; Weight Checking System; Product Checking Time; Spray Checking; Finished Products; Cleaning Effectiveness.	18,750
3	Others	Workshop; Public Utilities; Computer System; Others	6,250
		Subtotal for One Production Line	37,500
		Number of Production Lines with Baseline Consumption	20
		Total	**750,000**

3.5. Staff Training

72. Due to the introduction of new substitute, it is necessary to provide training for the staff of the manufacturers. Those people who should receive training include Quality Control technicians, operators, recorders, engineers, management staff and those working for procurement, transportation and maintenance. It is estimated that each manufacturer has 20 for production and 40 for sales.

Table 6-10 Staff Training Cost

	Production Staff	**Sales Staff**
Number of Trainees	20	40
Unit Cost (US$/person)	125	375
Subtotal (US$)	2500	15,000
Subtotal for One Production Lines(US$)	17,500	
Number of Production Lines with Baseline Consumption	20	
Total	**350,000**	

3.6. Incremental Operating Cost

73. The calculation is based on the data collected from manufacturers during the survey undertaken by NICPBP, SFDA and SEPA. Baseline production data is shown in Table 2-3. Calculation of IOC is based on the ExCom guidelines and using Incremental Operating Cost for a period of two years.

74. For the new production, the propellant, valve and canister etc. have to be changed. Table 6-11 shows the prices of CFCs and HFA-134a in 2005, which is consistent with the baseline year.

Table 6-11 Price of Propellant

	Baseline Consumption (MT)	Price (USD/MT)
CFC-11	112.723	1,643
CFC-12	365.964	2,366
CFCs Weighted Price		2,196
HFC-134a Price		7,380

75. The total production quantity of baseline year is 10,121,216 pieces of aerosol products, of which 9,590,363 are of skin aerosols. The average CFCs consumption for skin aerosol products is 47.50 gram/canister, while that for cavity aerosol is 16.57gram/canister. Literature reviews indicates that on average, HFA aerosols uses 30% less propellant than CFCs aerosols. Therefore, it is assumed that after conversion, the average HFA-134a consumption for skin aerosol products is 33.25 gram/canister, while that for cavity aerosol is 11.60 gram/canister. Calculation for Incremental Operation Cost is shown in Table 6-12.

76. Due to the price difference of HFA-134a and CFCs, it is proposed that those manufacturers be financed with two years of Incremental Operation Cost only (USD 3,536,824) (and not four year as per the general rules until the Excom decides). The IOC will be allocated to eligible pharmaceutical aerosol manufacturers based on their baseline year production.

3.7. Contingency

77. Contingency is calculated as 10% of the TA and total Incremental Capital(IC).

3.8. Deduction Due to Foreign Share

78. Out of 32 eligible manufacturers, there are three joint ventures (#13, #14, and #22) with foreign shares (i.e. British Virgin Islands and USA). Funding for these enterprises is prorated according to Chinese share. Total USD 460,230 will be deducted (see Annex I).

Table 6-12 Incremental Operation Cost

I. IOC for Skin Aerosol							
Items	Before Conversion (CFCs as propellant)		After Conversion (HFA-134a as propellant)		IOC for One Piece of Aerosol	Skin Aerosol Production Quantity	IOC for Skin Aerosol
		Unit Cost (US$/can)		Unit Cost (US$/can)			
1. Propellant		0.10433		0.24523	0.14090		
Price(USD/g)	*0.00220*		*0.00738*				
Average Propellant Consumption(g/can)	*47.50*		*33.25*				
2. Canister		0.16875		0.19125	0.02250		
3 Valve		0.04813		0.05188	0.00375		
Subtotal		**0.32120**		**0.48835**	**0.16715**	**9,590,363**	**1,603,058**
II. IOC for Cavity Aerosol							
Items	Before Conversion (CFCs as propellant)		After Conversion (HFA-134a as propellant)		IOC for One Piece of Aerosol	Cavity Aerosol Production Quantity	IOC for Cavity Aerosol
		Unit Cost (US$/can)		Unit Cost (US$/can)			
1. Propellant		0.03638		0.08552	0.04914		
Price(USD/g)	*0.00220*		*0.00738*				
Average Propellant Consumption(g/can)	*16.57*		*11.60*				
2. Canister		0.16875		0.19125	0.02250		
3 Valve		0.12250		0.47500	0.35250		
Subtotal		**0.32763**		**0.75177**	**0.42414**	**530,853**	**225,156**
III. Total IOC for one year							**1,828,214**

IOC (discount @7%)		**Cumulative**
IOC for one year	1,828,214	1,828,214
IOC for 2nd year	1,708,611	**3,536,824**[2]
ICO for 3rd year	1,596,833	5,133,657
IOC for 4th year	1,492,367	6,626,024

[2] IOC for two years is reduced to USD3,509,474 after the fund request for Heilongjiang Tianlong(Plant #28) is withdrawn.

Summary: Incremental Cost

No.	Components	Cost (USD)	
A	**Technical Assistance**	**1,100,000**	
B	**Incremental Capital Cost (Manufacturer Conversion Cost**	**7,312,500**	
B.1	Screening Substitutes		1,793,500
B.2	Cost for Preparation for Technical Dossier for Registration Application		3,318,750
B.3	Modification on Existing Facilities		1,100,000
B.4	Validation		750,000
B.5	Staff Training		350,000
C	**IOC of Two Years (discount rate@7%)**	**3,509,474**	
D	**Contingency (10% of A+B)**	**841,250**	
	Subtotal (A+B+C+D)		12,763,224
E	**Deduction Due to Foreign Share**	**- 460,223**	
	Total(A+B+C+D+E)	**12,302,994**	
	Total Requested Funding	**12,302,994**	

Chapter 7 Operation Mechanism

79. This Chapter explains the procedures for establishing funding arrangements and operating mechanisms for project management, coordination, supervision and evaluation as well as the responsibilities of various institutions involved in implementation of this Sector Plan.

1. Umbrella Grant Agreement

80. China and the World Bank have signed an Umbrella Grant Agreement in December 1997. The Agreement sets forth the terms and conditions under which grant resources approved by the ExCom in sector approaches in China would be carried out. This Agreement includes provisions that allow the Bank to disburse funds to China based on performance indicators, and will also be extended to the pharmaceutical aerosol sector.

2. Funding Arrangements

81. MLF Approval: it is anticipated that funds for this Sector Plan would be approved in two steps:

    a The Government, through the World Bank, will request that the ExCom consider this overall sector plan and agree to fund the phase-out with tranches, provided that China meets agreed annual phase-out targets for the previous year. At the same time, the Government will also apply for approval of the First Biennial Program, presently proposed to cover activities in the calendar years from 2007 to 2008, which will be submitted to the ExCom as a separate document.

    b From 2007 onwards, another Biennial Programs will be submitted to the last ExCom meeting of 2008, setting out the annual targets and funding requests. The amount of annual funding request would be consistent with the funding amounts indicated in the overall sector plan. The ExCom would be asked to release funds at the levels agreed to in the sector plan based on achievement of previous phase-out targets, so that the next Biennial Program could start in the following January. In general, approval of funds would be based on achievement of agreed ODS phase-out targets.

82. In case China fails to reach the phase-out targets for a given year, i.e., if CFCs consumption for pharmaceutical Aerosol Sector exceeds the agreed targets or the phase-out amount contracted is less than that required to meet the target, the Bank and China would agree on remedial actions before applying for the next funding. The remedial actions proposed would be to bring the program back on track in the coming year, and would be further subject to ExCom approval. Other conditions as stated in the Umbrella Grant Agreement would also apply.

83. The Biennial Program would contain the following sections:

    a Sector phase-out schedule, including phase-out activities, manufacturers involved, phase-out

approaches adopted and the phase-out timetable arranged;

b Status of all activities of previous year(s) and any agreed remedial actions if necessary, for the current year;

c Objectives of Biennial Program – phase-out targets and funding requirements for activities in the following year;

d Description of activities in the Biennial Program, including phase-out activities for the manufacturers involved, any new policies to be taken up, and technical assistance activities;

e Performance indicators of the Biennial program.

84. The World Bank would approve the technical assistance consistent with the Biennial Program, based on agreed Terms of reference for each TA (including the funding level of TA) in that year's Biennial Program.

3. Disbursement Mechanism

85. MLF disbursement to the World Bank: Upon approval of the Biennial Program by the ExCom, the Multilateral Fund will transfer the funding to the World Bank account.

86. World Bank disbursement to China: There would be four disbursements into the ODS Phase-out Account at SEPA for each Biennial Program. The Government would be allowed to request these four disbursements at any time during the year, provided that the disbursement conditions have been met. In any particular year, disbursement to China will start only when the Bank receives grants for that Biennial Program from the MLF. Disbursement conditions and amounts to be disbursed are as follows:

a ***First disbursement*** – funds for technical assistance and DIA's agency fees. ***Condition:*** Approval of the Biennial Program by the ExCom and release of funding to the World Bank.

b ***Second disbursement*** – 50% of funds allocated for manufacturer activities and 50% of China's management fees.

Conditions:

I) 30% of all contracts covering target phase-out amount of the current year's Biennial Program have been signed by government with manufacturers;

II) Progress report on this sector plan implementation is satisfactory to the Bank; and

III) Any other conditions as specified in the current Biennial Program.

c ***Third disbursement*** – 30% of funds allocated to manufacturer activities and 30% of China's management fees.

Conditions*:*

I) 100% of all contracts covering target phase-out amount and TA contracts of the current year's

Biennial Program have been signed;

II) The government reports the actual consumption does not exceed the consumption target set for the previous year (not applicable to the first implementation program);

III) A Progress report should be provided to the Bank, which is satisfactory to the Bank;

IV) the Biennial Program implementation should be considered satisfactory to the Bank; and

V) Any other conditions as specified in the current Biennial Program.

d ***Fourth disbursement*** – 20% of funds allocated to manufacturer activities and 20% of China's management fees.

Conditions:

I) Performance audit of the previous year's Biennial Program is acceptable to the Bank;

II) Progress report on sector plan implementation is satisfactory to the Bank; and

III) Any other conditions as specified in the current Biennial Program.

87. In the event that any phase-out target is not met, the Bank will suspend further disbursements to China. Disbursements will resume only after China and the Bank agree on and carry out remedial actions.

88. The grant funds will be allocated to manufacturers in consistence with the MLF funding approved for the sector. Manufacturers would sign ODS reduction contracts with SEPA.

89. The contracts will stipulate, among others, (a) Date and amount of ODS phase-out in applications; (b) the disposal equipment list, if any; (c) and agreed disposal dates.

4. Management and Coordination

90. The Government would be responsible for implementing this Sector Plan. PMO will manage and coordinate execution of each Biennial Program. In addition, SFDA and SEPA will select a qualified firm as a Domestic Implementing Agency (DIA) to help manage day-to-day activities at manufacturer level. The World Bank will supervise overall implementation of this Sector Plan, replenish the ODS IV project account, report implementation progress to the ExCom and submit future funding requests to the ExCom.

A) State Food and Drug Administration

91. State Food and Drug Administration (SFDA) will play an important role in the preparation and execution of the yearly program. Responsibilities of SFDA include the following

(i) To establish CFCs phase-out policies for pharmaceutical aerosol sector;

(ii) To organize local FDAs to impalement phase-out policies and undertake irregular spot check to the pharmaceutical aerosol manufacturers

(iii) To supervise CFCs consumption of pharmaceutical aerosol manufacturers;

(iv) To ensure adequate clinical supply of pharmaceutical aerosol products.

B) Foreign Economic Cooperation Office (FECO)

92. FECO is a management department to implement the environmental protection projects financed by the organizations of the United Nations and international or regional financial organizations. It hosts the project management office (PMO) for ODS projects. Responsibilities of FECO include the following:

a To supervise PMO activities,

b The financial division of FECO manages the ODS IV phase-out special account,

I) prepare and submit withdrawal applications to WB for advance deposit;

II) review the application of disbursement from beneficiaries according to the manufacturer contracts and TA contracts and make disbursement,

III) keep financial records and account details,

IV) Provide financial information on the ODS IV account to the audit agency and assist the work of the audit agency.

c On behalf of SEPA, sign the ODS phase-out contracts, including manufacturer contracts and TA project contracts;

d On behalf of SEPA, handover the ownership of all the equipment purchased under the ODS project to the manufacturers after the project commissioning.

C) *Project Management Office (PMO)*

93. PMO is the National Ozone Unit (NOU) of China with full responsibility to implement the international and national policies and regulations, and manage the information concerning the ozone layer protection. It is also in charge of the project selection, development and submission to the Multilateral Fund. Once the ExCom approves project, the PMO will coordinate, manage and monitor its implementation. PMO consists of the staff from Pollution Control Department, International Cooperation Department of SEPA and FECO. It is responsible for the routine management of all the activities of ODS phase-out consistent with the MP and reports to the Leading Group on key issues. PMO is set up in the FECO of SEPA. Its responsibilities are as follows:

a. To coordinate with related line ministries, industrial departments and related industrial association to jointly prepare the sector plans for completely phasing out ODS in a given sector, including the implementation mechanism and the policies in favor of ODS phase-out to ensure healthy development of industries;

b. To select the domestic implementing agents (DIA) and endorse procurement agents selected;

c. To organize and implement sector plans strictly in accordance with the agreement signed between the Chinese Government and the ExCom;

I) review of the Biennial Programs prepared by the special working groups (SWG) and submit the Biennial Programs to the ExCom through the World Bank for approval,

II) review of the work plans prepared by the SWGs,

III) approval of project documents prepared and submitted by SWGs,

IV) review of progress reports submitted by SWGs,

V) helping SWGs to solve problems encountered during project implementation,

VI) Coordinating SWGs on ODS data reporting, policy formulation, training, and information exchange.

d. To supervise SWGs' activities and provide with necessary working conditions,

e. To communicate and reach an agreement with the World Bank on the important issues during the implementation of projects,

f. To cooperate with audit agency to carry out audit,

g. To assist the World Bank and the ExCom in necessary project evaluation.

h. To be responsible for implementation of Technical Assistant Projects (TAs)

I) To define the demand on TA projects;

II) To review all of the TORs of TA projects written by the SWG;

III) To review the selection of consultants for TA projects;

IV) To authorize disbursement to all the technical assistant project;

V) To evaluate the results of technical assistant projects and determine if further improvement is necessary.

D) ***Local Environmental Protection Bureau(EPB) and Local Food and Drug Administration(FDAs)***

94. Local EPB and FDAs are bureaus with jurisdiction over the geographical areas where the project manufacturers are located. The responsibilities of local FDAs and EPBs are the following:

a. To implement the ODS phase-out policies in the region;

b. To assist to resolve the issues in the region during the implementing of the project with the request of the SFDA and SEPA;

c. To assist to verify the ODS consumption of the manufacturers, attend the project commissioning with the request of the SEPA and SFDA;

d. To supervise the disposal of the ODS equipment, if any;

e. To supervise the manufacturers to comply with ODS quota system;

f. To attend the training with the request of SFDA and SEPA.

E) ***Domestic Implementation Agent (DIA)***

95. A DIA will be competitively selected by PMO for the Sector Plan (SP) after it is approved. The DIA will assist PMO in managing the implementation of SPs and Biennial Programs. Staffs from DIA usually work with staff from PMO in the SWGs. Under the guidance of PMO, DIA will carry out the following activities:

a. Overall management --

I) Assist SWGs in project preparation and implementation;

II) Keep all project preparation and implementation documentation for audit by the audit agency during annual performance audit and for the annual verification by the Bank,

III) Input data into (monitoring and information system) MIS in a timely manner and generate various project progress reports; and

IV) Review project implementation status and report identified problems to SWGs.

b. During project Preparation --

I) Prepare work plan with SWGs for each Biennial Program;

II) Assist SWGs in publicizing the sector plan;

III) Assist SWGs in training manufacturers, local experts, and general contractor(s) if needed;

IV) Review project application submitted by manufacturers;

V) Assist SWGs to organize experts to help manufacturers in preparing project proposals and feasibility study,

VI) Assist SWGs to organize experts to help manufacturers in evaluating project proposals and feasibility study; Assist SWGs to organize experts to provide technical support to manufacturers during project implementation

VII) Supervise expert activities and verify its working load and cost, and report to the SWGs accordingly; and

VIII) Assist SWGs in project appraisal.

c. During project implementation --

I) Prepare ODS phase-out contracts and its annexes;

II) Review project implementation status and verify the progress report submitted by beneficiary manufacturers and general contractor through plant visits;

III) Review of payment applications submitted by beneficiary manufacturers, and submission of applications to sector team;

IV) Assist PMO to select the procurement agency and review the procurement organized by the procurement agency in conform with the agreed procedures;

V) Assume responsibility for supervising equipment destruction and maintain relevant data and information;

VI) Assist PMO in selecting general contractors for sub-projects, if needed, including:

- Advertise the procurement notices in specified newspaper;

- Organize local experts to prepare bidding document for general contractor and submit to PMO for approval;
- Invite bids, organize bid opening and bid evaluation;
- Prepare bid evaluation reports and submit to PMO for approval;
- Prepare contract for general contractor and sign the contract with the winning bidder together with FECO and manufacturers;

VII) Review payment requests from project beneficiaries and general contractors, and prepare disbursement requests to FECO;

VIII) maintain project documentation and coordinate sector teams to provide all information necessary for financial and performance audit, and assist audit agency whenever necessary,

IX) Organize necessary training for manufacturers,

X) Assist PMO in implementing TA projects.

d. Reporting

I) reporting on technical, financial, procurement, and management problems occurred during project implementation in a timely manner, and submission of reports to PMO with recommendations to solve problems;

II) compilation of progress reports on manufacturer activities;

III) preparation of project completion reports and commissioning report and,

IV) input of information into the MIS in a timely manner on the status of implementation of manufacturer projects.

96. The World Bank plays a major role in assisting developing countries to meet their obligations as Parties to the Montreal Protocol. The Bank partners with developing countries in its role as an implementing agency for the Multilateral Fund. The World Bank and China began their partnership on Montreal Protocol program in 1993 to help China meet its national phase-out obligations. The WB is responsible for a range of activities specified in the project document along the lines of the following:

a. assisting China in preparation of the Biennial Programs;
b. verifying for the Executive Committee that consumption of the substances have been eliminated in accordance with the targets;
c. providing a verification report to the Executive Committee bringing evidence that the targets have been met and associated annual activities have been completed as indicated in the Biennial Program;
d. ensuring that achievements in previous Biennial Program are reflected in future Biennial Programs and will serve as the progress report;
e. Reporting on the implementation status of all previous years' Biennial programs activities will be included in Biennial Program.
f. carrying out supervision missions;

g. helping China to set up an operating mechanism to allow effective and transparent implementation of the Biennial Program;

h. co-coordinating the activities of the co-coordinating Implementing Agencies, if any;

i. ensuring that disbursements made to China are based on the use of the indicators; and

j. Providing China with the necessary policy, management and technical support.

5. Monitoring and Evaluation

97. PMO is the core organization for monitoring the implementation of Biennial Programs with the responsibility for reporting to the World Bank. PMO will be responsible for tracking the implementation of policy measures and the technical assistance activities; submit progress reports to the Bank every quarter. PMO will also report on specific issues if requested.

98. DIA will oversee the progress of Biennial Programs, and submit written reports to PMO quarterly.

99. The implementation status of all activities in Biennial Programs will be reported to ExCom once a year during preparation of following year's Biennial Program, and at other times if specifically requested.

100. There are two means for monitoring and evaluating the implementation of ODS PA phase-out plan.

A) Verification

101. The Bank will conduct an independent verification annually to verify CFCs consumption and conversion activities. The Bank will supervise the implementation of Biennial Programs and will have access to any ongoing or completed manufacturers for spot checks of the records of projects, including random factory visits. The Bank will also carry out such additional verifications as are required by the ExCom.

B) Audit

102. There will be an annual financial audit of the ODS Phase-out Account at SEPA, conducted by an independent audit agency acceptable to the Bank, and a performance audit, also by an independent audit agency acceptable to the Bank.

Chapter 8 Action Plan

103. This Chapter presents the Action Plan and schedule for implementing CFCs phase-out for the pharmaceutical aerosol sector. This is a rolling plan where the impact of a Biennial Program can be spread over subsequent years. Every Biennial Program will provide detailed progress of all program activities of previous years, including policy implementation, manufacturer activities and technical assistance activities. The proposed Action Plan is summarized in table 8-1.

Table 8-1 Phase-out Targets and Funding Request from 2007 to 2010 in Action Plan

Line		Baseline (average of 03-05)	2007	2008	2009	2010
1	CFCs Consumption (newly produced CFCs)	485.089	485.089	0	0	0
2	CFCs from Stockpiled CFCs	0	0	1/	1/	1/
3	Total CFCs Consumption	485,089	485.089	0	0	0
Funding Request(US$)						
4	Enterprise-Level Activities[1]		7,693,520		3,509,474	
5	Technical Assistance Activities		1,100,000		0	
6	Support Cost		659,514		263,211	
7	Total MLF Cost		9,453,034		3,772,685	

1/. Use of stockpiled CFCs as needed during the conversion.

1. Biennial Program

1). 2007-2008 Biennial Program: The following activities will be covered under this program:

a Substitute screening. To support manufacturers to identify substitutes for their aerosol products before the first half year of 2007.

b Registration Application. To support the registration for new CFCs-free aerosol products.

c Modification of Existing Facilities, Validation and New Production.

d Workshops, trainings and public awareness promotion.

e Development of a MIS system and other TA activities as necessary.

f Verification on CFCs consumption;

3). 2009-2010 Biennial Program: This will be submitted to the last ExCom meeting of 2008. It will consist of the following, but not limited to:

a Registration Application. To support the registration for new CFCs-free aerosol products.

b Modification of Existing Facilities, Validation and New Production.

c Workshops, Trainings and public awareness promotion.

d Verification on CFCs consumptions, including final verification of all phase out targets under the sector plan.

e Project Completion Report covering all sector plan activities will be prepared.

2. Implementation Schedule

Stage	Activities
Start-up	To complete policy development and substitute screening
Registration Application	To complete registration for new aerosol products. Registration application for new aerosol, if possible, will be initiated in the first year.
Production	To complete modification on the existing facilities, validation for production process and training for staff.
Commissioning	To undertake project commissioning organized by SFDA and attended by SEPA, the World Bank and DIA. All the original record, report and related documents should be retained.

Table 8-2 Implementation Schedule

Year / Process	2007				2008				2009				2010			
	1Q	2Q	3Q	4Q	1Q	2Q	3Q	4Q	1Q	2Q	3Q	4Q	1Q	2Q	3Q	4Q
Start-up	X	X	X	X												
Registration Application	X	X	X	X	X	X	X	X	X	X						
Production	X	X	X	X	X	X	X	X	X	X	X	X				
Acceptance													X	X	X	X

Annex I. Incremental Cost for Pharmaceutical Aerosol Manufacturers

Incremental Cost for Aerosol Producers (USD'000)

Enterp. ID	Enterprise Name	Chinese Share (%)	Line Type	CFCs Baseline (kg)	SA Prodt. Quantity (can)	CA Prodt. Quantity (can)	Incremental Capital					IOC	Subtotal	Adjusted Total
							Substitute Screening	Dossier Preparation	Modification	Validation	Training			
01	Wuxi Shanhe No.1	100%	A, B	823	26,667	0	88	150	102.5	75	35	8.62	459	459
02	Beijing Haiderun Pharmaceutical Co., Ltd	100%	-	0	0	0	131	225	0	0	0	0.00	356	356
03	Guangzhou Baiyunshan Hejigong	100%	-	0	0	0	0	0	0	0	0	0.00	0	0
04	Externally Applied Agent Factory of Guangzhou Baiyunshan	100%	-	0	0	0	0	0	0	0	0	0.00	0	0
05	Guiyang Dechangxiang Pharmaceutical Co., Ltd	100%	A	13	0	100	44	93.75	63.75	37.5	17.5	0.08	256	256
06	Beijing Double-Crane Modern Pharmaceutical Technology Co., Ltd	100%	-	0	0	0	0	0	0	0	0	0.00	0	0
07	Beijing Tongrentang	100%	B	14	0	1,267	131	262.5	38.75	37.5	17.5	1.04	489	489
08	Xinyi Pharmaceutical General Plant	100%	-	0	0	0	131	243.75	0	0	0	0.00	375	375
09	Fujian Nanshaolin	100%	A	10,684	48,571	0	88	150	63.75	37.5	17.5	15.71	372	372

Enterp. ID	Enterprise Name	Chinese Share (%)	Line Type	CFCs Baseline (kg)	SA Prodt. Quantity (can)	CA Prodt. Quantity (can)	Incremental Capital					IOC	Subtotal	Adjusted Total
							Substitute Screening	Dossier Preparation	Modification	Validation	Training			
	Pharmaceutical Co., Ltd													
10	Shanghai Fuxingzhaohui	100%	-	0	0	0	0	0	0	0	0	0.00	0	0
11	Penglai Nuokang Pharmaceutical Co., Ltd	100%	A	3,491	100,600	0	44	75	63.75	37.5	17.5	32.53	270	270
13	Hubei Nanyang Pharmaceutical Co., Ltd	70%	A	49,393	1,171,333	0	44	75	63.75	37.5	17.5	378.77	616	431
14	Shenyang Jingcheng Pharmaceutical Co., Ltd	50%	A	57,717	968,533	0	44	75	63.75	37.5	17.5	313.20	551	275
15	Harbin Hengcang Pharmaceutical Co., Ltd	100%	-	0	0	0	0	0	0	0	0	0.00	0	0
16	Pharmaceutical Plant of Hunan Bencao	100%	B	1,300	58,333	0	44	75	38.75	37.5	17.5	18.86	231	231
17	Shandong Bencao Pharmaceutical Co., Ltd	100%	B	428	0	56,720	88	187.5	38.75	37.5	17.5	46.54	415	415
18	Shandong Jewim Pharmaceutical Co.,	100%	A	12,080	276,314	41,967	131	262.5	63.75	37.5	17.5	123.79	636	636
19	Suizhou Pharmaceutical Co. Ltd.	100%	B	13	700	0	88	150	38.75	37.5	17.5	0.23	331	331
20	Guizhou Antai Pharmaceutical Co., Ltd	100%	A	20,827	580,000	0	88	150	63.75	37.5	17.5	187.56	544	544
21	Guizhou Xinyi	100%	A	229	8,333	0	44	75	63.75	37.5	17.5	2.69	240	240
22	Hangzhou Sino-US	75%	-	0	0	0	0	0	0	0	0	0.00	0	0

Enterp. ID	Enterprise Name	Chinese Share (%)	Line Type	CFCs Baseline (kg)	SA Prodt. Quantity (can)	CA Prodt. Quantity (can)	Incremental Capital					IOC	Subtotal	Adjusted Total
							Substitute Screening	Dossier Preparation	Modification	Validation	Training			
	Huadong													
23	Xinjiang Biochemistry Pharmaceutical Co., Ltd	100%	A	2,592	0	50,000	44	93.75	63.75	37.5	17.5	41.03	297	297
24	Yunnan Baiyao Group Corporation	100%	A	273,333	5,306,667	0	44	75	63.75	37.5	17.5	1716.02	1,954	1,954
25	Chongqing Kerui Pharmaceutical Co., ltd	100%	-	0	0	0	0	0	0	0	0	0.00	0	0
26	Huayi Pharmaceutical Co., Ltd	100%	B	380	0	70,000	44	93.75	38.75	37.5	17.5	57.44	289	289
27	Zhanjiang Xintongde Pharmaceutical Co., Ltd	100%	A	29,397	1,036,667	203,333	306	562.5	63.75	37.5	17.5	502.07	1,490	1,490
28	Heilongjiang Tianlong Pharmaceutical Co., Ltd	100%	A,B	300	0	33,333	0	0	0	0	0	0	0	0
29	Guizhou Hongyu Pharmaceutical Co., Ltd	100%	A	1,230	2,800	74,133	88	168.75	63.75	37.5	17.5	61.73	437	437
31	Guangzhou Dongkang Pharmaceutical Co.	100%	-	0	0	0	0	0	0	0	0	0.00	0	0
32	Shanghai Yishengyuan Pharmaceutical Co., Ltd	100%	B	112	4,845	0	44	75	38.75	37.5	17.5	1.57	214	214
37	Nantong Zhongbao Pharmaceutical Co., Ltd	100%	-	0	0	0	0	0	0	0	0	0.00	0	0
39	Anshan No.1	100%	-	0	0	0	0	0	0	0	0	0.00	0	0

Enterp. ID	Enterprise Name	Chinese Share (%)	Line Type	CFCs Baseline (kg)	SA Prodt. Quantity (can)	CA Prodt. Quantity (can)	Incremental Capital					IOC	Subtotal	Adjusted Total
							Substitute Screening	Dossier Preparation	Modification	Validation	Training			
	Pharmaceutical Plant													
30	Sanpu Pharmaceutical Co., Ltd	100%	-	13	1,700	0	0	0	0	0	0	0	0	0
33	Sanjing Pharmaceutical Co., Ltd of Harbin Pharmaceutical Group	100%	A	145	0	15,210	0	0	0	0	0	0	0	0
34	Hubei Lishizhen Medical Group Co., Ltd	100%	A	137	86,667	0	0	0	0	0	0	0	0	0
35	Shannxi Fengwuchendayaotang	100%	A	48	0	6,000	0	0	0	0	0	0	0	0
36	Harbin Guangji Pharmaceutical Factory	100%	-	0	0	0	0	0	0	0	0	0	0	0
38	Xian Lisheng Pharmaceutical Co., Ltd	100%	-	0	0	0	0	0	0	0	0	0	0	0
12	Glaxo SmithKline (Tianjin)	0%	A	20,390	0	1,216,000	0	0	0	0	0	0	0	0
	Eligible for MLF Fund						**1,794**	**3,319**	**1,100**	**750**	**350**	**3,509**	**10,822**	**10,362**
													Deduction	**-460**