

**MINISTRY OF THE ENVIRONMENT
MINISTRY OF HEALTH**

**Strategy of the Czech Republic for the Phaseout
of Medical Preparations Containing
Chlorofluorocarbons
(MDI - CFCs)**

Implementation of the Provisions of the Montreal Protocol on Substances that
Deplete the Ozone Layer

Basic Document
Prague, May 2001

1. Strategy of the Czech Republic for the Phaseout of Medical Preparations Containing Chlorofluorocarbons (MDI – CFCs) (basic document)

The procedure for limiting and terminating consumption of medical preparations containing CFCs in the Czech Republic will be gradually prepared and implemented in cooperation between the Ministry of Health and the Ministry of the Environment. In the first step, a steering working group (SWG) will be established, which will provide for organization of the preparatory and implementation work. The group will consist of professional workers from both ministries and invited professionals from the relevant area of health care. This working group will be established on the basis of an agreement between the Director of the Department of Pharmacy and Regulation of Medical Substances of the Ministry of Health and the Air Protection Department of the Ministry of the Environment by May 25, 2001.

The steering working group:

- Will establish the most suitable variant for implementation and the timetable for fulfillment. Suitable economic stimuli will be selected. Consideration will be given to the possibility of provision of essential financial support for the initial phase of implementation and specification of the relevant financial sources. Part of the financial means from the State Environmental Fund, obtained from payments for import and production of the regulated substances pursuant to Act No. 86/1995 Coll., on protection of the Ozone Layer of the Earth, can be used for these purposes. SWG will regularly monitor and direct the progress of implementation.
- Will provide for informing the public of commencement of limitation of the use of medical preparations containing CFCs, including organization, conditions and purpose. Professional information will be regularly disclosed in relation to the use of suitable available substitute medical preparations that do not contain CFC substances.
- Will regularly inform the top officials of the two cooperating ministries of the progress in implementation and the results achieved. All important decisions, especially in the area of provision of potential financial support, will be submitted for approval to the relevant ministries. Information will be provided through the Ministry of the Environment to the relevant authorities of the Montreal Protocol and, as required, also the authorities in EU.

1.1. Initial assumptions and general conditions for the further procedure

The European Communities, as the largest global producer of medical preparations in the form of aerosols, has prepared a very detailed strategy for transition from medical preparations containing CFCs to freon-free medical preparations.

The strategy is developed uniformly and in a coordinated manner for all the EU member states and, in the light of the prepared accession of the Czech Republic to EU, it is undoubtedly necessary to take this aspect into account to the maximum degree in developing the procedure to be adopted.

Introduction

The economically developed country Parties to the Montreal Protocol on substances that deplete the Ozone Layer eliminated the production and consumption of a set group of chlorofluorocarbons (CFC substances) as of January 1, 1996. As of the same date, the production, import and export of CFC substances, including products containing these substances, has been prohibited in the Czech Republic pursuant to Act No. 86/1995 Coll., on protection of the Ozone Layer of the Earth.

The Montreal Protocol permits the prohibition of CFC substances not to be implemented in cases of essential provision for protection of human health and lives. This possibility has been applied to medical substances containing CFCs as a propellant. This is particularly true of medical preparations in the form of aerosols for treatment of asthmatics and persons suffering from chronic pulmonary diseases, where the use of CFC as a propellant was irreplaceable until recently.

On the basis of requests by the individual states, the plenary meeting of the Parties to the Montreal Protocol approves special use of CFC substances for basic needs in countries that are Parties to the Montreal Protocol and compliance is monitored by the Secretariat of the Montreal Protocol in Nairobi. The Technical and Economic Advisory Panel to the Montreal Protocol (TEAP) is concerned with the professional aspects of this process; on the basis of trends in science and technology, it recommends the conditions under which and the time for which regulated substances of this group can be used because of lack of suitable replacements.

At the present time, the interest of foremost international pharmaceutical companies is concentrated on accelerated development of suitable replacements for medical preparations containing CFCs (for treating asthmatics and persons suffering from chronic pulmonary diseases). These consist primarily of medical preparations in the form of metered dose inhalers (MDIs), containing hydrofluorocarbons (HFCs) as propellants, i.e. such as HFC-135a (norfluran) or HFC-227. This range of products is supplemented by dose powder inhalers (DPIs), which do not require a propellant.

The authorities responsible for the Montreal Protocol are attempting to gradually decrease consumption and, in the final stage, to eliminate production of medical preparations containing CFCs, with a transition to medical preparations that do not contain CFCs (which can be termed "freon-free medical preparations"). However, it is necessary to reliably provide for protection of the health and lives of patients, who must not be endangered. The transition to the use of new forms of medical preparations (DPI and MDI) should proceed according to a certain coordinated strategy. The eighth meeting of the Parties to the Montreal Protocol, held in 1996 in San José (Costa Rica), thus laid down that the Parties to the agreement, in which medical preparations containing CFCs are produced and used, are to prepare a national strategy to limit such preparations and for transition to the use of freon-free medical preparations. The national strategies are to be submitted to the Secretariat of the Montreal Protocol in Nairobi by the end of 2001.

The Czech Republic is also bound by this decision.

In this process, it is necessary to take the following initial assumptions into consideration:

- The total amount of substances, including substances contained in products, that can be manufactured or imported into the Czech Republic in 2001 for the purposes of providing for protection of human health and lives - for serious cases of pulmonary disease - is equal to 14 tons and is laid down in Decree of the Ministry of the Environment No. 109/2000 Coll.
- The EU strategy is directed towards terminating the production of medical preparations containing CFCs at the site of manufacture within EU and rapid introduction of freon-free medical preparations. Materially, this depends on the local chemical and pharmaceutical industry that manufactures and puts into circulation these medical preparations.
- The transition to freon-free substances is expected to be completed by the year 2003, i.e. prior to the probable accession of this country to EU.
- The EU legislation for decreasing the consumption and terminating production of medical preparations containing CFCs is more consistent than the Czech legislation.

The general conditions for the further procedure in the Czech Republic follow from these facts:

- considerations should be based on the deadline of 2003, when only new medical preparations (freon-free) will be available in EU,
- the legislation should be modified for faster introduction of new medical preparations, as it will no longer be possible to request exemptions and the original medical preparations (containing CFCs) will no longer be available. It will thus be especially necessary to specify which medical preparations with CFCs are currently irreplaceable and how registration of essential medical preparations can be cancelled, etc.,
- preparations containing CFCs in the form of aerosols should be gradually phased out.

Phasing-out can occur under the following conditions:

- medical substances with CFCs containing salbutamol will no longer be considered irreplaceable as soon as two freon-free medical preparations become available from two different manufacturers,
- medical substances with CFCs containing beklomethason will no longer be considered irreplaceable as soon as two freon-free medical preparations become available from two different manufacturers,
- medical substances with CFCs containing some other medical substance will no longer be considered irreplaceable as soon as one freon-free medical preparation with an equally effective substance becomes available.

This approach can be employed for medical preparations in the following individual categories:

- MDI medical preparations with CFCs substances in category A will no longer be considered irreplaceable as soon as two freon-free substances containing salbutamol and one other freon-free substance containing some other active substance become available,
- MDI medical preparations with CFCs substances in category B will no longer be considered irreplaceable as soon as two freon-free substances containing beklomethason

and two other freon-free substances containing various active substances become available,

- MDI medical preparations with CFCs substances in categories C, D and E will no longer be considered irreplaceable as soon as one freon-free substance becomes available for each medical substance, or the status of essential use will no longer apply to the relevant category or medical preparation. Freon-free MDI will not be considered as replacements for both its components until technically suitable and available alternatives become available.

In order for it to be possible to completely eliminate medical substances containing CFCs from circulation, it is necessary to fulfill the following conditions:

- determine basic information on the number of users of medical preparations, the trend in the occurrence of serious pulmonary disease and the necessary range and amount of medical preparations,
- to discuss the freon-free program with insurance companies (consider price advantages for freon-free medical preparations),
- register a sufficient number of equivalent freon-free medical preparations, from the point of view of both the active substance and of dosage,
- provide for a suitable production and distribution capacity for freon-free MDI medical preparations for patient requirements,
- also provide for medical preparations with suitable dosages for groups of patients such as children and seniors,
- the effectiveness and treatment by substitute medical preparations must correspond to the medical preparations containing CFCs,
- provide for a survey of medical preparations in circulation (post marketing surveillance) for the purpose of safety monitoring,
- discuss the freon-free MDI program with the recipients of care (associations of patients).

These measures must be supplemented by an extensive information campaign directed towards health-care workers and patients and essential monitoring and control of imports of medical preparations containing CFCs in the form of aerosols. These activities will be considered by the steering working group, which will lay down the means of implementation and the timetable for fulfillment.

1.2. Basic tasks to be resolved

The Ministry of Health

shall provide conditions:

- a) for preferential prescribing of freon-free medical preparations that are environmentally preferable but more expensive, increasing the costs of medical care,
- b) for ensuring sufficient provision of information for health-care workers on the importance of replacing medical preparations containing CFCs with freon-free medical preparations,
- c) for monitoring and identifying any difficulties in introducing a new medical preparation.

Preliminary deadline: 3 Q. 2001

The Ministry of the Environment

- a) shall provide for conditions for monitoring and control of imports of medical preparations containing CFCs in the form of aerosols, or of the stocks of medical preparations containing CFCs. This consists primarily in cooperation with the customs authorities and obtaining of data from the customs records in the framework of the competence laid down in the draft of the new Act on protection of the air,
- b) shall consider the potential and conditions for provision of financial assistance from the means of the State Environmental Fund in introducing freon-free medical preparations.

Preliminary deadline: 3 Q. 2001

State Institute for Control of Pharmaceuticals

Following specification of exemptions from Act No. 86/1995 Coll. (see point 1), shall prepare proposals for conditions:

- a) for deletion from registration of medical preparations containing CFCs that would no longer correspond to exemption from above mentioned,
- b) for not accepting new applications for registration of medical preparations containing CFCs, to which the exemption does not apply and not accepting new applications for registration of medical preparations to which the exemption applies. This procedure would be used only under the precondition that corresponding medical preparations with propellant not depleting the Ozone Layer of the Earth have already been registered,
- c) for setting a time limit for the use of medical preparations containing CFCs also for treatment of asthmatics and persons suffering from chronic pulmonary diseases in dependence on newly registered, environmentally friendly medical preparations according to the EU scheme (see the Annex).

In order to provide for these requirements, consideration will be given to amendment of Act No. 79/1997 Coll., on medical substances and on amending and supplementing of some laws, as amended.

Preliminary deadline: 4 Q. 2001

Professional associations of health-care workers, associations of patients

shall provide for:

- a) information dissemination on transition to new medical preparations, explaining that this approach is necessary,
- b) explaining to patients the reasons for the new changes and pointing out that the safety and effectiveness is identical with the originally used medical preparations, emphasizing that

any changes in the appearance, taste, smell and other properties of the medical preparation are not related to a decrease in its quality.

Preliminary deadline: 4 Q. 2001

Producers and distributors of medical preparations

Will prepare suitable information materials, in particular for the professional periodical and nonperiodical press.

Preliminary deadline: 3 Q. 2001

1.3. Personnel requirements

This aspect will be the responsibility of existing employees of the above organizations. It will be necessary to utilize a specialized agency only for an information campaign. Similarly, a specialized agency can be employed if required for obtaining and processing the monitored data.

1.4. Financial requirements

Finances will be required not only for the information and public awareness campaign, preliminarily estimated at about 0.5 to 1 mil. CZK, but also for transition to treatment with new freon-free medical preparations.

2. Current conditions in the Czech Republic

2.1. Production of medical preparations containing CFCs in the Czech Republic

In 1986, the use of CFCs was considerable for the production of medical preparations in the Galena Opava and Dental Praha companies - a total of about 750 tons. The production of these medical preparations is gradually decreasing. Between 1993 and 1996, the only manufacturer was Galena Opava. The consumption of CFCs for these purposes in 1993 - 1994 equaled about 100 tons p.a., which decreased to about 70 tons in 1995. On the basis of an exemption provided by Act No. 86/1995 Coll., the Galena Opava company was granted exemptions for about 60 tons of CFCs in 1996 in connection with the relevant medical preparations. This limit was not fully used and the actual consumption of CFCs equaled only 42 tons in 1996. In 1997, production was stopped at this sole manufacturer. The consumption of these medical preparations in the Czech Republic is covered to the present time solely through imports, which are gradually decreasing. Imports are limited by the implementing Decree to Act No. 86/1995 Coll., on protection of the Ozone Layer of the Earth. The limit equaled 61 tons for 1998, 50 tons for 1999 and 28 tons for 2000.

2.2 Provision for requirements for medical preparations for treating asthma and chronic pulmonary diseases in the Czech Republic and the present legislation

Requirements for medical preparations in the Czech Republic are met by imports both from the countries of the European Union (EU) and from other countries, whose manufacturers have preparations registered in the Czech Republic.

This approach is made possible by the provisions of § 4 par. 6 letter b) of Act No. 86/1995 Coll., according to which the prohibition of production and import does not apply to products containing CFCs essential for providing for the protection of human health and lives.

The permitted consumption of CFCs for these purposes is laid down for the individual years in a Decree of the Ministry of the Environment. In contrast to EU, however, no legal regulation specifically names the individual products (here medical preparations), that are permitted for reasons of essential provision for protection of human health and lives. This aspect is left to the Ministry of Health to decide in specific cases. The import of medical preparations to provide for this consumption is possible only on the basis of a permit issued by the Ministry of the Environment under the conditions of a favorable standpoint of the Ministry of Health.

In the EU, legislation pursuant to Regulation of the European Parliament and Council (EU) No. 2037/2000, that replaced Council Regulation (EU) No. 3093/94, this exemption applies only to medical preparations in the form of aerosols for treating asthma and chronic pulmonary diseases. In the Czech Republic in recent years, a somewhat different procedure has been followed, as this exemption has also been employed for the use of medical preparations externally in dermatology. An example is the use of CFC-12, corresponding to about 5.4 t in 1998, more than 10% of which (0.68 t) was used in the manufacture of the medical preparation Triamcinolin (dermatologicum). The use of this type of medical preparation is considered to be nonessential in the EU countries. This aspect has been incorporated in the Czech legislation through a Decree dealing with the consumption of medical preparations only for the purposes of serious pulmonary diseases after the year 2000.

In contrast to the European legislation, the legislation valid in the Czech Republic (Act No. 86/1995 Coll., and its Decree for implementation, issued pursuant to § 5 par. 8 of this Act No. 109/2000 Coll., valid for period 2000 to 2002) does not contain any further specification as to which medical preparations containing CFCs are specifically permitted for the purpose of providing for essential uses in 2000 to 2002, in the framework of providing for the protection of human health and lives. It should be pointed out in relation to intervention in the process of registration of medical preparations containing CFCs (not prolonging registration, not accepting new applications for registration of medical preparations containing CFCs, etc.) that the relevant legal regulation, i.e. Act No. 79/1997 Coll., on medical preparations and amending and supplementing some other laws, does not currently permit such an approach.

Replacements for medical preparations containing CFCs are gradually being introduced in the Czech Republic. DPI have been registered for treating asthma and chronic pulmonary diseases; 1 medical preparation is currently registered containing propellant HFC 134, containing the active substance salbutamol, together with 1 medical preparation in three various concentrations containing the active substance flutikason. In addition, medical

preparations containing salbutamol, beklomethason and fenoterol are currently in the registration procedure

3. EU Strategy (according to the document COM/1998/603 final)

3.1. Principles of the procedure

EU is the largest global manufacturer of medical preparations in the form of aerosols (50% of global production). 25% of the production of these medical preparations in EU is exported. Thus, it has a special responsibility for the development and introduction of replacements for medical preparations containing CFCs. The transition strategy has been developed as a whole for the entire EU. Its main principles can be summarized in the following points:

- To provide for the currently essential medical preparations containing CFCs, EU submits an application every year for permitting their production to the Secretariat of the Montreal Protocol, jointly for all its member states. Every year, EU specifies the essential indications for which medical preparations containing CFCs are to be permitted, the manufacturer of these medical preparations and the requested amount of CFC substances (in practice this applies only to medical preparations for treating asthma and chronic pulmonary disease).
- It is considered absolutely essential to phase-out medical preparations containing CFCs and it is expected that they will be completely eliminated in provision of health care by the end of the year 2003. Mainly DPI and medical preparations in the form of aerosols with propellants based on HFC substances are to replace these products.
- Prior to putting new freon-free medical preparations, it is necessary to obtain approval (registration) from the relevant authorities. Registration is a relatively long process that must be accelerated as much as possible. Thus, it is proposed that the manufacturers of these medical preparations submit an application for their registration jointly for the entire EU, that the member states cooperate in making decisions on registration, and that new medical preparations be registered for all the EU member states simultaneously.
- The health and safety of patients must not be endangered. Medical substances containing CFCs will thus be available in EU 12 months after introduction of medical preparations not containing CFCs (freon-free).
- Any difficulties that appear in the use of freon-free medical preparations will be evaluated and resolved as rapidly as possible. They must be resolved to the time of definitive withdrawal of preparations containing CFCs from circulation.
- Studies will be made of the safety of freon-free medical preparations by the holder of the registration decision. On the basis of clinical evaluation, they will compare freon-free medical preparations and medical preparations containing CFCs.
- The manufacturer will provide for professional information activities for medical doctors, pharmacists and patients, related to freon-free medical preparations.
- EU will submit information to the Secretariat of the Montreal Protocol, in which it will annually state the medical preparations for which the use of CFCs is still essential and where CFCs have been replaced.

3.2. The EU system in replacing medical preparations containing CFCs

The category of medical preparations for treating asthmatics and persons suffering from chronic pulmonary diseases, where medical preparations containing CFCs are still used:

A. *short-action bronchodilatancia* - e.g. salbutamol, terbutalin, fenoterol

B. *steroid hormones* - e.g. beklomethason, budesonit, flutikason

C. *nonsteroid antiophlogistica* - e.g. disodium chromoglycan, nedocromil

D. *anticholinergic bronchodilatancia* - e.g. ipratropin, oxytropin

E. *prolonged-action bronchodilatancia* - e.g. salmeterol, fomoterol

F. *combined preparations*.

About 80% of medical preparations containing CFCs fall in categories A and B. The forecast for ending their availability is given in the table in Annex A (planned deadline according to information from manufacturers).

It can be stated that freon-free medical preparations are already available at the present time.

Phasing-out of medical preparations containing CFCs from use in health care

According to EU, in phasing out these preparations, the following general procedures should be followed, consisting particularly in providing for:

- a technically and economically feasible alternative,
- a sufficient number of freon-free medical preparations both from the standpoint of the active substance and from the standpoint of dosage,
- supervision of new (reformulated) medical preparations after introduction into circulation,
- adequate informing of health-care workers and patients,
- participation of the manufacturers of medical preparations containing CFCs in the development of freon-free medical preparations,
- registration of new freon-free medical preparations concurrently with phasing-out of medical preparations containing CFCs.

The use of HFC substances requires a new composition of the medical preparation; HFC substances are not compatible with the auxiliary substances and elastomers of the dosage valves in the preparations used to date. In DPIs, there can be a change in the size of the inhaled particles that, together with a change in the time regime of supply of the particles to the respiratory tract, can lead to a different distribution of the active substance, different availability and different clinical properties of the medical preparation. Thus, during the registration process for a new medical preparation, it must be demonstrated that it is of high quality, safe and effective. As medical preparations containing CFCs are used by a large number of patients, they cannot be withdrawn from circulation before adequate replacement is ensured. It is expected that both medical preparations containing CFCs and freon-free preparations will be available for a period of about 12 months.

There are several possible approaches in the specific procedure for the introduction of freon-free medical preparations:

- phase out the individual types of freons, where, in introducing the new medical preparation, the manufacturer phases out the original medical preparation according to a certain timetable,
- phase out the individual types of freons contained in medical preparations with the same active substance, i.e. if a freon-free substance containing a certain active substance is in circulation, all similar medical preparations containing CFCs with the same active substance will be withdrawn from circulation,
- phase-out the individual types of medical preparations containing CFCs in the above categories, i.e. so that medical preparations containing CFCs can be phased out after a sufficient number of freon-free medical preparations become available,
- phase-out medical preparations containing CFCs according to targets and timetables; e.g. annually decrease the amounts of CFCs used in the production of medical preparations.

It seems advantageous to employ a strategy in based on determination of the actual availability of freon-free medical preparations, where such a preparation need not be identical - active substance - with the medical preparation containing the CFC substance. It would seem optimum to proceed one category at a time.

Technical and economically suitable alternatives and their introduction:

The strategy must also select criteria as to whether a certain alternative is technically and economically feasible and whether a medical preparation containing CFCs can be withdrawn from circulation. The criteria are given in Table B of the Annex. Withdrawal of medical preparations containing CFCs from circulation requires a transition period of 12 months.

In this strategy, there is a certain danger that the manufacturers of medical preparations containing CFCs in the form of aerosols with official seat outside of EU will fill the gap in the market and import these preparations to EU. Thus it is necessary to introduce a system of monitoring the remaining stocks of freons, medical preparations containing CFCs and their import. Imports may be permitted only for medical preparations that fulfill the condition of essential use.

Information and public awareness campaign in the transition to freon-free medical preparations:

The choice of a medical preparation is made by the medical doctor. Consequently, it is very important to provide doctors with information and cooperation in gradual phasing-out the use of medical preparations containing CFCs in the transition period.

Underestimation of this aspect was manifested, e.g. for the medical preparation in the form of an aerosol containing salbutamol and HFC as a propellant, that was registered in EU 4 years ago. In 1998, the consumption of this substance corresponded to only 1.5% of the total consumption of MDI, demonstrably because of lack of information for patients, lack of interest on the part of doctors and its higher price.

To increase information levels, it will be necessary to adopt measures:

- at the level of the state administration (provided for by the Ministry of Health),
- at the level of health-care workers and patients - professional information texts and professional symposia for health-care workers, material of professional medical societies, including pharmaceutical societies, workshops at schools and the influence of the mass media on patients can all be used for this purpose,
- at the level of the manufacturers of medical preparations, professional information materials, sponsoring of medical symposia, organization of informative events for patients, etc.

The manufacturers of medical preparations in EU should also influence their customers in third countries to which they export their medical preparations, in support of the fastest possible registration and introduction of new medical preparations into circulation (i.e. including the Czech Republic).

Forecast for terminating the availability of CFCs in the EU

Active substance	First specified date for administration	Last specified date for administration	When the product will probably lose the status of "essential use"*)
salbutamol	1994	2001	1998-1999
terbutalin	2000	2004	2001-2002
fenoterol	1998	2002	1999-2000
beklomethason	1996	2002	1999-2000
budesonid	2000	2002	2001-2002
chromoglyc. acid	1998	1999	1999-2000
ipratropium bromide	1999	2000	2000-2001

**) the period of time during which freons in a certain medical preparation will probably lose their status of "essential use" in some or all EU member states according to the provisions of this strategy, unless there is a disproportionate delay in registration and bringing into circulation of freon-free preparations*

Category A		
Beta agonist bronchodilatancia with short-term action		
Preparation	<i>number of alternatives</i>	<i>number of manufacturers</i>
salbutamol*	2 freon-free preparations	2 different manufacturers
terbutalin*	Preparations with CFCs for all of category A will not longer be considered essential when 2 alternative salbutamol preparations, manufactured by 2 different manufacturers, PLUS 1 other preparation, defined by this strategy as essential, become available . These preparations will thus be replaced by at least three freon-free medical preparations in the form of aerosols (two salbutamol and one other).	
Klenbuterol		
Fenoterol* bitolterol		
Orciprenalin prokaterol		
Reproterol		
Karbuterol		
Hexoprenalin		
Pirbuterol		

Category B		
Steroid hormones		
Preparation	<i>number of alternatives</i>	<i>number of manufacturers</i>
Beklomethason*	2 freon-free beklomethason preparation	2 different manufacturers
Dexamethason	Preparations with CFCs for all of category B will not longer be considered essential when 2 alternative beklomethason preparations, manufactured by 2 different manufacturers, PLUS 2 other preparations containing different active substances, defined by this strategy as essential, become available. These preparations will thus be replaced by at least four freon-free medical preparations in the form of aerosols (two beklomethason and two other preparations).	
flunisolid		
flutikason*		
budesonid*		

Category C Nonsteroid antiphlogistic substances	
<i>disodium chromoglycan*</i> <i>nedokromil*</i> <i>Note:</i> <i>Both these preparations are considered essential in some member states</i>	Preparations with CFCs for both medical preparations in category C will not longer be considered essential when 1 alternative freon-free preparation replacing one of the current freon preparations becomes available. Thus two freon preparations will be replaced by at least one freon-free preparation, unless both preparations are considered essential.
Category D Anticholinergic bronchodilatancia	
<i>ipratropium bromide</i> <i>oxytropium bromide</i>	Preparations with CFCs or both medical preparations in category D will no longer be considered essential when 1 alternative freon-free preparation, that replaces one of the two current medical preparations containing CFCs, becomes available.
Category E Beta agonist bronchodilatancia with long-term action	
<i>salmeterol*</i> <i>formoterol*</i> <i>Note:</i> <i>Both these preparations are considered essential in some member states</i>	Preparations with CFCs for both medical preparations in category E will not longer be considered essential when 1 alternative freon-free preparation becomes available to replace one of the two current preparations containing CFCs. Two preparations in category E will thus be replaced by at least one freon-free medical preparation except for cases where both preparations will be considered essential
Category F Combined preparations	
	Combined preparations will be dealt with separately in each individual case. Combined preparations containing CFCs will not longer be considered essential when freon-free preparations become available for each separate active substance in the given combination.

* the asterisks denote medical preparations that are considered essential for the purposes of this strategy in one or more EU member states.