

# **OUTLINE OF THE JAPANESE INITIAL TRANSITION STRATEGY FOR THE PHASE-OUT OF CHLOROFLUOROCARBON (CFC) USE IN METERED DOSE INHALERS (MDIs)**

December, 1998

## **1. BACKGROUND**

1.1. The manufacture of CFCs used for MDIs had been discontinued in Japan. The amount of CFCs used as essential use exemption for MDI production is being reduced in stages.

1.2 It is estimated that about 400,000 patients are using MDIs for the treatment of asthma and chronic obstructive pulmonary disease(COPD) in Japan.

1.3 One non-CFC alternative MDI is now on the market in Japan, another alternative has been approved and two other alternatives are in the reviewing process by the Government. Research and development of non-CFC alternatives to other existing CFC MDIs is being pursued by the pharmaceutical industry. In addition to this, one non-CFC product containing new drug substance has been launched, and other two are in reviewing process.

1.4 The degree of transition to non-CFC alternatives in Japan depends highly on the success of these alternatives in the countries which are developing them. About 40% of CFC MDIs sold in Japan are imported, and about 40% are manufactured in Japan under the license of foreign companies.

## **2. DEVELOPMENT OF non-CFC ALTERNATIVES**

2.1 It is expected that about 95% of existing CFC MDIs sold in Japan will be replaced by those of non-CFC alternatives by the year 2005, taking the development status of the alternative products into consideration.

2.2 The prospective situation of the transition of the remaining about 5% of CFC MDIs to alternatives is recognized to be unclear.

## **3. TIMEFRAME OF TRANSITION**

The timeframe of transition to non-CFC alternatives is as follows;

3.1 Major part of research and development activities to develop non-CFC alternatives is projected to be completed by the year 2000.

3.2 Major part of non-CFC alternatives are to be marketed by the year 2003. The Government will verify the schedule for development and transition to non-CFC alternatives, if such alternatives are not on the market at this time.

3.3 The manufacturing and importing of CFC MDIs will, in principle, be discontinued by the year 2005.

#### **4. MECHANISMS OF TRANSITION**

4.1 As the number of generic drugs in Japan is few and taking the development situation of non-CFC alternatives into consideration, it is anticipated that the brand-by-brand rule for the transition to non-CFC MDIs is likely to be acceptable in Japan.

4.2 The Government will encourage companies to transfer the supply of CFC MDIs to their non-CFC alternatives by the year 2005 when the manufacturing and importing of CFC MDIs will in principle be discontinued.

4.3 If a company does not succeed in developing the non-CFC alternative to a CFC MDI, the Government will make a decision at an appropriate time before 2005 as to whether or not the manufacturing or importing of the particular CFC MDI is to be permitted.

4.4 For the exceptional cases where the CFC MDI contains a medically important chemical moiety which has been unable to be reformulated as an alternative, or where the complete transition to the alternative is considered to be inappropriate due to patient safety concerns, the Government will consider whether continuing supply of such CFC MDI for a limited period beyond the year 2005 is necessary.

#### **5. PRODUCT REVIEW AND APPROVAL**

5.1 The Government will review the license applications of non-CFC alternatives as promptly as possible.

5.2 If a non-CFC alternative contains the same dosage of the same drug substance under the same administration route as the existing CFC MDI, specified parts of the documents required for the application can be omitted. Data and documents originating in foreign countries can also be used for license application.

5.3 The standard processing time in the above case is expected to be 12 months.

5.4 The Government will encourage companies not to submit new CFC MDIs applications.

## **6. SAFETY OF PATIENTS AND PENETRATION OF ALTERNATIVES**

6.1 The transition to non-CFC alternatives is to be pursued while paying due attention to the safety of patients and acceptance by physicians and patients. The Government will encourage the companies which manufacture or import alternatives to conduct sufficient post-marketing surveillance.

6.2 As it is anticipated that the variety of non-CFC alternative products put on the Japanese market will be limited, the Government must take a good care in phasing-out CFC MDIs.

## **7. INFORMATION FOR HEALTH PROFESSIONALS AND PATIENTS**

7.1 The Government will encourage companies, in consultation with medical community, to inform health professionals of the status of transition to non-CFC alternatives and to bring forth sound understanding on the alternative products. The Government will make efforts in circulating appropriate information to both companies and health professionals.

7.2 The Government will encourage companies to provide health professionals with information on the transition such that patients can understand the alternatives well. The Government will make efforts in providing relevant information to the parties concerned.

## **8. LABELING**

Since both CFC MDIs and non-CFC MDIs may be on the market during a certain limited term of the transition processes, the Government is considering measures for labeling to distinguish these products from each other.

## **9. ADVERTISING**

Whilst the advertising of ethical drugs is regulated with respect to target and contents in Japan, the Government will encourage companies not to engage in false or misleading advertising for or against either non-CFC alternatives or CFC MDIs.

## **10. PRICING**

The price of ethical drugs for reimbursement is determined officially in Japan.

## **11. REDUCTION OF EMISSION OF CFCs**

The Government will encourage companies to minimize the emissions of CFCs from CFC MDI

manufacturing plants. The Government will urge companies to investigate the measure for recovery and destruction of CFCs from expired, defective, and returned MDIs to minimize CFC emissions from MDI use.

## **12. INTERNATIONAL COOPERATION**

12.1 Since the majority of MDI products marketed in Japan are either imported from or manufactured under the license of foreign companies, and therefore Japan is greatly dependent on these foreign companies in introducing non-CFC alternatives, the Government are anticipating the overseas development of the alternatives and will encourage domestic companies to introduce the alternatives without delay after their successful development abroad.

12.2 The Government will encourage domestic companies to explain the Japanese transition strategies to MDI exporting or licensing companies abroad.