NOTIFICATION UNDER ARTICLE 2.6.1

The following notification, received from the delegation of Japan, is being circulated in accordance with Article 10.4.

80.12.1(a) Provision: Adoption of a technical regulation (2.6.1).

(b) Party:

The Evaluation and Registration Division and the Biologics and Antibiotics Division, Pharmaceutical Affairs Bureau of the Ministry of Health and Welfare. (Address: 1-2, Kasumigaseki, Chiyoda-ku, Tokyo. Tel: 03-501-4876, 03-501-2052).

(c) Pharmaceutical products.

(d) Objective and rationale:

Simplification of the administrative procedure for examination of new pharmaceutical products for which approval is sought.

Under the amendment, results of the stability test conducted by a relevant body of a foreign country concerned may be accepted by the Japanese Government as data in conducting the examination.

(e) Statement:

Amendment to the regulation on the stability test for new drugs which is required in making application for approval of their manufacture or import. (For further details, see Annex below).

The amendment was put into effect on 1 April 1980.

Annex to 80.12.1

Notification by the Director-General of the Pharmaceutical Affairs Bureau of the Ministry of Health and Welfare on the New Regulation concerning the Stability Test for New Drugs

1. The stability test (hereinafter called "test") shall be carried out in a well-equipped laboratory by experienced researchers in accordance with the standards given below. (*)
The test data submitted in application for approval must be accompanied with the following information:

1. Name and location of the institute which conducted the test, date of the establishment of the institute, the institute's parent body and its organizational structure, and an outline of the facilities of the institute (types, etc.).

2. Personal history and record of experiences in research work of all researchers who conducted the test.

2. All test data must be written in Japan. If the material is translated from a foreign language, a total translation must be submitted as well as the original. It is also required to give the name, title and qualification of the translator and the expert technician who finally checked the translation.

3. In submitting a report prepared on the basis of the results of a test conducted overseas, the test must have been carried out in accordance with the relevant required standards of the Japanese Government.

   New drugs which are submitted for import approval accompanied by data from tests carried out overseas must have already been given approval or permission overseas. In such case, complete data of the stability test on the basis of which the approval of that product was granted by the government of the country of origin must be submitted, together with a certificate of the competent authority of that Government stating that the approval was granted as a result of the examination of such test data.

4. All the records relating to the test must be kept for at least five years after the Japanese Government's approval for manufacture (import) of the product.
1. Stability test (hereinafter called "test") for new drugs shall be conducted in accordance with the following:

   (1) The test should be "long-term stability test" and "accelerated stability test", as provided for, respectively, in 2 and 3 hereunder.

   (2) The long-term stability test should be conducted according to either "A" or "B" method described below:

   (i) In using "A" method, storage conditions (temperature, humidity, etc.) during the test shall be recorded and mentioned in the report of the results of the test. If the preservation conditions are judged to differ extremely from the normal climate conditions in Japan, the results of the test conducted under such climate conditions shall not be adopted.

   (ii) When "A" method is employed, if a special condition or a period for expiration is set for storage, it is required, in all such cases, to indicate the ground for the setting of such condition or period.

   (iii) Where approval for manufacture (or import) was granted in respect of a new product on the basis of the results of the test conducted using "B" method, confirmation of the stability of the product shall be performed by means of "A" method for the purpose of quality control after the starting of manufacture or import.

2. Long-term stability test.

   (1) Objective

       To ensure the quality of a new drug during a certain specific period when it is on the market.

   (2) Test procedure, etc.

       (i) "A" method

           Sample: Final product. (When the product to be tested contains a new active ingredient, the substance as well shall be subject to the test.)
Number of lots to be tested: Three

Condition for storage: Room temperature. (If a special storage condition is stated in the application for government approval, the test shall be conducted under such condition.)

Test period: Three years or more. (If the period for expiration is stated in the application, the test period shall be that period or longer than that.)

Measurement dates: Initially, at the time of the starting of the test and, subsequently, at intervals of not more than six months.

Measurement items: Items which are considered to require checking from the viewpoint of quality control.

Measurement times per testing: Three times. However, the times may be reduced depending on the accuracy of the measurement method to be employed and measuremental variation of individual characteristics of the product to be tested.

(ii) "B" method.

Sample: Same as "A" method.

Number of lots to be tested. Same as "A" method.

Condition for storage: 25°C (+ 1°C) 75% R.H. (+ 5%)

Test period: Two years.

Measurement dates: Initially, at the time of the starting of the test, and subsequently, each after the elapse of 3, 6, 9, 12, 18 and 24 months.

Measurement items: Same as "A" method.

Measurement times per testing: Same as "A" method.

3. Accelerated stability test.

(1) Objective

To estimate the stability of the product at room temperature, and investigate decomposed products.
(2) Test conditions

(i) Test conditions shall be fixed, taking into consideration the three factors: light, temperature, humidity. As for the substance, the test in aqueous solution must be included as a rule.

(ii) Identification of decomposed products shall be carried out, and, with regard to principal decomposed products, they shall be subjected to both toxicological examination and examination on pharmacological actions.

(iii) Examination for confirming the absence of any decomposed products shall be conducted by means of chromatography under no less than three different conditions or by means of any other suitable methods.

4. This regulation shall apply with regard to applications submitted on 1 April 1980 or thereafter, for government approval of manufacture or import of pharmaceutical products. However, in principle, the old regulation may be applied with regard to applications submitted before 1 April 1981.