Commission communication on the implementation of the new marketing authorization procedures for medicinal products for human and veterinary use in accordance with Council Regulation (EEC) No 2309/93 of 22 July 1993 and Council Directives 93/39/EEC, 93/40/EEC and 93/41/EEC, adopted on 14 June 1993

(94/C 82/04)

In 1993, on a proposal from the Commission, the Council adopted four texts establishing two types of procedure (centralized and decentralized) for authorizing the marketing of medicinal products in the Community. These were [1]:

— Regulation (EEC) No 2309/93 of 22 July laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products,

— Directive 93/39/EEC of 14 June 1993 amending Directives 65/65/EEC, 75/318/EEC and 75/319/EEC in respect of medicinal products,

— Directive 93/40/EEC of 14 June 1993 amending Directives 81/851/EEC and 81/852/EEC on the approximation of the laws of the Member States relating to veterinary medicinal products,

— Directive 93/41/EEC of 14 June 1993 repealing Directive 87/22/EEC on the approximation of national measures relating to the placing on the market of high-technology medicinal products, particularly those derived from biotechnology.

This new framework encompasses everything except the homeopathic medicinal products covered by Article 9 (2) of Council Directive 92/73/EEC (medicinal products for human use) [2] and Article 9 (2) of Council Directive 92/74/EEC (medicinal products for veterinary use) [3].

To facilitate the implementation of these acts, the Commission wishes to pass on the following information to the interested parties:

A. Medicinal products for human and veterinary use subject to the centralized procedure for marketing authorization

1. The practical scope of Regulation (EEC) No 2309/93 is defined in the Annex thereto. This comprises two parts:

Part A, listing medicinal products which are automatically subject to the centralized (Community) marketing authorization procedure set up by the Regulation.

Part B, listing medicinal products to which the centralized procedure may be applied at the request of the person responsible for placing on the market.

Moreover, Article 3 (3) and (4) of the Regulation lays down that before the Regulation enters into force and after consultation of the Committee for Proprietary Medicinal Products or the Committee for Veterinary Medicinal Products, as appropriate, Parts A and B of the Annex must be examined 'in the light of scientific and technical progress with a view to making any amendments necessary'.

2. Having carried out the necessary consultations, the Commission does not feel that there has been any technical and/or scientific progress since the Council adopted these texts such as would necessitate a review of Parts A and B. However, it would point out to all the parties affected by the implementation of this Regulation that the following medicinal products must be deemed to be covered by Part A:

The definition of medicinal products developed by means of recombinant DNA technology must be deemed to include products intended for gene therapy.

The products covered by Part A also include vaccines from strains developed by means of recombinant DNA technology, including gene deletion.

Any medicinal product for which a monoclonal antibody is used at any stage in the manufacturing process.

B. Transitional measures for the implementation of the new marketing authorization procedures

1. The centralized Community procedure laid down by Regulation (EEC) No 2309/93 for the marketing authorization of medicinal products will apply from 1 January 1995. New applications will then no longer be subject to the procedure laid down by Council Directive 87/22/EEC [4], which will be repealed on the same date by Directive 93/41/EEC.

In addition, the provisions of Council Directives 93/39/EEC (medicinal products for human use) and

[1] OJ No L 214, 24. 8. 1993, p. 1, 22, 31 and 40 respectively.

[2] Council Directive 92/73/EEC of 22 September 1992 widening the scope of Directives 65/65/EEC and 75/319/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to medicinal products and laying down additional provisions on homeopathic medicinal products (OJ No L 297, 13. 10. 1992, p. 8).

[3] Council Directive 92/74/EEC of 22 September 1992 widening the scope of Directive 81/851/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to veterinary medicinal products and laying down additional provisions on homeopathic veterinary medicinal products (OJ No L 297, 13. 10. 1992, p. 12).

[4] OJ No L 15, 17. 1. 1987, p. 38.

93/40/EEC (medicinal products for veterinary use) will enter into force on 1 January 1995 replacing the earlier provisions laid down by the current texts of Directives 65/65/EEC (1), 75/318/EEC (2), 75/319/EEC (3) (medicinal products for human use) and 81/851/EEC (4) and 81/852/EEC (5) (medicinal products for veterinary use).

In the interest of a smooth switch from one procedural system to another, the Commission, having consulted the Committee for Proprietary Medicinal Products and the Committee for Veterinary Medicinal Products, feels it would be useful to recall or recommend the following measures:

Implementation of the decentralized procedure

2. Article 3 of Directive 65/65/EEC, as amended by Directive 93/39/EEC, and Article 4 (1) of Directive 81/851/EEC, as amended by Directive 93/40/EEC, dealing with medicinal products for human and veterinary use respectively, replace the current 'multi-state' procedure with a decentralized procedure. Within this new framework, applications for authorization to place medicinal products on the market will fall within the scope of one of the following Articles:

   — Article 9 (1) of Directive 75/319/EEC, as amended by Directive 93/39/EEC, which lays down that 'In order to obtain the recognition according to the procedures laid down in this chapter in one or more of the Member States of an authorization issued by a Member State in accordance with Article 3 of Directive 65/65/EEC, the holder of the authorization shall submit an application to the competent authorities of the Member State or Member States concerned ...'

   — Article 7 (2) of Directive 65/65/EEC, as amended by Directive 93/39/EEC, or Article 8 (2) of Directive 81/851/EEC, as amended by Directive 93/40/EEC, which lays down that 'Where a Member State notes that an application for authorization submitted after 1 January 1995 is already under active examination in another Member State in respect of that medicinal product, the Member State concerned may decide to suspend the detailed examination of the application in order to await the assessment report prepared by the other Member State ...'

   — Article 11 of Directive 75/319/EEC, as amended by Directive 93/39/EEC, or Article 19 of Directive 81/851/EEC, as amended by Directive 93/40/EEC, which lays down that 'If several applications ... have been made for marketing authorization for a particular medicinal product and Member States have adopted divergent decisions concerning the authorization of the medicinal product or its suspension or withdrawal from the market, a Member State, or the Commission, or the person responsible for placing the medicinal product on the market may refer the matter to the Committee for application of the procedure (to obtain a Community decision).';

   — Article 12 of Directive 75/319/EEC, as amended by Directive 93/39/EEC, or Article 20 of Directive 81/851/EEC, as amended by Directive 93/40/EEC, which lays down that 'The Member States or the Commission or the applicant or holder of the marketing authorization may, in specific cases where the interests of the Community are involved, refer the matter to the Committee for the application of the procedure (to obtain a Community decision).'.

3. On 1 January 1995 an inventory will be made of applications for authorization submitted before that date which come under the 'multi-state' procedure and for which the competent Committee for medicinal products has not delivered an opinion. Management of pending dossiers wil be entrusted to the Agency in order that any current application proceedings may be completed. Opinions finally delivered at this point will, however, still be deemed to be covered by the 'multi-state' procedure, and therefore not binding. Member States will have to give notice of the action taken on this opinion within 60 days, as laid down in the relevant Community rules.

Details of the transition from the conciliation procedure to the centralized procedure

4. In accordance with Article 2 of Directive 93/41/EEC, 'Applications for marketing authorizations which have been referred to the Committee for Proprietary Medicinal products or to the Committee for Veterinary Medicinal products before 1 January 1995 in accordance with Article 2 of Directive 87/22/EEC and in respect of which the Committee concerned has not given an opinion by 1 January 1995 shall be considered in accordance with Regulation (EEC) No 2309/93.'

A number of practical measures will be needed to ensure a smooth transition. From an operational point of view, the Commission will recommend the following two measures to the European Agency for the Evaluation of Medicinal Products, which will be ultimately responsible for organizing the evaluation work.

(1) OJ No L 22, 9. 2. 1965, p. 369. Directive last amended by Directive 92/27/EEC (OJ No L 113, 30. 4. 1992, p. 8).

(2) OJ No L 147, 9. 6. 1975, p. 1. Directive last amended by Directive 91/507/EEC (OJ No L 270, 26. 9. 1991, p. 32).

(3) OJ No L 147, 9. 6. 1975, p. 13. Directive last amended by Directive 92/27/EEC (OJ No L 113, 30. 4. 1992, p. 8).

(4) OJ No L 317, 6. 11. 1981, p. 1. Directive last amended by Directive 90/676/EEC (OJ No L 373, 31. 12. 1990, p. 15).

(5) OJ No L 317, 6. 11. 1981, p. 16. Directive last amended by Directive 92/18/EEC (OJ No L 97, 10. 4. 1992, p. 1).

— Under the current conciliation procedure, applicants for marketing authorization select a Member State, which acts as rapporteur. Depending on the stage reached in the procedure, this rapporteur may by 1 January 1995 have already drawn up an evaluation report or prepared a draft opinion for the relevant committee on medicinal products. In order that due account may be taken of such applications during the transition to the centralized procedure, the Commission will recommend to the Agency that the role of rapporteur be assumed by a member of the Committee belonging to the competent authority of the Member State which previously fulfilled that role.

— In the same spirit, the Commission will recommend to the Agency that work by previous rapporteurs and committees to evaluate a medicinal product should remain usable and valid under the new procedure. To facilitate the use of earlier evaluation dossiers, the working methods of the committees which meet during 1994 will need to be adapted to the new procedural framework.

5. The Commission would also stress that pharmaceutical companies could facilitate the transition from one procedure to another by ensuring that authorization applications are sent to all the Member States in accordance with the conciliation procedure. If this is not done, committee members who are not involved under the conciliation procedure could raise new queries under the centralized procedure or even ask that a new evaluation be carried out.

   In addition, the Community rules lay down that examination of an application for marketing authorization under the conciliation procedure should not exceed 210 days, not including any postponed deadlines. In view of the likely timetable of meetings of the relevant committees for medicinal products in 1994, the Commission would draw the attention of the pharmaceutical companies to the fact that applications submitted after 1 May 1994 will probably receive an opinion under the centralized procedure in accordance with Article 2 of Directive 93/41/EEC. (The exact address of the Agency in London will be supplied to the companies concerned as soon as possible.)

   Cases involving the switch from the conciliation procedure to the decentralized procedure

6. National marketing authorization has been granted to medicinal products indicated in Lists A and B of the Annex to Directive 87/22/EEC for which a favourable opinion has been delivered before 1 January 1995 by the relevant committee for medicinal products. However, these medicinal products have been subject to a Community procedure designed to produce harmonized national decisions. To maintain the necessary harmonization in the event of applications to vary the terms of this type of marketing authorization, Article 15b of Directive 75/319/EEC, as amended by Directive 93/39/EEC, and Article 23b of Directive 81/851/EEC, as amended by Directive 93/40/EEC, lay down that the abovementioned applications to vary a national authorization will come under the decentralized procedure as from 1 January 1995.

   In addition, these Articles lay down that the decentralized procedure will also apply to these medicinal products should a Member State consider that the variation of the terms of a marketing authorization, or its suspension or withdrawal is necessary for the protection of public health.

C. **Lists of experts**

1. The Commission considers that, under the new procedures, there must be an ongoing effort to maintain the high level of scientific expertise and of medicinal product evaluation. This means that the pool of expertise available to the Agency will be decisive. Article 53 (2) of Regulation (EEC) No 2309/93 therefore lays down that 'Member States shall transmit to the Agency a list of experts with proven experience in the assessment of medicinal products who would be available to serve on working parties or expert groups of the Committee for Proprietary Medicinal Products or the Committee for Veterinary Medicinal Products, together with an indication of their qualifications and specific areas of expertise. This list shall be updated as necessary.'

2. The Commission therefore asks the Member States to send it their lists of experts at their earliest convenience, and if possible before 1 September 1994, in order that the Agency may have access to them before it assumes its responsibilities.