COUNCIL DIRECTIVE

of 3 May 1989

extending the scope of Directives 65/65/EEC and 75/319/EEC and laying down additional provisions for radiopharmaceuticals

(89/343/EEC)

THE COUNCIL OF THE EUROPEAN COMMUNITIES,

Having regard to the Treaty establishing the European Economic Community, and in particular Article 100a thereof,

Having regard to the proposal from the Commission (1),

In cooperation with the European Parliament (2),

Having regard to the opinion of the Economic and Social Committee (3),

Whereas disparities in the provisions currently laid down by law, regulation or administrative action by Member States may hinder trade in radiopharmaceuticals within the Community;

Whereas the essential aim of any rules governing the production, distributio or use of medicinal products must be to safeguard public health;

Whereas the provisions laid down by Directive 65/65/EEC (4), as last amended by Directive 87/21/EEC (5), and by Second Directive 75/319/EEC (6), as last amended by Directive 83/570/EEC (7), on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, although appropriate, are inadequate for radiopharmaceuticals;

Whereas, in accordance with Article 5 of Council Directive 87/22/EEC of 22 December 1986 on the approximation of national provisions relating to the placing on the market of high technology medicinal products, particularly those derived from biotechnology (8), the Commission is required to submit proposals to harmonize, along the lines of Directive 75/319/EEC, the conditions for authorizing the manufacture and placing on the market of radiopharmaceuticals before 22 December 1987;

Whereas, in the case of radiopharmaceuticals, generators, kits and precursors, authorization should be required; whereas, however, a specific authorization should not be required for radiopharmaceuticals in their finished form which are made up exclusively from authorized kits, generators or precursor radiopharmaceuticals in health care establishments;

Whereas the Commission should be empowered to adopt any necessary changes in the requirements for the testing of proprietary medicinal products set out in the Annex to Council Directive 75/318/EEC of 20 May 1975 on the approximation of the laws of the Member States relating to analytical, pharmacotoxicological and clinical standards and protocols in respect of the testing of proprietary medicinal products (9), as last amended by Directive 87/19/EEC (10), to take account of the special nature of radiopharmaceuticals in close cooperation with the Committee for the Adaptation to Technical Progress of the Directives on the Removal of Technical Barriers to Trade in the Proprietary Medicinal Products Sector, thus ensuring the greater quality, safety and efficacy of the medicinal products;

Whereas any rules governing radiopharmaceuticals must take into account the provisions of Council Directive 84/466/Euratom of 3 September 1984 laying down basic measures for the radiation protection of persons undergoing medical examination or treatment (11); whereas account should also be taken of Council Directive 80/836/Euratom of 15 July 1980 amending the Directives laying down the basic safety standards for the health protection of the general public and workers against the dangers of ionizing radiation (12), as last amended by Directive 84/467/Euratom (13), the objective of which is to prevent the exposure of workers or patients to excessive or unnecessarily high levels of ionizing radiation, and in particular of Article 5c thereof, which requires prior authorization for the addition of radioactive substances to medicinal products as well as for the importation of such medicinal products,

HAS ADOPTED THIS DIRECTIVE:

Article 1

1. In derogation from Article 34 of Directive 75/319/EEC, and subject to the provisions of this Directive,

(1) OJ No C 36, 8. 2. 1988, p. 30.
(2) OJ No C 290, 14. 11. 1988, p. 136; OJ No C 120, 16. 5. 1989.
(3) OJ No C 208, 8. 8. 1988, p. 64.
(4) OJ No 22, 9. 2. 1965, p. 369/65.
(5) OJ No L 15, 17. 1. 1987, p. 36.
(6) OJ No L 147, 9. 6. 1975, p. 13.
(7) OJ No L 332, 28. 11. 1983, p. 1.
(8) OJ No L 15, 17. 1. 1987, p. 38.
(9) OJ No L 147, 9. 6. 1975, p. 1.
(10) OJ No L 15, 17. 1. 1987, p. 31.
(11) OJ No L 265, 5. 10. 1984, p. 1.
(12) OJ No L 246, 17. 9. 1980, p. 1.
(13) OJ No L 265, 5. 10. 1984, p. 4.

the provisions of Directives 65/65/EEC and 75/319/EEC shall apply to radiopharmaceuticals for human use, excluding radionuclides in the form of sealed sources.

2. For the purposes of this Directive, the following definitions apply:

— 'radiopharmaceutical' shall mean any medicinal product which, when ready for use, contains one or more radionuclides (radioactive isotopes) included for a medicinal purpose,

— 'generator' shall mean any system incorporating a fixed parent radionuclide from which is produced a daughter radionuclide which is to be removed by elution or by any other method and used in a radiopharmaceutical,

— 'kit' shall mean any preparation to be reconstituted or combined with radionucliedes in the final radiopharmaceutical, usually prior to its administration,

— 'precursor' shall mean any other radionuclide produced for the radio-labelling of another substance prior to administration.

3. Nothing in this Directive shall in any way derogate from the Community rules for the radiation protection of persons undergoing medical examination or treatment or from the Community rules laying down the basic safety standards for the health protection of the general public and workers against the dangers of ionizing radiation.

Article 2

The authorization referred to in Article 3 of Directive 65/65/EEC shall be required for generators, kits, precursor radiopharmaceuticals and industrially prepared radiopharmaceuticals. However, authorization shall not be required for a radiopharmaceutical prepared at the time of use by a person or by an establishment authorized, according to national legislation, to use such medicinal products in an approved health care establishment exclusively from authorized generators, kits or precursor radiopharmaceuticals in accordance with the manufacturer's instructions.

Article 3

In addition to the requirements set out in Article 4 of Directive 65/65/EEC, an application for authorization to market a generator shall also contain the following information and particulars:

— a general description of the system together with a detailed description of the components of the system which may effect the composition or quality of the daughter nucleid preparation,

— qualitative and quantitative particulars of the eluate or the sublimate.

Article 4

For radiopharmaceuticals, in addition to the information referred to in Article 4a of Directive 65/65/EEC, the summary of product characteristics referred to in point 9 of the second paragraph of Article 4 of Directive 65/65/EEC shall contain the following additional points 7 and 8:

'7. Full details of internal radiation dosimetry.

8. Additional detailed instructions for extemporaneous preparation and quality control of such preparation and, where appropriate, maximum storage time during which any intermediate preparation such as an eluate or the ready to use pharmaceutical will conform with its specifications.'

Article 5

The outer carton and the container of medicinal products containing radionuclides shall be labelled in accordance with the regulations for the safe transport of radioactive materials laid down by the International Atomic Energy Agency. Moreover, the labelling shall comply with the following provisions:

(a) The label on the shielding shall include the particulars mentioned in Article 13 of Directive 65/65/EEC. In addition, the labelling on the shielding shall explain in full the codings used on the vial and shall indicate, where necessary, for a given time and date, the amount of radioactivity per dose or per vial and the number of capsules, or, for liquids, the number of millilitres in the container;

(b) The vial shall be labelled with the following information:

— the name or code of the medicinal product, including the name or chemical symbol of the radionuclide;

— the batch identification and expiry date,

— the international symbol for radioactivity,

— the name of the manufacturer,

— the amount of radioactivity as specified under (a).

Article 6

1. Member States shall ensure that a detailed instruction leaflet is enclosed with the packaging of radiopharmaceuticals, generators, kits or precursor radiopharmaceuticals. The text of this leaflet shall be established in accordance with the provisions of Article 6 of Directive 75/319/EEC and shall contain all the information referred to therein. In addition, the leaflet shall include any precautions to be taken by the user and the patient during the

preparation and administration of the product and special precautions for the disposal of the container and its unused contents.

2. Without prejudice to Article 8 of Directive 65/65/EEC and Article 6 of Directive 75/319/EEC, Member States shall permit the use of user information leaflets which have been established in more than one of the languages of the Community provided that the information contained in all the language versions of the leaflet is identical.

Article 7

Any amendments which are necessary in the testing requirements for medicinal products set out in the Annex to Directive 75/318/EEC to take account of the extension of the scope of Directives 65/65/EEC and 75/319/EEC to cover radiopharmaceuticals shall be adopted in accordance with the procedure laid down in Article 2c of Directive 75/318/EEC.

Article 8

1. Save in the case provided for in paragraph 2, Member States shall take the necessary measures to comply with this Directive not later than 1 January 1992. They shall forthwith inform the Commission thereof.

2. If the amendments to Directive 75/318/EEC referred to in Article 7 have not been adopted by the date referred to in paragraph 1, this Directive shall come into force on the same date as those amendments.

3. Requests for marketing authorization for products covered by ths Directive lodged after the date of entry into force must comply with the provisions of this Directive.

4. This Directive shall be progressively extended to existing radiopharmaceutical medicinal products covered by this Directive before 31 December 1992.

Article 9

This Directive is addressed to the Member States.

Done at Brussels, 3 May 1989.

For the Council

The President

P. SOLBES