STATUTORY INSTRUMENTS

1992 No. 2846

MEDICINES

The Medicines (Standard Provisions for Licences and Certificates) Amendment Regulations 1992

Made - - - -	*12th November 1992*
Laid before Parliament	*20th November 1992*
Coming into force - -	*11th December 1992*

The Secretary of State concerned with health in England, the Secretaries of State respectively concerned with health and with agriculture in Wales and in Scotland, the Minister of Agriculture, Fisheries and Food, the Department of Health and Social Services for Northern Ireland and the Department of Agriculture for Northern Ireland, acting jointly, in exercise of powers conferred upon them by section 47(1) of the Medicines Act 1968(**1**) or, as the case may be, those conferred by the said provisions and now vested in them(**2**) and of all other powers enabling them in that behalf, after consulting such organisations as appear to them to be representative of interests likely to be substantially affected by these Regulations(**3**), hereby make the following Regulations:

Citation, commencement and interpretation

1.—(1) These Regulations may be cited as the Medicines (Standard Provisions for Licences and Certificates) Amendment Regulations 1992, and shall come into force on11th December 1992.

(2) In these Regulations, "the Principal Regulations" means the Medicines (Standard Provisions for Licences and Certificates) Regulations 1971(**4**).

(**1**) 1968 c. 67. The expression "the Ministers", used in section 47(1), is defined in section 1(1) of that Act as amended by S.I.1969/388, Schedule 1.

(**2**) In the case of the Secretaries of State concerned with health in England and in Wales by virtue of article 2(2) of, and Schedule 1 to, the Transfer of Functions (Wales) Order 1969 (S.I. 1969/388); in the case of the Secretary of State concerned with agriculture in Wales by virtue of article 2(3) of, and Schedule 1 to, the Transfer of Functions (Wales) (No. 1) Order 1978 (S.I. 1978/272); in the case of the Northern Ireland Departments by virtue of section 40 of, and Schedule 5 to, the Northern Ireland Constitution Act 1973 (c. 36) and section 1(3) of, and paragraph 2(1)(b) of Schedule 1 to, the Northern Ireland Act 1974 (c. 28).

(**3**) *See*section 129(6) of the Medicines Act 1968.

(**4**) S.I. 1971/972; the relevant amending instruments are S.I. 1972/1226, 1974/1523, 1977/675, 1977/1039, 1977/1053, 1983/1730.

Amendment of regulation 2(1) of the Principal Regulations

2.—(1) Regulation 2(1) of the Principal Regulations (interpretation) shall be amended in accordance with the following provisions of this regulation.

(2) After the definition of "advertisement" there shall be inserted the following definition—

""allergen product" means any product which is intended to identify or induce a specific acquired alteration in the immunological response to an allergising agent;"

(3) After the definition of "BCG vaccine", there shall be inserted the following definition—

""blood product" means any industrially prepared medicinal product for human use derived from human blood or human plasma and includes albumin, coagulating factors and immunoglobulins of human origin, but does not include whole human blood, human plasma or blood cells of human origin;"

(4) After the definition of "clinical trial certificate of right" and "animal test certificate of right", there shall be inserted the following definitions—

""expiry date", in relation to a medicinal product, means the date after which the medicinal product should not be used;

"good manufacturing practice" means the part of quality assurance which ensures that medicinal products are consistently produced and controlled to the quality standards appropriate to their intended use, the principles and guidelines of which are specified in Chapter II of Commission Directive 91/356/EEC(**5**);".

(5) After the definition of "parenteral administration", there shall be inserted the following definition—

""relevant period" means the period of five years from the date of certification of the relevant batch referred to in paragraph 16(3)(b) of Schedule 2 to these Regulations or the period of one year from the expiry date of the relevant batch, whichever expires later;"

Insertion of regulation 3A into the Principal Regulations

3. After regulation 3 of the Principal Regulations there shall be inserted the following regulation—

"**Standard provisions for product licences, including product licences of right, for blood products and immunological medicinal products for human use**

3A. In addition to the standard provisions for product licences set out in Part I of Schedule 1 to these Regulations—

(a) the standard provisions for product licences, including product licences of right, in relation to blood products shall be those provisions set out in paragraphs 1 and 2 of Schedule 1A to these Regulations, and

(b) the standard provisions for product licences, including product licences of right, in relation to vaccines, toxins, serums or allergen products for human use shall be those provisions set out in paragraph 3 of Schedule 1A to these Regulations.".

Insertion of Schedule 1A into the Principal Regulations

4. After Schedule 1 to the Principal Regulations, there shall be inserted the following—

(**5**) OJ No. L193, 17.7.91, p.30.

"SCHEDULE 1A Regulation 3A

ADDITIONAL STANDARD PROVISIONS FOR PRODUCT LICENCES INCLUDING PRODUCT LICENCES OF RIGHT RELATING TO BLOOD PRODUCTS AND CERTAIN IMMUNOLOGICAL MEDICINAL PRODUCTS

Blood products

1. The licence holder shall take all necessary measures to ensure that the manufacturing and purifying processes used in the preparation of the blood products to which the licence relates—

(a) are properly validated,

(b) attain batch-to-batch consistency, and

(c) guarantee, in so far as the state of technology permits, the absence of specific viral contamination,

and shall take all necessary measures to ensure that appropriate records relating to relevant control measures are—

(i) signed by the qualified person referred to in paragraph 16 of Schedule 2 to these Regulations,

(ii) kept for the relevant period, and

(iii) if so requested by the licensing authority, submitted to the licensing authority.

2. The licence holder shall take all necessary measures to ensure that the manufacturer of the blood products to which the product licence relates notifies the licensing authority of the method or methods used to reduce or eliminate pathogenic viruses liable to be transmitted by the blood products.

Immunological products

3. The licence holder shall take all necessary measures to ensure that the processes used in the production of vaccines, toxins, serums or allergen products to which the product licence relates—

(a) are properly validated, and

(b) attain batch-to-batch consistency,

and shall take all necessary measures to ensure that appropriate records relating to control measures are—

(i) signed by the qualified person referred to in paragraph 16 of Schedule 2 to these Regulations,

(ii) kept for the relevant period, and

(iii) if so requested by the licensing authority, submitted to the licensing authority.".

Amendment of Schedule 2 to the Principal Regulations

5.—(1) Schedule 2 to the Principal Regulations (standard provisions for manufac turer's licences including manufacturer's licences of right) shall be amended in accordance with the following paragraphs of this regulation.

(2) At the end of paragraph 3, there shall be inserted the words "and, in relation to medicinal products for human use, shall conduct all such operations in accordance with the principles and guidelines of good manufacturing practice".

(3) After paragraph 3, there shall be inserted the following paragraph—

"**3A.** The licence holder shall, in relation to medicinal products for human use, establish and implement an effective pharmaceutical quality assurance system involving the active participation of the management and personnel of the different services involved.".

(4) In paragraph 5 there shall be inserted after the words "The licence holder shall" the words ", in relation to medicinal products, other than for human use,"

(5) After paragraph 5 there shall be inserted the following paragraphs—

"**5A.**—(1) The licence holder shall, in relation to medicinal products for human use—

(a) provide and maintain a designated quality control department having authority in relation to quality control and being independent from all other departments in the exercise of that authority; and

(b) place the quality control department under the authority of the person notified to the licensing authority in accordance with paragraph 7(2) of Schedule 1 to the Medicines (Applications for Manufacturer's and Wholesale Dealer's Licences) Regulations 1971(**6**) as being responsible for quality control.

(2) Subject to paragraph 5B of this Schedule, the licence holder shall, in order to support the quality control department, provide and maintain such staff, premises and plant as are necessary for carrying out—

(a) such tests of the strength, quality and purity of the medicinal products which he manufactures for human use under the manufacturer's licence as are required by the relevant product licences, and

(b) any tests or controls which relate to the conditions of production and in-process controls.

(3) Any animals used for the tests referred to in sub-paragraph (2) of this paragraph shall be suitably housed and managed.

(4) The licence holder shall ensure that the quality control department, in determining whether finished medicinal products for human use are to be released for sale or distribution, takes into account, in addition to analytical results—

(a) the conditions of production,

(b) the result of in-process controls,

(c) the examination of manufacturing documents, and

(d) the conformity of products to the specification in the relevant product licence.

5B. A licence holder need not himself provide and maintain such staff, premises and plant as are necessary for carrying out such tests as are specified in paragraph 5A(2) of this Schedule provided that he makes arrangements with a person approved by the licensing authority to carry out such tests on his behalf in accordance with paragraph 5A(2) and (3) of this Schedule.".

(6) In paragraph 8, for the words from "for a period" to the end of that paragraph there shall be substituted the following—

"without the consent of the licensing authority—

(a) in relation to a medicinal product for human use, for the relevant period,

(b) in any other case, for a period of five years from the date when the manufacture or assembly of the relevant batch ocurred."

(7) After paragraph 8, there shall be inserted the following paragraphs—

(**6**) S.I. 1971/1974.

"**8A.** The licence holder shall keep readily available for examination by a person authorised by the licensing authority samples of each batch of finished medicinal products for human use manufactured or assembled under his licence for at least a period of one year from their expiry date and shall retain samples of starting materials (other than solvents, gases or water) for at least a period of two years from the date of the release of the relevant batch of which the relevant starting materials formed part, except where the licence holder is authorised by the licensing authority to destroy any such sample earlier.

8B. The licence holder shall make suitable arrangements to ensure that any record or sample referred to in paragraph 8 or 8A above relating to a medicinal product for human use is retained for the relevant period.".

(8) In paragraph 9 after the word "shall" there shall be inserted the words ", in relation to medicinal products other than for human use," and after the word "any" there shall be inserted the word "such".

(9) After paragraph 9 there shall be inserted the following—

"**9A.**—(1) The licence holder shall implement a system for recording and reviewing complaints in relation to medicinal products for human use manufactured or assembled under his licence, together with an effective system for recalling promptly and at any time any such medicinal product in the distribution network.

(2) The licence holder shall record and investigate all complaints described in sub-paragraph (1) of this paragraph and shall immediately inform the licensing authority of any defect which could result in a recall from sale, supply or exportation or in an abnormal restriction on such sale, supply or exportation.".

(10) In sub-paragraph (5) of paragraph 16 the words "medicinal products consisting of vaccines, toxins or serums, medicinal products based on human blood or blood constituents, radioactive isotopes or" shall be omitted.

Amendment of Schedule 3 to the Principal Regulations

6.—(1) Schedule 3 to the Principal Regulations (standard provisions for wholesale dealer's licences including wholesale dealer's licences of right), shall be amended in accordance with the following paragraph.

(2) After paragraph 8 there shall be inserted the following paragraph—

"**8A.** Where the licence relates to imported proprietary products, the licence holder shall in relation to medicinal products for human use—

(a) ensure that all manufacture and assembly operations have been carried out by a duly authorised manufacturer or assembler and that the products have been manufactured and assembled in accordance with the principles and guidelines of good manufacturing practice;

(b) keep readily available for examination by a person authorised by the licensing authority samples of each batch of finished products for at least one year after their expiry date except where the licence holder is authorised by the licensing authority to destroy such samples earlier;

(c) implement a system for recording and reviewing complaints relating to the medicinal products to which his licence relates, together with an effective system for recalling promptly and at any time any such medicinal product in the distribution network; and

(d) record and investigate all such complaints and immediately inform the licensing authority of any defect which could result in a recall from sale, supply or exportation or in an abnormal restriction on such sale, supply or exportation.".

Amendment of Schedule 4 to the Principal Regulations

7. Paragraph 1 of each of Parts I, IV and V of Schedule 4 to the Principal Regulations shall be omitted.

Amendment of Schedule 5 to the Principal Regulations

8. Paragraph 1 of Part I of Schedule 5 to the Principal Regulations shall be omitted.

Signed by authority of the Secretary of State for Health.

Department of Health
12th November 1992

Brian Mawhinney
Minister,

12th November 1992

David Hunt
Secretary of State for Wales

12th November 1992

Fraser of Carmyllie
Minister of State, Scottish Office

In Witness whereof the Official Seal of the Minister of Agriculture, Fisheries and Food is hereunto affixed on 12th November 1992.

L.S.

John Selwyn Gummer
Minister of Agriculture, Fisheries and Food

Sealed with the Official Seal of the Department of Health and Social Services for Northern Ireland on 12th November 1992.

L.S.

F. A. Elliott
Permanent Secretary

Sealed with the Official Seal of the Department of Agriculture for Northern Ireland on 12th November 1992.

L.S.

W. J. Hodges
Permanent Secretary

EXPLANATORY NOTE

(This note is not part of the Regulations)

These Regulations further amend the Medicines (Standard Provisions for Licences and Certificates) Regulations 1971 ("the Principal Regulations"). They implement in part Commission Directive 91/356/EEC (OJNo. L193, 17.7.91, p.30) ("the Directive") which lays down the requirements of good manufacturing practice to be adopted by manufacturers of medicinal products for human use within the European Community and by importers of medicinal products for human use into the Community. Good manufacturing practice is defined in regulation 2(4) (articles 2 and 4 of the Directive) and manufacturers are required to comply with its principles and guidelines (regulation 5(2)).

In particular these Regulations require the holder of a manufacturer's licence to—

- establish and implement an effective pharmaceutical quality assurance system (regulation 5(3), article 6 of the Directive);
- provide and maintain an independent quality control department under the authority of the person nominated as being responsible for overall quality control (regulation 5(5), article 11(1) of the Directive);
- make arrangements with a person approved by the licensing authority in respect of the carrying out of tests if the licence holder does not provide and maintain his own staff, premises and plant (regulation 5(5), article 11(2) of the Directive);
- retain records and samples of starting materials and finished products for the periods defined in the Regulations (regulation 5(6) and (7), article 11(4) of the Directive); and
- maintain an effective system whereby complaints are reviewed and products may be recalled (regulation 5(9), article 13 of the Directive).

Similar obligations are imposed on the holder of a wholesale dealer's licence who is authorised to import medicinal products from outside the European Community into the United Kingdom (regulation 6(2), articles 4 and 13 of the Directive) insofar as the requirements of good manufacturing practice can be applied to him.

These Regulations also amend the Principal Regulations by imposing additional requirements to be incorporated into standard provisions for product licences and manufacturer's licences relating to certain immunological products, radiopharmaceuti cals and products derived from human blood or human plasma, in each case being a product for human use. The Regulations implement in part Council Directives—

89/342/EEC relating to immunological products (OJ No. L142, 25.5.1989, p.14) (regulations 2(2), 3, 4, 5(10) and 7 which implement articles 1 and 4 of that Directive);

89/343/EEC relating to radiopharmaceuticals (OJ No. L142 25.5.1989, p.16) (regulation 5(10) which implements part of article 1 of that Directive); and

89/381/EEC relating to medicinal products derived from human blood or human plasma (OJ No. L181, 28.6.1989, p.44) (regulations 2(3), 3, 4 and 5(10) which implement articles 1 and 4 of that Directive).

These Directives each extend the scope of Council Directives 65/65/EEC (OJ No. 22, 9.2.1965, p.369/65) and 75/319/EEC (OJ No. L147, 9.6.1975, p.13) on the approxima tion of provisions relating to medicinal products.