STATUTORY INSTRUMENTS

2004 No. 1031

The Medicines for Human Use (Clinical Trials) Regulations 2004

PART 6

MANUFACTURE AND IMPORTATION OF INVESTIGATIONAL MEDICINAL PRODUCTS

Requirement for authorisation to manufacture or import investigational medicinal products

36.—(1) Subject to paragraph (2) and regulation 37, no person shall manufacture, assemble or import any investigational medicinal product except in accordance with an authorisation granted by the licensing authority for the purposes of this regulation ("a manufacturing authorisation").

(2) The restriction in paragraph (1) shall not apply to the manufacture or assembly of a medicinal product to the extent that such manufacture or assembly is in accordance with the terms and conditions of a marketing authorization relating to that product.

Exemption for hospitals and health centres

37.—(1) The restriction imposed by regulation 36(1) shall not apply to the assembly of an investigational medicinal product where the conditions specified in paragraph (2) are satisfied.

(2) The conditions referred to in paragraph (1) are that—

(a) the assembly is carried out in—

(i) in a hospital or health centre, and

(ii) by a doctor, a pharmacist or a person acting under the supervision of a pharmacist; and

(b) the investigational medicinal products are assembled exclusively for use in—

(i) that hospital or health centre, or

(ii) any other hospital or health centre which is a trial site for the clinical trial in which the product is to be used.

Application for manufacturing authorisation

38.—(1) An application for the grant of a manufacturing authorisation shall be—

(a) made to the licensing authority;

(b) in writing; and

(c) signed by or on behalf of the applicant.

(2) Every application for the grant of a manufacturing authorisation shall specify which, if any, of the standard provisions referred to in regulation 40(4) it is desired shall be excluded or modified in relation to the grant of the authorisation.

(3) Every application for the grant of a manufacturing authorisation shall be accompanied by—

(a) the particulars specified in Schedule 6 to these regulations; and

(b) any fee which may be payable in connection with that application under the Medicines (Products for Human Use—Fees) Regulations 1995(**1**).

(4) The application and any accompanying material shall be supplied to the licensing authority in the English language.

Consideration of application for manufacturing authorisation

39.—(1) Subject to paragraph (3) and regulation 40, the licensing authority shall consider a valid application for a manufacturing authorisation and grant, or refuse to grant, an authorisation within a period not exceeding 90 days from the date the application is received.

(2) Following receipt of an application, the licensing authority may give a notice in writing to the applicant requesting him to provide further information relating to—

(a) the particulars referred to in regulation 38(3); or

(b) the qualified person referred to in regulation 43.

(3) Where the licensing authority give a notice pursuant to paragraph (2), the period specified in paragraph (1) shall be suspended from the date the notice is given and shall recommence only on receipt of the information requested.

(4) If the application for a manufacturing authorisation relates (wholly or partially) to the importation of investigational medicinal products, the licensing authority may, if they think fit, require the production by the applicant of an undertaking, given by the manufacturer of any such products, to permit—

(a) the premises where they are or are to be manufactured; and

(b) the operations carried on or to be carried on in the course of manufacturing them,

to be inspected by or on behalf of the licensing authority.

(5) In this regulation, "valid application" means an application which complies with the provisions of regulation 38.

Grant or refusal of manufacturing authorisation

40.—(1) The licensing authority shall grant a manufacturing authorisation only if—

(a) the applicant—

(i) has complied with the requirements of regulation 38,

(ii) has at his disposal suitable and sufficient premises, technical equipment and control facilities complying with the requirements of Commission Directive 2003/94/EC, as regards the manufacture or import, and control, of the products to which the authorisation relates and the storage of such products,

(iii) has at his disposal the services of at least one qualified person, and

(iv) if a notice has been given under regulation 39(2), has provided the information requested by the licensing authority; and

(b) they have established that the particulars supplied pursuant to regulation 38(3) are accurate.

(2) Subject to paragraph (1), the licensing authority may grant a manufacturing authorisation in respect of any or all of—

(**1**) S.I. 1995/1116.

(a) the descriptions of investigational medicinal products;

(b) the manufacturing, assembling or importation operations; or

(c) the premises,

specified in the application made pursuant to regulation 38.

(3) The licensing authority may grant a manufacturing authorisation containing—

(a) any provisions to be incorporated in the authorisation in accordance with paragraph (4); or

(b) such other provisions as the licensing authority consider appropriate.

(4) The provisions specified—

(a) in the case of a manufacturing authorisation relating to the manufacture or assembly of investigational medicinal products, in Part 2 of Schedule 7; and

(b) in the case of a manufacturing authorisation relating to the importation of investigational medicinal products, in Part 3 of Schedule 7,

may be incorporated by the licensing authority in any manufacturing authorisation, with or without modifications and either generally or in relation to investigational medicinal products of any particular class.

(5) The provisions of Schedule 8 shall have effect where the licensing authority propose—

(a) to refuse to grant a manufacturing authorisation; or

(b) to grant a manufacturing authorisation otherwise than in accordance with the application.

(6) Where the licensing authority—

(a) refuse to grant a manufacturing authorisation; or

(b) grant a manufacturing authorisation otherwise than in accordance with the application,

and the applicant requests the authority to state their reasons, the licensing authority shall give the applicant a notice in writing stating the reasons for their decision.

Application and effect of manufacturing authorisation

41. A manufacturing authorisation shall apply only in relation to—

(a) the descriptions of investigational medicinal products;

(b) the manufacturing, assembling or importation operations; and

(c) the premises,

specified in the application made pursuant to regulation 38 and in respect of which the authorisation is granted.

Obligations of manufacturing authorisation holder

42. The holder of a manufacturing authorisation shall comply with—

(a) the principles and guidelines of good manufacturing practice; and

(b) the provisions referred to in regulation 40(3).

Qualified persons

43.—(1) Subject to paragraphs (4) and (5), the holder of a manufacturing authorisation must have at his disposal the services of at least one qualified person who is responsible for carrying out the duties referred to in paragraph 2.

(2) A qualified person shall be responsible for carrying out the duties specified in Article 13(3) and (4) of the Directive, in accordance with that Article, in respect of the investigational medicinal products manufactured, assembled or imported in accordance with the authorisation in question.

(3) A qualified person shall perform his functions under these Regulations in accordance with the Code of Practice for Qualified Persons in the Pharmaceutical Industry, published jointly by the Institute of Biology, the Royal Pharmaceutical Society of Great Britain and the Royal Society of Chemistry in March 2004(**2**).

(4) If the holder of the authorisation satisfies the requirements as to qualifications and experience specified in paragraph (a) or (b) of the definition of "qualified person" in regulation 2(1), he may act as the qualified person in accordance with paragraph (2) for the purposes of that authorisation.

(5) For the purposes of this paragraph, but without prejudice to paragraph (6) below, the holder of the authorisation may regard a person as satisfying the provisions of the said Article 49 or 50, as respects formal qualifications if he produces evidence that—

(a) he is a member of—

(i) the Institute of Biology,

(ii) the Pharmaceutical Society,

(iii) the Royal Society of Chemistry, or

(iv) such other body as may appear to the licensing authority to be an appropriate body for the purpose of this paragraph; and

(b) he is regarded by the body of which he is a member as so satisfying those provisions.

(6) Where, after giving the holder of the authorisation and the person acting as a qualified person the opportunity of making representations to them (orally or in writing), the licensing authority are of the opinion that—

(a) the person so acting does not satisfy—

(i) the provisions of the said Articles 49 and 50 of Directive 2001/83/EC as respects qualifications and experience, or

(ii) the requirements as to qualifications and experience specified in paragraph (b) of the definition of "qualified person" in regulation 2(1); or

(b) he is failing to carry out the duties referred to in paragraph (2) adequately or at all,

and have notified the holder of the authorisation accordingly in writing, the holder of the authorisation shall not permit that person to act as a qualified person.

Variation of manufacturing authorisation

44.—(1) The licensing authority may vary a manufacturing authorisation, whether on the application of the holder of the authorisation or otherwise.

(2) Subject to the following provisions of this regulation, if the holder of a manufacturing authorisation makes a valid application to vary the manufacturing authorisation the licensing authority shall consider the application and—

(a) in a case where the effect of the variation would be to change the—

(i) the types of investigational medicinal products,

(ii) the manufacturing, assembling or importation operations,

(iii) the premises,

(**2**) A copy of the Code of Practice may be obtained by writing to the Institute of Biology, 20 Queensbury Place, London SW7 2DZ, the Royal Pharmaceutical Society of Great Britain, 1 Lambeth High Street, London SE1 7JN or the Royal Society of Chemistry, Burlington House, Piccadilly, London W1V 0BN.

(iv) the technical equipment and control facilities,

in respect of which the authorisation has been granted, may vary or refuse to vary the authorisation within a period not exceeding 30 days from the date the application is received;

(b) in any other case, may vary or refuse to vary the authorisation within such period as the licensing authority consider appropriate.

(3) If the application falls within paragraph (2)(a), but it appears to the licensing authority to be necessary to conduct an inspection of any premises to which the variation relates, the authority may vary or refuse to vary the authorisation within a period not exceeding 90 days from the date the application is received.

(4) Following receipt of a valid application to vary a manufacturing authorisation, the licensing authority may give a notice in writing to the applicant requesting him to provide further information relating to the contents of the application or any particulars relevant to the application.

(5) Where the licensing authority give a notice pursuant to paragraph (4), and a period specified in paragraph (2)(a) or paragraph (3) applies, that period shall be suspended from the date the notice is given and shall recommence only on receipt of the information requested.

(6) The provisions of Schedule 8 shall have effect where the licensing authority propose to vary a manufacturing authorisation otherwise than on the application of the holder of the authorisation.

(7) Where the licensing authority—

(a) vary a manufacturing authorisation, otherwise than in accordance with a valid application by the holder of the authorisation; or

(b) after consideration of such an application, refuse to vary a manufacturing authorisation,

the licensing authority shall notify the holder of that authorisation in writing, stating the reasons for their decision.

(8) In this regulation, "valid application" means an application—

(a) made to the licensing authority;

(b) in writing and signed by or on behalf of the applicant;

(c) specifying the variation requested by the applicant;

(d) accompanied by—

(i) such particulars as are necessary to enable the licensing authority to consider the application, and

(ii) any fee which may be payable in connection with that application under the Medicines (Products for Human Use—Fees) Regulations 1995(**3**); and

(e) where the application, and any accompanying material, is in the English language.

Suspension and revocation of manufacturing authorisation

45.—(1) The licensing authority may by a notice in writing to the holder of a manufacturing authorisation, forthwith or from a date specified in the notice, suspend the authorisation for such period as the authority may determine, or revoke the authorisation, on one or more of the following grounds—

(a) the holder is not carrying out, or has indicated by a notice in writing that he is no longer to carry out, the manufacturing, assembly or importation operations to which the authorisation relates;

(**3**) S.I. 1995/1116.

(b) the particulars accompanying the application in accordance with regulation 38(3), were false or incomplete in a material particular;

(c) a material change of circumstances has occurred in relation to any of those matters or particulars;

(d) the holder of the authorisation has failed to any material extent to comply with his obligations under regulation 42 or 43(1);

(e) the holder has manufactured, assembled or, as the case may be, imported investigational medicinal products otherwise than in accordance with the terms of the authorisation;

(f) the holder has manufactured or assembled investigational medicinal products otherwise than in accordance with—

(i) in the case of products manufactured before a request for authorisation to conduct the clinical trial involving those products has been made in accordance with regulation 17 or any equivalent provisions in any EEA State other than the United Kingdom, the specification for the product provided by the person who is to act as the sponsor of the proposed clinical trial,

(ii) in the case of products manufactured for the purpose of export, the specification for the product provided by the person to whose order the products are manufactured, or

(iii) in any other case, the specification for the product contained in the investigational medicinal product dossier for that product;

(g) the qualified person has failed to carry out the duties referred to in regulation 43(2), adequately or at all; and

(h) the holder of the authorisation does not have the staff, premises, equipment or facilities necessary for carrying out properly—

(i) the manufacture or assembly operations to which the authorisation relates, or

(ii) the importation operations to which the authorisation relates,

including any handling, storage or distribution activities relating to those operations.

(2) The suspension or revocation of an authorisation under this regulation may be—

(a) total; or

(b) limited to investigational medicinal products—

(i) of one or more descriptions, or

(ii) manufactured, assembled or stored on any particular premises or in a particular part of any premises.

(3) The provisions of Schedule 8 shall have effect where the licensing authority propose to suspend or revoke a manufacturing authorisation in accordance with this regulation.

(4) Where the licensing authority suspend or revoke a manufacturing authorisation in accordance with this regulation, they shall notify the holder of that authorisation in writing, stating the reasons for their decision to suspend or revoke the authorisation.