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STATUTORY INSTRUMENTS

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**2004 No. 1031**

**MEDICINES**

The Medicines for Human Use  
(Clinical Trials) Regulations 2004

<i>Made</i>	- - - -	<i>31st March 2004</i>
<i>Laid before Parliament</i>		<i>1st April 2004</i>
<i>Coming into force</i>	- -	<i>1st May 2004</i>

The Secretary of State, being a Minister designated<sup>(1)</sup> for the purposes of section 2(2) of the European Communities Act 1972<sup>(2)</sup> in relation to medicinal products, in exercise of the powers conferred by the said section 2(2), and of all other powers enabling him in that behalf, hereby makes the following Regulations:

PART 1

INTRODUCTORY PROVISIONS

**Citation and commencement**

1. These Regulations may be cited as the Medicines for Human Use (Clinical Trials) Regulations 2004 and shall come into force on 1st May 2004.

**Interpretation**

2.—(1) In these Regulations—

“the Act” means the Medicines Act 1968<sup>(3)</sup>;

“adult” means a person who has attained the age of 16 years;

“adverse event” means any untoward medical occurrence in a subject to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product;

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(1) S.I. 1972/1811.  
(2) 1972 c. 68.  
(3) 1968 c. 67.

“adverse reaction” means any untoward and unintended response in a subject to an investigational medicinal product which is related to any dose administered to that subject;

“authorised health professional” means—

- (a) a doctor,
- (b) a dentist,
- (c) a nurse, or
- (d) a pharmacist;

“appropriate committee”, for the purpose of any provision of these Regulations under which a function falls to be performed, means such committee established under section 4 of the Act for purposes which consist of or include any of those specified in section 4(3) of the Act as the authority performing that function considers appropriate in the circumstances;

“assemble”, in relation to an investigational medicinal product, means—

- (a) enclosing the product (with or without other medicinal products of the same description) in a container which is labelled before the product is sold or supplied, or used in a clinical trial, or
- (b) where the product (with or without other medicinal products of the same description) is already contained in the container in which it is to be sold or supplied, or used in a clinical trial, labelling the container before the product is sold or supplied, or used in a clinical trial, in that container,

and “assembly” has a corresponding meaning;

“business”, except in Schedule 2, includes a professional practice and includes any activity carried on by a body of persons, whether corporate or unincorporate;

“chief investigator” means—

- (a) in relation to a clinical trial conducted at a single trial site, the investigator for that site, or
- (b) in relation to a clinical trial conducted at more than one trial site, the authorised health care professional, whether or not he is an investigator at any particular site, who takes primary responsibility for the conduct of the trial;

“clinical trial” means any investigation in human subjects, other than a non-interventional trial, intended—

- (a) to discover or verify the clinical, pharmacological or other pharmacodynamic effects of one or more medicinal products,
- (b) to identify any adverse reactions to one or more such products, or
- (c) to study absorption, distribution, metabolism and excretion of one or more such products, with the object of ascertaining the safety or efficacy of those products;

“Commission Directive [2003/94/EC](#)” means Commission Directive [2003/94/EC](#)(4) laying down the principles and guidelines of good manufacturing practice for medicinal products for human use and for investigational medicinal products for human use;

“conditions and principles of good clinical practice” means the conditions and principles specified in Schedule 1;

“conducting a clinical trial” includes—

- (a) administering, or giving directions for the administration of, an investigational medicinal product to a subject for the purposes of that trial,

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(4) OJ No. L262, 14.10.2003, p.22.

- (b) giving a prescription for an investigational medicinal product for the purposes of that trial,
- (c) carrying out any other medical or nursing procedure in relation to that trial, and
- (d) carrying out any test or analysis—
  - (i) to discover or verify the clinical, pharmacological or other pharmacodynamic effects of the investigational medicinal products administered in the course of the trial,
  - (ii) to identify any adverse reactions to those products, or
  - (iii) to study absorption, distribution, metabolism and excretion of those products,but does not include any activity undertaken prior to the commencement of the trial which consists of making such preparations for the trial as are necessary or expedient;

“container”, in relation to an investigational medicinal product, means the bottle, jar, box, packet or other receptacle which contains or is to contain it, not being a capsule, cachet or other article in which the product is or is to be administered, and where any such receptacle is or is to be contained in another such receptacle, includes the former but does not include the latter receptacle;

“dentist” means a person registered in the dentists register under the Dentists Act 1984<sup>(5)</sup> or entered in the list of visiting EEC practitioners under Schedule 4 to that Act;

“the Directive” means Directive 2001/20/EC of the European Parliament and of the Council on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use<sup>(6)</sup>;

“Directive 2001/83/EC” means Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to medicinal products for human use<sup>(7)</sup>, as amended<sup>(8)</sup>;

“doctor” means a registered medical practitioner<sup>(9)</sup>;

“EEA State” means a State which is a Contracting Party to the EEA Agreement;

“EEA Agreement” means the Agreement on the European Economic Area signed at Oporto on 2nd May 1992<sup>(10)</sup> as adjusted by the Protocol signed at Brussels on 17th March 1993<sup>(11)</sup>;

“electronic signature” means data in electronic form which are attached to or logically associated with other electronic data and which serve as a method of authentication;

“European Economic Area” means the European Economic Area created by the EEA Agreement;

“the European Medicines Agency” means the European Agency for the Evaluation of Medicinal Products established by Council Regulation (EEC) No. 2309/93 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<sup>(12)</sup>;

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(5) 1984 c. 24.

(6) OJ No. L121, 1.5.2001, p.34.

(7) OJ No. L311, 28.11.2001, p.67.

(8) See Article 31 of Directive 2002/98/EC (OJ No. L33, 8.2.2003, p.30) and Commission Directive 2003/63/EC (OJ No. L159, 27.6.2003, p.46).

(9) See Schedule 1 of the Interpretation Act 1978 (c. 30), as amended by paragraph 18 of Schedule 5 to the Medical Act 1983 (c. 54).

(10) OJ No. L1, 3.1.1994, p.3.

(11) OJ No. L1, 3.1.1994, p.572.

(12) OJ No. L214, 24.8.93, p.1.

“ethics committee” means—

- (a) a committee established or recognised in accordance with Part 2,
- (b) the Ethics Committee constituted by regulations made by the Scottish Ministers under section 51(6) of the Adults with Incapacity (Scotland) Act 2000<sup>(13)</sup>, or
- (c) the Gene Therapy Advisory Committee;

“export” means export to a third country from an EEA State, whether by land, sea or air;

“the Gene Therapy Advisory Committee” means the Gene Therapy Advisory Committee appointed by the Secretary of State to—

- (a) consider and advise on the acceptability of proposals for gene therapy research on human subjects, on ethical grounds, and
- (b) provide advice on developments in gene therapy research and their implications;

“Health and Social Services Board” means a Health and Social Services Board established under the Health and Personal Social Services (Northern Ireland) Order 1972<sup>(14)</sup>;

“Health Board” means a Health Board established under the National Health Service (Scotland) Act 1978<sup>(15)</sup>;

“health care” means services for or in connection with the prevention, diagnosis or treatment of illness;

“health care professional” means—

- (a) a doctor,
- (b) a dentist,
- (c) a nurse,
- (d) a pharmacist,
- (e) a person registered in a register of ophthalmic opticians maintained under section 7 of the Opticians Act 1989<sup>(16)</sup>,
- (f) a person registered in a register established and maintained under article 5 of Health Professions Order 2001<sup>(17)</sup>,
- (g) a registered osteopath as defined by section 41 of the Osteopaths Act 1993<sup>(18)</sup>, or
- (h) a registered chiropractor as defined by section 43 of the Chiropractors Act 1994<sup>(19)</sup>;

“health centre” means a health centre maintained under section 2 or 3 of the National Health Service Act 1977, section 36 of the National Health Service (Scotland) Act 1978 or Article 5 of the Health and Personal Social Services (Northern Ireland) Order 1972;

“health service body” means—

- (a) a Strategic Health Authority, Health Board or Health and Social Services Board,
- (b) a Special Health Authority, Primary Care Trust or Local Health Board established under the National Health Service Act 1977,
- (c) a Special Health Board established under the National Health Service (Scotland) Act 1978,

<sup>(13)</sup> 2000 asp. 4; see S.S.I. 2002/190.

<sup>(14)</sup> S.I. 1972/1265 (N.I. 14).

<sup>(15)</sup> 1978 c. 29.

<sup>(16)</sup> 1989 c. 44.

<sup>(17)</sup> S.I. 2002/254.

<sup>(18)</sup> 1993 c. 21.

<sup>(19)</sup> 1994 c. 17.

- (d) a special health and social services agency established under the Health and Personal Social Services (Special Agencies) (Northern Ireland) Order 1990<sup>(20)</sup>,
- (e) the Dental Practice Board constituted under section 37(1) of the National Health Service Act 1977,
- (f) the Scottish Dental Practice Board or the Common Services Agency for the Scottish Health Service established under the National Health Service (Scotland) Act 1978,
- (g) the Northern Ireland Central Services Agency for the Health and Social Services established under the Health and Personal Social Services (Northern Ireland) Order 1972,
- (h) a National Health Service trust established under the National Health Service and Community Care Act 1990<sup>(21)</sup> or the National Health Service (Scotland) Act 1978,
- (i) an NHS foundation trust within the meaning of section 1(1) of the Health and Social Care (Community Health and Standards) Act 2003<sup>(22)</sup>, or
- (j) a Health and Social Services trust established under the Health and Personal Social Services (Northern Ireland) Order 1991<sup>(23)</sup>;

“hospital” includes a clinic, nursing home or similar institution;

“import”, other than in regulation 13 and Schedule 3, means import into the United Kingdom from a third country, whether by land, sea or air;

“informed consent” shall be construed in accordance with paragraph 3 of Part 1 of Schedule 1;

“insurance or indemnity” includes provision for meeting losses or liabilities—

- (a) under a scheme established under—
  - (i) section 21 of the National Health Service and Community Care Act 1990 (schemes for meeting losses and liabilities etc. of certain health service bodies in England and Wales)<sup>(24)</sup>,
  - (ii) section 85B of the National Health Service (Scotland) Act 1978 (schemes for meeting losses and liabilities etc. of certain health service bodies in Scotland)<sup>(25)</sup>,  
or
  - (iii) Article 24 of the Health and Personal Social Services (Northern Ireland) Order 1991 (schemes for meeting losses and liabilities etc. of certain health service bodies in Northern Ireland)<sup>(26)</sup>, or
- (b) in accordance with guidance issued by—
  - (i) the Secretary of State,
  - (ii) the Scottish Ministers,
  - (iii) the National Assembly for Wales, or
  - (iv) the Department for Health, Social Services and Public Safety,as to the arrangements to be adopted by health service bodies for meeting the costs arising from clinical negligence (known as NHS Indemnity);

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<sup>(20)</sup> S.I. 1990/247 (N.I.3)

<sup>(21)</sup> 1990 c. 19.

<sup>(22)</sup> 2003 c. 43.

<sup>(23)</sup> S.I. 1991/194 (N.I.1).

<sup>(24)</sup> 1990 c. 19; section 21 was amended by paragraph 79 of Schedule 1 to the Health Authorities Act 1995 (c. 17) and paragraph 81 of Schedule 4 to the Health Act 1999 (c. 8).

<sup>(25)</sup> 1978 c. 29; section 85 was inserted by section 41 of the National Health Service and Community Care Act 1990 (c. 19) and was amended by paragraph 56 of Schedule 4 to the Health Act 1999 (c. 8).

<sup>(26)</sup> S.I. 1991/194 (N.I. 1).

“investigational medicinal product” means a pharmaceutical form of an active substance or placebo being tested, or to be tested, or used, or to be used, as a reference in a clinical trial, and includes a medicinal product which has a marketing authorization but is, for the purposes of the trial—

- (a) used or assembled (formulated or packaged) in a way different from the form of the product authorised under the authorization,
- (b) used for an indication not included in the summary of product characteristics under the authorization for that product, or
- (c) used to gain further information about the form of that product as authorised under the authorization;

“investigational medicinal product dossier” means, in relation to an investigational medicinal product, the dossier relating to that product which accompanies a request for authorisation to conduct a trial in which that product is or is to be used, in accordance with paragraph 11 of Schedule 3;

“investigator” means, in relation to a clinical trial, the authorised health professional responsible for the conduct of that trial at a trial site, and if the trial is conducted by a team of authorised health professionals at a trial site, the investigator is the leader responsible for that team;

“investigator’s brochure” means a document containing a summary of the clinical and non-clinical data relating to an investigational medicinal product which are relevant to the study of the product in human subjects;

“labelling”, in relation to an investigational medicinal product, means affixing to or otherwise displaying on it a notice describing or otherwise relating to the contents, and “label” has a corresponding meaning;

“legal representative”, other than in regulation 3 and Parts 2 to 4 of Schedule 3, has the meaning given by Part 1 of Schedule 1;

“licensing authority” shall be construed in accordance with section 6 of the Act;

“manufacture”, in relation to an investigational medicinal product, includes any process carried out in the course of making the product, but does not include dissolving or dispersing the product in, or diluting it or mixing it with, some other substance used as a vehicle for the purposes of administering it;

“manufacturing authorisation” has the meaning given by regulation 36(1);

“marketing authorization” means—

- (a) a marketing authorization granted by the licensing authority under the Medicines for Human Use (Marketing Authorisations Etc.) Regulations 1994<sup>(27)</sup>,
- (b) a marketing authorization issued by the competent authority of an EEA State, other than the United Kingdom, in accordance with Directive 2001/83/EC,
- (c) a marketing authorization granted by the European Commission under Council Regulation (EEC) 2309/93<sup>(28)</sup>, or
- (d) a product licence granted by the licensing authority for the purposes of section 7 of the Medicines Act 1968<sup>(29)</sup>;

“medicinal product” means—

- (a) a medicinal product within the meaning given by Article 1 of Directive 2001/83/EC, or

<sup>(27)</sup> S.I. 1994/3144, as amended by S.I. 1998/3105, 2000/292, 2001/795, 2002/236, 2002/542 and 2003/????.

<sup>(28)</sup> OJ No. L214, 24.8.1993, p.1.

<sup>(29)</sup> Section 7 does not apply to “relevant medicinal products” within the meaning given by S.I. 1994/3144.

- (b) any product which is not a medicinal product within the meaning given by Article 1 of Directive [2001/83/EC](#), but which is a medicinal product within the meaning given by section 130 of the Act;

“minor” means a person under the age of 16 years;

“non-interventional trial” means a study of one or more medicinal products which have a marketing authorization, where the following conditions are met—

- (a) the products are prescribed in the usual manner in accordance with the terms of that authorization,
- (b) the assignment of any patient involved in the study to a particular therapeutic strategy is not decided in advance by a protocol but falls within current practice,
- (c) the decision to prescribe a particular medicinal product is clearly separated from the decision to include the patient in the study,
- (d) no diagnostic or monitoring procedures are applied to the patients included in the study, other than those which are ordinarily applied in the course of the particular therapeutic strategy in question, and
- (e) epidemiological methods are to be used for the analysis of the data arising from the study;

“nurse” means a registered nurse or registered midwife;

“pharmaceutical form of an active substance” includes any substance or article to which these Regulations have effect by virtue of an order under section 104 or 105 of the Act (which relate to the application of Act to certain articles and substances which are not medicinal products);

“Pharmaceutical Society” in relation to Great Britain means the Royal Pharmaceutical Society of Great Britain, and in relation to Northern Ireland means the Pharmaceutical Society of Northern Ireland;

“pharmacist” means—

- (a) in relation to Great Britain, a person registered in the register of pharmaceutical chemists established in pursuance of the Pharmacy Act 1952 and maintained in pursuance of the Pharmacy Act 1954, and
- (b) in relation to Northern Ireland, a person registered in the register of pharmaceutical chemists for Northern Ireland made out and maintained under Articles 6 and 9 of the Pharmacy (Northern Ireland) Order 1976;

“Phase I trial” means a clinical trial to study the pharmacology of an investigational medicinal product when administered to humans, where the sponsor and investigator have no knowledge of any evidence that the product has effects likely to be beneficial to the subjects of the trial;

“the principles and guidelines of good manufacturing practice” means the principles and guidelines of good manufacturing practice set out in Commission Directive [2003/94/EC](#);

“protocol” means a document that describes the objectives, design, methodology, statistical considerations and organisation of a clinical trial;

“qualified person” means—

- (a) a person who as respects qualifications and experience satisfies the requirements of Article 49 or 50 of Directive [2001/83/EC](#), or
- (b) a person who, without satisfying the requirements referred to in paragraph (a)—
  - (i) has been engaged in activities equivalent to those to be performed in accordance with regulation 43(2) in respect of investigational medicinal products for a period of at least 6 months prior to 1st May 2004,

- (ii) has, in accordance with paragraph 6(1) of Schedule 6, been named as a qualified person in a valid application for a manufacturing authorisation made prior to 1st May 2006, and
- (iii) is—
  - (aa) a member of the Institute of Biology, the Pharmaceutical Society, the Royal Society of Chemistry, or such other body as may appear to the licensing authority to be an appropriate body for the purpose of this paragraph, or
  - (bb) the holder of a diploma, certificate or other evidence of formal qualifications awarded on completion of a university or other higher education course of study in pharmacy, chemistry, medicine, biology or a related life science, which the licensing authority have stated in a notice in writing to that person to be qualifications sufficient for the purpose of performing the functions of a qualified person;

“relevant ethics committee”, in relation to a clinical trial, means—

- (a) in a case where an ethics committee has given a favourable opinion in relation to that trial and paragraph 13 of Schedule 2 applies, the ethics committee which is the relevant ethics committee for that trial by virtue of sub-paragraph (5) of that paragraph;
- (b) in a case where an ethics committee has given an unfavourable opinion in relation to that trial but a favourable opinion has been given by an appeal panel in accordance with paragraph 4(4) of Schedule 4, that committee, or
- (c) in any other case, the ethics committee which has given a favourable opinion in relation to that trial in accordance with regulation 15;

“serious adverse event”, “serious adverse reaction” or “unexpected serious adverse reaction” means any adverse event, adverse reaction or unexpected adverse reaction, respectively, that—

- (a) results in death,
- (b) is life-threatening,
- (c) requires hospitalisation or prolongation of existing hospitalisation,
- (d) results in persistent or significant disability or incapacity, or
- (e) consists of a congenital anomaly or birth defect;

“sponsor” shall be construed in accordance with regulation 3;

“Strategic Health Authority” means a Strategic Health Authority established under the National Health Service Act 1977(30);

“subject” means, in relation to a clinical trial, an individual, whether a patient or not, who participates in a clinical trial—

- (a) as a recipient of an investigational medicinal product or of some other treatment or product, or
- (b) without receiving any treatment or product, as a control;

“third country” means a country or territory outside the European Economic Area;

“trial site” means a hospital, health centre, surgery or other establishment or facility at or from which a clinical trial, or any part of such a trial, is conducted;

“unexpected adverse reaction” means an adverse reaction the nature and severity of which is not consistent with the information about the medicinal product in question set out—

(30) See section 8 of the National Health Service Act 1977 (c. 49) as substituted by section 1(2) of the National Health Service Reform and Health Care Professions Act 2002 (c. 17).



- (a) in the case of a product with a marketing authorization, in the summary of product characteristics for that product,
- (b) in the case of any other investigational medicinal product, in the investigator's brochure relating to the trial in question.

(2) Any reference in these Regulations to the holder of a manufacturing authorisation shall be construed as a reference to the holder of such an authorisation which is for the time being in force.

(3) Any reference in these Regulations to an application, request or other document that is signed includes a reference to an application, request of other document that is signed with an electronic signature.

### **Sponsor of a clinical trial**

**3.—**(1) In these Regulations, subject to the following paragraphs, “sponsor” means, in relation to a clinical trial, the person who takes responsibility for the initiation, management and financing (or arranging the financing) of that trial.

(2) If two or more persons take responsibility for the matters specified in paragraph (1) in relation to a clinical trial, those persons may—

- (a) take joint responsibility for carrying out the functions of the sponsor of that trial under these Regulations; or
- (b) allocate responsibility for carrying out the functions of the sponsor of that trial in accordance with paragraphs (4) to (10).

(3) If two or more persons take joint responsibility in accordance with paragraph (2)(a)—

- (a) any reference to the sponsor in these Regulations shall, in relation to that trial, be construed as a reference to those persons; and
- (b) paragraphs (4) to (10) shall not apply.

(4) One of the persons referred to in paragraph (2) shall be responsible for carrying out the functions of a sponsor under Part 3 (authorisation for clinical trials and ethics committee opinion) and shall make the request for authorisation to conduct the trial in accordance with regulation 17.

(5) The request for authorisation referred to in regulation 17 shall specify—

- (a) who, in accordance with paragraph (4), is responsible for carrying out the functions of the sponsor under Part 3;
- (b) who is to be responsible for carrying out the functions of the sponsor under Part 4 (good clinical practice and the conduct of clinical trials); and
- (c) who is to be responsible for carrying out the functions of the sponsor under Part 5 (pharmacovigilance).

(6) After the clinical trial has been authorised by the licensing authority in accordance with regulation 18, 19 or 20, a different person may be specified as responsible for carrying out the functions of the sponsor under Part 3, 4 or 5 by making a substantial amendment to the terms of a clinical trial authorisation in accordance with regulations 24 to 26.

(7) Where a person is responsible for carrying out the functions of the sponsor under Part 3 by virtue of paragraph (5), or is specified in accordance with paragraph (6) as responsible for those functions, any reference to the sponsor in—

- (a) that Part, except regulation 15,
- (b) Parts 2 to 4 of Schedule 3,
- (c) Schedule 5, in so far as it relates to decisions of the licensing authority under Part 3, and
- (d) Schedule 12,

shall, in relation to the trial, be construed as a reference to that person.

(8) Where a person is specified in accordance with paragraph (5) or (6) as responsible for carrying out the functions of the sponsor under Part 4, any reference to the sponsor in—

- (a) that Part, except regulation 28(1), or
- (b) Schedule 5, in so far as it relates to notices under regulation 31(1),

shall, in relation to the trial, be construed as a reference to that person.

(9) Where a person is specified in accordance with paragraph (5) or (6) as responsible for carrying out the functions of the sponsor under Part 5, any reference to the sponsor in that Part shall, in relation to the trial, be construed as a reference to that person.

(10) Any reference to the sponsor in—

- (a) regulations 15 and 28(1),
- (b) Parts 2 and 6 to 9, and
- (c) Schedules 1 and 7, and Part 1 of Schedule 3,

shall, in relation to the trial, include a reference to a person specified in accordance with paragraph (5) or (6).

(11) A person who is a sponsor of a clinical trial in accordance with this regulation must—

- (a) be established in the European Community, or
- (b) have a legal representative who is so established.

### **Responsibility for functions under the Directive**

4.—(1) For the purposes of the Directive, the competent authority of the United Kingdom shall be the licensing authority.

(2) Subject to paragraph (3), the licensing authority shall perform, as respects the United Kingdom, the functions of the Member State under the Directive.

(3) Paragraph (2) shall not apply in so far as any functions fall to be performed by the exercise of any powers or duties which are conferred by any provision of these Regulations, or by any provision of the Act as applied by these Regulations, on a person or body other than the licensing authority.

## **PART 2**

### **ETHICS COMMITTEES**

#### **United Kingdom Ethics Committees Authority**

5.—(1) The body responsible for establishing, recognising and monitoring ethics committees in the United Kingdom in accordance with these Regulations is the United Kingdom Ethics Committees Authority, which is a body consisting of—

- (a) the Secretary of State for Health;
- (b) the National Assembly for Wales;
- (c) the Scottish Ministers; and
- (d) the Department for Health, Social Services and Public Safety for Northern Ireland.

(2) The functions of the Authority—

- (a) may, by agreement between them, be performed by any one of the Secretary of State for Health, the National Assembly for Wales, the Scottish Ministers and the Department for

Health, Social Services and Public Safety for Northern Ireland acting alone, or any two or more of them acting jointly; and

- (b) may be performed by any one of the Secretary of State for Health, the National Assembly for Wales, the Scottish Ministers and the Department for Health, Social Services and Public Safety for Northern Ireland acting alone solely in relation to a part of the United Kingdom with respect to which the Secretary of State, the Assembly, the Ministers or the Department, as the case may be, have responsibilities.

(3) In accordance with the preceding provisions of this regulation, in these Regulations “the United Kingdom Ethics Committees Authority” (“the Authority”) means any one or more of the Secretary of State for Health, the National Assembly for Wales, the Scottish Ministers and the Department for Health, Social Services and Public Safety for Northern Ireland, and, in the case of anything falling to be done by the Authority, means any one or more of them acting as mentioned in paragraph (2).

(4) The Authority may appoint such persons as they think necessary for the proper discharge by them of their functions, and those persons shall be appointed on such terms and conditions (including conditions as to remuneration, benefits, allowances and reimbursement for expenses) as the Authority think fit.

(5) Arrangements may be made between the Authority and any relevant authority for—

- (a) any functions of the Authority to be exercised by, or by members of staff of, the relevant authority; or
- (b) the provision of staff, premises or administrative services by the relevant authority to the Authority.

(6) Any arrangements under paragraph (5) for the exercise of any functions of the Authority shall not affect the responsibility of the Authority.

(7) In this regulation, “relevant authority” means any government department, local or public authority or holder of public office.

#### **Establishment of ethics committees**

6.—(1) The Authority may establish ethics committees to act—

- (a) for the entire United Kingdom or for such areas of the United Kingdom; and
- (b) in relation to such descriptions or classes of clinical trials,

as the Authority consider appropriate.

(2) The Authority may—

- (a) vary the area for which any committee they have established acts or, as the case may be, the descriptions or classes of clinical trials in relation to which such a committee acts; and
- (b) abolish any such committee.

#### **Recognition of ethics committees**

7.—(1) Subject to paragraph (3), the Authority may, by a notice in writing, recognise a committee as an ethics committee for the purposes of these Regulations if—

- (a) an application in relation to that committee has been made in accordance with paragraph (2); and
- (b) they are satisfied that the proposed arrangements for the membership and operation of that ethics committee would—

- (i) enable that committee to perform the functions of an ethics committee adequately; and
  - (ii) comply with the provisions of Schedule 2.
- (2) An application for recognition of an ethics committee shall be—
- (a) made in writing to the Authority; and
  - (b) accompanied by such information, documents and particulars as are necessary to enable the Authority to determine the application.
- (3) If any committee—
- (a) was established or recognised by—
    - (i) the Secretary of State,
    - (ii) the Scottish Ministers,
    - (iii) the National Assembly for Wales,
    - (iv) the Department of Health, Social Services and Public Safety, or
    - (v) a Strategic Health Authority, Health Board or Health and Social Services Board,
 for the purpose of advising on the ethics of research investigations on human beings, and
  - (b) was in existence on 30th April 2004,
- the Authority may recognise that committee in accordance with paragraph (1) without an application for recognition being submitted.
- (4) When recognising a committee the Authority shall specify—
- (a) whether the committee may act for the entire United Kingdom or only for a particular area of the United Kingdom;
  - (b) the description or class of clinical trial in relation to which it may act as an ethics committee; and
  - (c) any other conditions or limitations that apply to that committee.
- (5) The Authority may—
- (a) vary the area for which a committee recognised under this regulation acts,
  - (b) vary the description or class of clinical trial in relation to which it may act as an ethics committee, or
  - (c) vary or revoke any conditions or limitations imposed under paragraph (5),
- where it considers it necessary or appropriate to do so.

### **Revocation of recognition**

8. The Authority may revoke a recognition of an ethics committee if they are satisfied that—
- (a) the provisions of Schedule 2 are not complied with in relation to that committee;
  - (b) the committee is failing to perform its functions under these Regulations adequately or at all; or
  - (c) it is otherwise necessary or expedient to do so.

### **Constitution and operation of ethics committees**

9. The provisions of Schedule 2 have effect in relation to ethics committees.

### **Other functions of the Authority**

10.—(1) The Authority shall monitor the extent to which ethics committees adequately perform their functions under these Regulations.

(2) The Authority may provide advice and assistance to ethics committees with respect to the performance of their functions.

## **PART 3**

### **AUTHORISATION FOR CLINICAL TRIALS AND ETHICS COMMITTEE OPINION**

#### **Interpretation of Part 3**

11. In this Part—

“amendment to the clinical trial authorisation” means an amendment to—

- (a) the terms of the request for authorisation to conduct that trial or the application for an ethics committee opinion in relation to that trial,
- (b) the protocol for that trial, or
- (c) the other particulars or documents accompanying that request for authorisation or application for ethics committee approval;

“substantial amendment to the clinical trial authorisation” means an amendment to the clinical trial authorisation which is likely to affect to a significant degree—

- (a) the safety or physical or mental integrity of the subjects of the trial,
- (b) the scientific value of the trial,
- (c) the conduct or management of the trial, or
- (d) the quality or safety of any investigational medicinal product used in the trial;

“valid application” means an application for an ethics committee opinion which complies with the provisions of regulation 14; and

“valid request for authorisation” means a request to the licensing authority for authorisation to conduct a clinical trial which complies with the provisions of regulation 17, and “valid amended request” shall be construed accordingly.

#### **Requirement for authorisation and ethics committee opinion**

12.—(1) No person shall—

- (a) start a clinical trial or cause a clinical trial to be started; or
- (b) conduct a clinical trial,

unless the conditions specified in paragraph (3) are satisfied.

(2) No person shall—

- (a) recruit an individual to be a subject in a trial;
- (b) issue an advertisement for the purpose of recruiting individuals to be subjects in a trial,

unless the condition specified in paragraph (3)(a) has been satisfied.

(3) The conditions referred to in paragraphs (1) and (2) are—

- (a) an ethics committee or an appeal panel appointed under Schedule 4 has given a favourable opinion in relation to the clinical trial; and
  - (b) the clinical trial has been authorised by the licensing authority.
- (4) For the purposes of these Regulations, a clinical trial has been authorised by the licensing authority if—
- (a) in the case of a trial to which regulation 18 relates—
    - (i) the trial is to be treated as authorised by virtue of regulation 18, or
    - (ii) the authority has accepted the request for authorisation in accordance with the procedure specified in Schedule 5; or
  - (b) in the case of a clinical trial to which regulation 19 or 20 applies—
    - (i) the authority has given a notice of authorisation in accordance with those regulations, or
    - (ii) the authority has accepted the request for authorisation in accordance with the procedure specified in Schedule 5.

### **Supply of investigational medicinal products for the purpose of clinical trials**

**13.**—(1) Subject to paragraphs (3) and (4), no person shall, in the course of a business carried on by him, sell or supply any investigational medicinal product to—

- (a) an investigator,
- (b) a health care professional who is a member of an investigator's team,
- (c) a person who provides or is to provide health care under the direction or control of a person referred to in sub-paragraphs (a) and (b), or
- (d) a subject,

for the purpose of administering that product in a clinical trial, unless the conditions specified in paragraph (2) are satisfied.

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

- (a) the licensing authority has authorised the clinical trial for the purposes of which the product is sold or supplied;
- (b) in the case of an investigational medicinal product manufactured or assembled in an EEA State, other than in accordance with the terms of a marketing authorization relating to that product, or imported into an EEA State—
  - (i) the product has been manufactured, assembled or imported in accordance with the terms of—
    - (aa) a manufacturing authorisation, or
    - (bb) an authorisation referred to in Article 13 of the Directive granted by a competent authority of an EEA State other than the United Kingdom, and
  - (ii) the production batch of investigational medicinal products of which the product is a part has been checked and certified by a qualified person pursuant to Article 13(3) and (4) of the Directive.

(3) If an investigational medicinal product has been manufactured or imported prior to 1st May 2004—

- (a) the condition specified in paragraph (2)(b)(i) shall apply only in relation to any assembly of that product which takes place on or after that date; and
- (b) the conditions specified in paragraph (2)(b)(ii) shall not apply.

(4) The restriction in paragraph (1) shall not apply to the sale or supply of a medicinal product in accordance with the terms of a marketing authorisation relating to that product, other than a marketing authorisation issued by the competent authority of an EEA State other than the United Kingdom.

### **Application for ethics committee opinion**

**14.**—(1) An application for an ethics committee opinion in relation to a clinical trial shall be made by the chief investigator for that trial.

(2) A chief investigator for a trial shall make an application for an ethics committee opinion in relation to that trial to one ethics committee only, regardless of the number of trial sites at which the trial is to be conducted.

(3) Subject to paragraphs (4) and (5), the application for an ethics committee opinion in relation to a clinical trial shall be made to an ethics committee established or recognised—

- (a) for—
  - (i) the entire United Kingdom, or
  - (ii) in relation to an area of the United Kingdom in which the chief investigator is professionally based; and
- (b) in relation to a description or class of clinical trial into which the proposed trial falls.

(4) If a clinical trial—

- (a) is conducted at one or more trial sites in Scotland;
- (b) involves adults unable by virtue of physical or mental incapacity to give informed consent; and
- (c) the chief investigator is professionally based at a hospital, health centre, surgery or other establishment or facility in Scotland,

the application for an ethics committee opinion in relation to that trial shall be made to the Ethics Committee constituted by regulations made by the Scottish Ministers under section 51(6) of the Adults with Incapacity (Scotland) Act 2000<sup>(31)</sup>.

(5) An application for an ethics committee opinion in relation to a clinical trial involving medicinal products for gene therapy, other than a trial falling within paragraph (4), shall be made to the Gene Therapy Advisory Committee.

(6) An application shall be—

- (a) in writing;
- (b) signed by the chief investigator making the application; and
- (c) accompanied by the particulars and documents specified in Part 1 of Schedule 3.

(7) The application and any accompanying material shall be supplied in the English language.

(8) For the purposes of this regulation, a chief investigator is professionally based at the hospital, health centre, surgery or other establishment or facility at or from which he primarily conducts his professional practice.

### **Ethics committee opinion**

**15.**—(1) Subject to paragraphs (3) and (4), an ethics committee shall within the specified period following receipt of a valid application, give an opinion in relation to the clinical trial to which the application relates.

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<sup>(31)</sup> 2000 asp. 4; see S.S.I. 2002/190.

(2) Where following receipt of a valid application it appears to the committee that further information is required in order to give an opinion on a trial, the committee may, within the specified period and before giving its opinion, send a notice in writing to the applicant requesting that he furnishes the committee with that information.

(3) Where the committee sends a request in accordance with paragraph (2), the specified period shall be suspended pending receipt of the information requested.

(4) If the clinical trial involves a medicinal product for xenogenic cell therapy, the time limits referred to in paragraphs (1) to (3) shall not apply and the ethics committee may give an opinion in relation to that trial or send a notice under paragraph (2) at any time after receipt of the valid application.

(5) In preparing its opinion, the committee shall consider, in particular, the following matters—

- (a) the relevance of the clinical trial and its design;
- (b) whether the evaluation of the anticipated benefits and risks as required under paragraph 2 of Part 2 of Schedule 1 is satisfactory and whether the conclusions are justified;
- (c) the protocol;
- (d) the suitability of the investigator and supporting staff;
- (e) the investigator's brochure;
- (f) the quality of the facilities for the trial;
- (g) the adequacy and completeness of the written information to be given, and the procedure to be followed, for the purpose of obtaining informed consent to the subjects' participation in the trial;
- (h) if the subjects are to include persons incapable of giving informed consent, whether the research is justified having regard to the conditions and principles specified in Part 5 of Schedule 1;
- (i) provision for indemnity or compensation in the event of injury or death attributable to the clinical trial;
- (j) any insurance or indemnity to cover the liability of the investigator or sponsor;
- (k) the amounts, and, where appropriate, the arrangements, for rewarding or compensating investigators and subjects;
- (l) the terms of any agreement between the sponsor and the owner or occupier of the trial site which are relevant to the arrangements referred to in sub-paragraph (k); and
- (m) the arrangements for the recruitment of subjects.

(6) If—

- (a) any subject of the clinical trial is to be a minor; and
- (b) the committee does not have a member with professional expertise in paediatric care,

it shall, before giving its opinion, obtain advice on the clinical, ethical and psychosocial problems in the field of paediatric care which may arise in relation to that trial.

(7) If—

- (a) any subject to the clinical trial is to be an adult incapable by reason of physical and mental incapacity to give informed consent to participation in the trial; and
- (b) the committee does not have a member with professional expertise in the treatment of—
  - (i) the disease to which the trial relates, and
  - (ii) the patient population suffering that disease,



it shall, before giving its opinion, obtain advice on the clinical, ethical and psychosocial problems in the field of that disease and patient population which may arise in relation to that trial.

(8) The ethics committee shall consider, and give an opinion on, any other issue relating to the clinical trial, if—

- (a) the committee has been asked by the applicant to consider the issue;
- (b) it is, in the committee's opinion, relevant to the other matters considered by the committee in accordance with this regulation.

(9) Where an ethics committee gives an opinion in accordance with this regulation, it shall publish a summary of that opinion.

(10) In this regulation—

“the specified period” means—

- (a) in the case of a clinical trial involving a medicinal product for gene therapy or somatic cell therapy or a medicinal product containing a genetically modified organism—
  - (i) where a specialist group or committee is consulted, 180 days, or
  - (ii) where there is no such consultation, 90 days; or
- (b) in any other case, 60 days;

“specialist group or committee” means a group or committee whose functions include the provision of advice on ethical or scientific issues in relation to—

- (a) in the case of medicinal products for gene therapy or somatic cell therapy, the use of such therapies in the treatment of humans; or
- (b) in the case of medicinal products containing genetically modified organisms, the administration of such products to humans.

### **Review and appeal relating to ethics committee opinion**

**16.**—(1) This regulation applies where a chief investigator for a trial has been notified by the ethics committee to which he made an application in accordance with regulation 13 that the committee's opinion in relation to that trial is not favourable.

(2) This regulation does not apply in relation to an opinion given by—

- (a) the Ethics Committee constituted by regulations made by the Scottish Ministers under section 51(6) of the Adults with Incapacity (Scotland) Act 2000; or
- (b) an ethics committee pursuant to paragraph 2 of Schedule 4.

(3) Where the opinion was given by an ethics committee other than the Gene Therapy Advisory Committee, the chief investigator may within 90 days of being notified that the committee's opinion is not favourable, give a notice to the United Kingdom Ethics Committees Authority—

- (a) stating his wish to appeal against the opinion; and
- (b) setting out his representations with respect to that opinion.

(4) Where the opinion was given by the Gene Therapy Advisory Committee, the chief investigator may, within 14 days of being notified of that opinion—

- (a) give a notice in writing to the Committee requiring the Committee to review its opinion; or
- (b) give a notice in writing to the United Kingdom Ethics Committee Authority—
  - (i) stating his wish to appeal against the opinion; and
  - (ii) setting out his representations with respect to that opinion.

(5) Where the Gene Therapy Advisory Committee is required by a notice under paragraph (4) to review its opinion, it must do so within 60 days of receipt of the notice.

(6) On a review pursuant to paragraph (5), the Gene Therapy Advisory Committee may vary or confirm their opinion and shall give notice in writing to the chief investigator of the variation or confirmation.

(7) If the Gene Therapy Advisory Committee confirm their opinion pursuant to paragraph (6), a chief investigator may within the 14 days of being notified of the confirmation give notice in writing to the United Kingdom Ethics Committees Authority—

- (a) stating his wish to appeal against the Committee's opinion; and
- (b) setting out his representations with respect to that opinion

(8) Schedule 4 shall have effect to regulate the procedure where the Authority receives a notice in accordance with paragraph (3), (4) or (7).

### **Request for authorisation to conduct a clinical trial**

**17.—**(1) A request for authorisation to conduct a clinical trial shall be made to the licensing authority by the sponsor of the trial.

(2) A request shall—

- (a) be in writing and signed by or on behalf of the sponsor; and
- (b) be accompanied by—
  - (i) the particulars and documents specified in Part 2 of Schedule 3, and
  - (ii) any fee which may be payable in connection with that application under the Medicines (Products for Human Use—Fees) Regulations 1995<sup>(32)</sup>.

(3) The request and any accompanying material shall be supplied in the English language.

### **Authorisation procedure for clinical trials involving general medicinal products**

**18.—**(1) This regulation applies to clinical trials involving medicinal products other than those to which regulations 19 and 20 apply.

(2) The licensing authority may, within the period of 30 days from the date of receipt of a valid request for authorisation of a clinical trial to which this regulation applies, give written notice to the sponsor—

- (a) setting out the licensing authority's grounds for not accepting the request;
- (b) stating that the licensing authority accepts the request for authorisation; or
- (c) stating that the licensing authority accepts the request for authorisation, subject to the conditions specified in the notice.

(3) Subject to paragraph (4), if—

- (a) a notice is given in accordance with paragraph (2)(b); or
- (b) no notice is given in accordance with paragraph (2),

the clinical trial is to be treated as authorised.

(4) If a notice is given in accordance with paragraph (2)(c), the clinical trial is to be treated as authorised only if the conditions specified in the notice are satisfied.

(5) If the sponsor is given a notice in accordance with paragraph (2)(a) or (c), he may, within the period of 14 days, or such extended period as the licensing authority may in any particular case

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(32) S.I. 1995/1116.

allow, from the date on which the notice was received, send an amended request to the licensing authority for further consideration.

(6) The licensing authority shall consider a valid amended request and may, within the period of 60 days from the date on which the original request was received give a written notice to the sponsor—

- (a) setting out the licensing authority's grounds for not accepting the amended request;
- (b) stating that the licensing authority accepts the amended request; or
- (c) stating that the licensing authority accepts the amended request, subject to the conditions specified in the notice.

(7) Subject to paragraph (8), if a valid amended request has been received and—

- (a) a notice is given in accordance with paragraph (6)(b); or
- (b) no notice is given in accordance with paragraph (6),

the clinical trial is to be treated as authorised.

(8) If a valid amended request has been received and a notice is given in accordance with paragraph (6)(c), the clinical trial is to be treated as authorised only if the conditions specified in the notice are satisfied.

(9) If—

- (a) the licensing authority gives written notice to the sponsor of grounds for non-acceptance in accordance with paragraph (2)(a) and the sponsor does not submit an amended request in accordance with paragraph (5), or
- (b) the sponsor has submitted an amended request in accordance with paragraph (5), but the licensing authority gives written notice to the sponsor of grounds for non-acceptance in accordance with paragraph (6)(a),

the request is to be treated as rejected and the authority shall not consider any further amendments to the request.

#### **Authorisation procedure for clinical trials involving medicinal products for gene therapy etc.**

**19.—**(1) This regulation applies to clinical trials involving—

- (a) medicinal products for gene therapy and somatic cell therapy, including xenogenic cell therapy; or
- (b) medicinal products containing genetically modified organisms.

(2) Subject to the following provisions of this regulation, the licensing authority may, within the period of 30 days from the date of receipt of a valid request for authorisation of a clinical trial to which this regulation applies—

- (a) issue a written authorisation to the sponsor; or
- (b) give a notice in writing to the sponsor setting out the grounds for not accepting the request.

(3) The licensing authority shall not authorise a clinical trial involving products for gene therapy if the use of those products in that trial would result in modifications to any subject's germ line genetic identity.

(4) If the licensing authority considers that it is appropriate to do so, they may consult the relevant committee before deciding whether to authorise a clinical trial.

(5) Where the authority consults the relevant committee in accordance with paragraph (4), the period specified in paragraph (2) shall be extended by a further 90 days.

(6) Where a sponsor is given a notice in accordance with paragraph (2)(b), he may, within the period of 30 days, or such extended period as the licensing authority may in any particular case

allow, from the date on which the notice was received, send an amended request to the licensing authority for further consideration.

(7) The licensing authority shall consider a valid amended request and, not later than 90 days, or, in a case falling within paragraph (5), 180 days, from the date on which the original request was received—

- (a) issue a written authorisation to the sponsor; or
- (b) give a notice in writing to the sponsor setting out the grounds for not accepting the request.

(8) A written authorisation issued under this regulation may contain such conditions as the licensing authority consider appropriate.

(9) If the clinical trial involves a medicinal product for xenogenic cell therapy, the time limits set out in paragraphs (2), (5) and (7) shall not apply and the authority may issue an authorisation or notice under those paragraphs at any time after receipt of the request.

(10) In this regulation, “the relevant committee” means—

- (a) the Committee on Safety of Medicines<sup>(33)</sup>; or
- (b) such other body or committee as the licensing authority may consider appropriate in relation to the application under consideration.

#### **Authorisation procedure for clinical trials involving medicinal products with special characteristics**

**20.**—(1) This regulation applies to clinical trials—

- (a) involving medicinal products—
  - (i) which do not have a marketing authorization and are referred to in Part A of the Annex to Regulation (EEC) No. 2309/93<sup>(34)</sup>, or
  - (ii) which have an active ingredient—
    - (aa) that is a biological product of human or animal origin,
    - (bb) containing biological components of human or animal origin, or
    - (cc) the manufacturing of which requires such components,
 other than products falling within regulation 19; or
- (b) where the licensing authority, within 7 days from the date of receipt of a valid request for authorisation of the trial, issues a notice to the sponsor specifying that by virtue of the special characteristics of the medicinal product to which the trial relates, written authorisation for that trial is required.

(2) The licensing authority may, within the period of 30 days from the date of receipt of a valid request for authorisation of a clinical trial to which this regulation applies—

- (a) issue a written authorisation to the sponsor; or
- (b) give a notice in writing to the sponsor setting out the grounds for not authorising the trial.

(3) Where a sponsor is given a notice in accordance with paragraph (2)(b), he may, within the period of 14 days, or such extended period as the licensing authority may in any particular case allow, from the date on which the notice was received, send an amended request to the licensing authority for further consideration.

(4) The licensing authority shall consider a valid amended request and, not later than 60 days from the date on which the original request was received—

<sup>(33)</sup> The Committee on Safety of Medicines was established under section 4 of the Act, by [S.I. 1970/1257](#), for the purposes set out in that instrument.

<sup>(34)</sup> OJ No. L214, 24.8.93, p.1.

- (a) issue a written authorisation to the sponsor; or
  - (b) give a notice in writing to the sponsor setting out the grounds for not accepting the request.
- (5) A written authorisation issued under this regulation may contain such conditions as the licensing authority consider appropriate.

### **Clinical trials conducted in third countries**

**21.**—(1) If the licensing authority receives a valid request for authorisation relating to a clinical trial which is or is to be conducted in a third country as well as the United Kingdom, the licensing authority may, if they think fit, require the production by the sponsor of any one or more of the following—

- (a) an undertaking, given by the sponsor, to permit their premises in that country to be inspected by or on behalf of the licensing authority for the purpose of establishing whether the conditions and principles of good clinical practice are satisfied or adhered to in relation to that trial; or
- (b) an undertaking, given by the owner or occupier of any premises in that country at which the clinical trial is or is to be conducted, to permit those premises to be inspected by or on behalf of the licensing authority for the purpose of establishing whether the conditions and principles of good clinical practice are satisfied or adhered to in relation to that trial.

(2) If a sponsor fails to produce an undertaking required by the licensing authority in accordance with paragraph (1), that failure constitutes a ground for not accepting the request for authorisation, for the purposes of regulations 18 to 20.

### **Amendments to clinical trial authorisation**

**22.** Subject to regulation 30, an amendment to a clinical trial authorisation may be made—

- (a) by the licensing authority, in accordance with regulation 23; or
- (b) by the sponsor, in accordance with regulation 24 or 25.

### **Amendments by the licensing authority**

**23.**—(1) Subject to paragraphs (1) and (2), the licensing authority may make amendments to a clinical trial authorisation if it appears to the authority to be necessary to ensure—

- (a) the safety or scientific validity of the clinical trial; or
- (b) that the conditions and principles of good clinical practice are satisfied or adhered to in relation to the clinical trial.

(2) Where the licensing authority propose to make an amendment in accordance with paragraph (1), the authority shall, at least 14 days before the date on which it is proposed the amendment should take effect, serve a notice on the sponsor stating their proposal and the reasons for it.

(3) If, within 14 days of the date a notice is served in accordance with paragraph (2), the sponsor makes representations in writing to the licensing authority, the authority—

- (a) shall take those representations into account before deciding whether to make the amendment; and
- (b) may delay the date the proposed amendment is to take effect, in order to allow time for them to consider those representations.

**Amendments by the sponsor**

**24.**—(1) A sponsor may make an amendment to a clinical trial authorisation, other than a substantial amendment, at any time.

(2) A sponsor shall—

- (a) keep records of the amendments made in accordance with paragraph (1); and
- (b) send those records, or copies of such records, to the licensing authority, where the authority send him a notice in writing requiring him to provide those records, or copies of such records.

(3) If the sponsor proposes to make a substantial amendment to a clinical trial authorisation which consists of, or includes, an amendment to—

- (a) the terms of the request for authorisation of the clinical trial; or
- (b) the particulars or documents that accompanied that request,

he shall send a valid notice of amendment to the licensing authority, whether or not he is also required to send a notice in accordance with paragraph (4).

(4) If the sponsor proposes to make a substantial amendment to a clinical trial authorisation which consists of, or includes, an amendment to—

- (a) the terms of the application for an ethics committee opinion in relation to the clinical trial; or
- (b) the particulars or documents that accompanied that application,

he shall send a valid notice of amendment to the relevant ethics committee, whether or not he is also required to send a notice in accordance with paragraph (3).

(5) The licensing authority may, within the period of 35 days from the date of receipt of a valid notice of amendment, give written notice to the sponsor—

- (a) setting out the licensing authority's grounds for not accepting the proposed amendment; or
- (b) stating that the licensing authority accepts the application for amendment, subject to any conditions which may be specified in the notice.

(6) A relevant ethics committee shall, within the period of 35 days from the date of receipt of a valid notice of amendment, give an opinion to the sponsor.

(7) Subject to paragraph (8), if the sponsor has sent a notice in accordance with paragraph (3), he may make the amendment only if—

- (a) the licensing authority have given him a notice in accordance with paragraph (5)(b); or
- (b) no notice has been given by the licensing authority in accordance with paragraph (5).

(8) If the sponsor has been given a notice in accordance with paragraph (5)(b), he may make the amendment subject to the conditions, if any, specified in the notice.

(9) If the sponsor has sent a notice in accordance with paragraph (4), he may make the amendment only if the relevant ethics committee has given a favourable opinion.

(10) In this regulation—

“valid notice of amendment” means a notice that is—

- (a) in writing; and
- (b) accompanied by—
  - (i) the particulars specified in Part 3 of Schedule 3, and

- (ii) any fee which may be payable in connection with that notice under the Medicines (Products for Human Use—Fees) Regulations 1995(35).

### **Modifying or adapting rejected proposals for amendment**

25.—(1) Subject to the following provisions of this regulation, if—

- (a) the ethics committee opinion on a proposed amendment to the protocol is not favourable; or
- (b) the sponsor has been notified by the licensing authority of any grounds for non-acceptance of a proposed amendment to the protocol,

and it is possible to modify or adapt the proposed amendment in order to meet the concerns of ethics committee or the licensing authority as set out in the opinion or, as the case may be, the grounds for non-acceptance, the sponsor may amend the protocol accordingly.

(2) If a sponsor proposes to amend the protocol in accordance with paragraph (1), the sponsor shall, at least 14 days before the amendment is to be made, give a notice in writing to the licensing authority and the relevant ethics committee.

(3) The licensing authority may, within the period of 14 days from the date of receipt of a notice under paragraph (1), give written notice to the sponsor setting out the licensing authority's further grounds for not accepting the modified or adapted amendment.

(4) The relevant ethics committee may, within the period of 14 days from the date of receipt of a notice under paragraph (1), give a written notice to the sponsor stating that its opinion of the modified or adapted amendment is unfavourable.

(5) If—

- (a) the sponsor receives a written notice under paragraphs (3) or (4), he may not make the amendment; and
- (b) if he receives no such notice, he may make the modified or adapted amendment.

### **Reference to the appropriate committee or the Medicines Commission**

26.—(1) If—

- (a) a sponsor has been notified by the licensing authority that—
  - (i) there are grounds for not accepting a request for authorisation, or
  - (ii) in accordance with regulation 18(2) or (6), 19(8) or 20(5), the trial is authorised subject to specified conditions;
- (b) the licensing authority has amended a clinical trial authorisation under regulation 23; or
- (c) the sponsor who has been notified by the licensing authority in accordance with regulation 24(4) or 25(3) that—
  - (i) the authority does not accept a proposed, modified or adapted amendment to the clinical trial authorisation, or
  - (ii) the authority accepts such an amendment subject to conditions,

the sponsor may, within 28 days, or such extended period as the licensing authority may in any particular case allow, of the notice being given, give notice in writing to the licensing authority of his wish to make written or oral representations to the appropriate committee or, if for the time being there is no such committee, the Medicines Commission(36).

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(35) S.I. 1995/1116.

(36) See section 2 of the Act.

(2) Schedule 5 shall have effect to regulate the procedure for reference to the appropriate committee, or as the case may be, the Medicines Commission following receipt of a notice in accordance with paragraph (1).

### **Conclusion of clinical trial**

**27.**—(1) Subject to paragraph (2), within 90 days of the conclusion of a clinical trial the sponsor shall notify the licensing authority and the relevant ethics committee in writing that the trial has ended.

(2) If a trial is terminated—

- (a) before the date for the conclusion of the trial specified in the protocol for that trial, or
- (b) before the event specified in the protocol as the event which indicates the end of the trial has occurred,

the sponsor shall notify the licensing authority and the relevant ethics committee in writing of the termination of the trial within 15 days of the date of termination.

(3) A notification made in accordance with paragraphs (1) or (2) shall contain the particulars specified in Part 4 of Schedule 3.

## **PART 4**

### **GOOD CLINICAL PRACTICE AND THE CONDUCT OF CLINICAL TRIALS**

#### **Good clinical practice and protection of clinical trial subjects**

**28.**—(1) No person shall—

- (a) conduct a clinical trial; or
- (b) perform the functions of the sponsor of a clinical trial (whether that person is the sponsor or is acting under arrangements made with that sponsor),

otherwise than in accordance with the conditions and principles of good clinical practice.

(2) Subject to paragraph (5), the sponsor of a clinical trial shall put and keep in place arrangements for the purpose of ensuring that with regard to that trial the conditions and principles of good clinical practice are satisfied or adhered to.

(3) Subject to paragraphs (4) and (5), the sponsor of a clinical trial shall ensure that—

- (a) the investigational medicinal products used in the trial, and
- (b) any devices used for the administration of such products,

are made available to the subjects of the trial free of charge.

(4) The restriction in paragraph (3) shall not apply in relation to any charge payable by a subject under regulations made under—

- (a) the National Health Service Act 1977(**37**);
- (b) the National Health Service (Scotland) Act 1978(**38**); or
- (c) the Health and Personal Social Services (Northern Ireland) Order 1972(**39**),

in respect of any medicinal products or devices provided in pursuance of those Acts or that Order.

(37) 1977 c. 49.

(38) 1978 c. 29.

(39) S.I. 1972/1265 (N.I. 14).



(5) If—

- (a) a clinical trial is conducted at more than one trial site; and
- (b) the request for authorisation to conduct that trial specifies that in relation to one or more trial sites the duties of the sponsor under paragraphs (2) and (3) are to be performed by a person other than the sponsor,

those duties shall, in relation to that site or those sites, be performed by the person so specified.

#### **Conduct of trial in accordance with clinical trial authorisation etc.**

**29.** Subject to regulation 30, no person shall conduct a clinical trial otherwise than in accordance with—

- (a) the protocol relating to that trial, as may be amended from time to time in accordance with regulations 22 to 25;
- (b) the terms of—
  - (i) the request for authorisation to conduct that trial,
  - (ii) the application for an ethics committee opinion in relation to that trial, and
  - (iii) any particulars or documents, other than the protocol, accompanying that request or that application,as may be amended from time to time in accordance with regulations 22 to 25; and
- (c) any conditions imposed by the licensing authority under regulation 18(2) or (6), 19(8), 20(5), 24(4) or Schedule 5.

#### **Urgent safety measures**

**30.—**(1) The sponsor and investigator may take appropriate urgent safety measures in order to protect the subjects of a clinical trial against any immediate hazard to their health or safety.

(2) If measures are taken pursuant to paragraph (1), the sponsor shall immediately, and in any event no later than 3 days from the date the measures are taken, give written notice to the licensing authority and the relevant ethics committee of the measures taken and the circumstances giving rise to those measures.

#### **Suspension or termination of clinical trial**

**31.—**(1) If, in relation to a clinical trial—

- (a) the licensing authority have objective grounds for considering that—
  - (i) any condition, restriction or limitation which applies to the conduct of the trial and is set out in the request for authorisation or the particulars or documents accompanying that request, or
  - (ii) any condition imposed by the licensing authority under regulation 18(2) or (6), 19(8), 20(5), 24(4) or Schedule 5,is no longer satisfied (either generally or at a particular trial site); or
- (b) the licensing authority have information raising doubts about the safety or scientific validity of the trial, or the conduct of the trial at a particular trial site,

the licensing authority may, by a notice served in accordance with paragraph (2), require that the trial, or the conduct of the trial at a particular trial site, be suspended or terminated.

(2) A notice in accordance with paragraph (1) shall be served—

- (a) in a case where the suspension or termination applies to the trial generally, on—

- (i) the sponsor, or
  - (ii) the investigator at each trial site;
- (b) in a case where the suspension or termination applies to the conduct of a trial at a particular trial site, on—
  - (i) the sponsor, or
  - (ii) the investigator at that trial site.
- (3) The notice shall specify—
  - (a) whether the notice applies to the trial generally or to one or more of the trial sites;
  - (b) whether the notice requires suspension or termination of the trial;
  - (c) if the notice requires suspension of the trial—
    - (i) whether the suspension applies until further notice from the licensing authority or for such period as may be specified in the notice, and
    - (ii) any conditions which are to be satisfied before the trial or, as the case may be, the conduct of the trial at a particular site, may be recommenced; and
  - (d) whether suspension or termination is to take effect immediately on receipt of the notice or on such date as may be specified in the notice.
- (4) If the licensing authority issues a notice under paragraph (1), they shall forthwith inform—
  - (a) where the notice has not been served on the sponsor, the sponsor;
  - (b) competent authorities of each EEA State, other than the United Kingdom;
  - (c) the relevant ethics committee;
  - (d) the European Medicines Agency; and
  - (e) the European Commission.
- (5) Subject to paragraph (6), at least one week before issuing a notice under paragraph (1) the licensing authority shall, by a notice in writing to the sponsor or the investigator—
  - (a) inform him that the authority is minded to issue a notice suspending or terminating the trial, or the conduct of a trial at a particular site, and of the reasons why they are so minded; and
  - (b) advise him that they may, within one week of the date of the notice, furnish the authority with written representations as to whether the trial, or the conduct of the trial at a particular site, should be so suspended or terminated.
- (6) Paragraph (5) shall not apply where it appears to the licensing authority that there is an imminent risk to the health or safety of any of the subjects of the clinical trial.
- (7) A person on whom a notice has been served in accordance with paragraphs (1) and (2) may, within 28 days, or such extended period as the licensing authority may in any particular case allow, of the notice being given, give notice of his wish to make written or oral representations to the appropriate committee or, if for the time being there is no such committee, the Medicines Commission.
- (8) Schedule 5 shall have effect to regulate the procedure for reference to the appropriate committee or, as the case may be, the Medicines Commission<sup>(40)</sup> following receipt of a notice in accordance with paragraph (7).
- (9) Where the notice of suspension or termination is referred to an appropriate committee or the Medicines Commission it shall remain in force unless revoked in accordance with Schedule 5.

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<sup>(40)</sup> See section 2 of the Act.

## PART 5

### PHARMACOVIGILANCE

#### **Notification of adverse events**

**32.**—(1) An investigator shall report any serious adverse event which occurs in a subject at a trial site at which he is responsible for the conduct of a clinical trial immediately to the sponsor.

(2) An immediate report under paragraph (1) may be made orally or in writing.

(3) Following the immediate report of a serious adverse event, the investigator shall make a detailed written report on the event.

(4) Paragraphs (1) to (3) do not apply to serious adverse events specified in the protocol or the investigator's brochure as not requiring immediate reporting.

(5) Adverse events, other than those to which paragraphs (1) to (3) apply, that are identified in the protocol as critical to evaluations of the safety of the trial shall be reported to the sponsor in accordance with the reporting requirements, including the time periods for such reporting, specified in that protocol.

(6) The reports made under paragraphs (1), (3) and (5) shall identify each subject referred to in the report by a number assigned to that subject in accordance with the protocol for the trial.

(7) The number assigned to a subject in accordance with the protocol must be different from the number of any other subject in that trial, including any subject at a trial site outside the United Kingdom.

(8) Where the event reported under paragraph (1) or (5) consists of, or results in, the death of a subject, the investigator shall supply—

(a) the sponsor; and

(b) in any case where the death has been reported to the relevant ethics committee, that committee,

with any additional information requested by the sponsor or, as the case may be, the committee.

(9) The sponsor shall keep detailed records of all adverse events relating to a clinical trial which are reported to him by the investigators for that trial.

(10) The licensing authority may, by sending a notice in writing to the sponsor, require him to send the records referred to in paragraph (9), or copies of such records, to the authority.

#### **Notification of suspected unexpected serious adverse reactions**

**33.**—(1) A sponsor shall ensure that all relevant information about a suspected unexpected serious adverse reaction which occurs during the course of a clinical trial in the United Kingdom and is fatal or life-threatening is—

(a) recorded; and

(b) reported as soon as possible to—

(i) the licensing authority,

(ii) the competent authorities of any EEA State, other than the United Kingdom, in which the trial is being conducted, and

(iii) the relevant ethics committee,

and in any event not later than 7 days after the sponsor was first aware of the reaction.

(2) A sponsor shall ensure that within 8 days of a report in accordance with paragraph (1)(b), any additional relevant information is sent to the persons or bodies listed in that paragraph.

(3) A sponsor shall ensure that a suspected unexpected serious adverse reaction which occurs during the course of a clinical trial in the United Kingdom, other than those referred to in paragraph (1), is reported as soon as possible to—

- (a) the licensing authority;
- (b) the competent authorities of any EEA State, other than the United Kingdom, in which the trial is being conducted; and
- (c) the relevant ethics committee,

and in any event not later than 15 days after the sponsor is first aware of the reaction.

(4) For the purposes of paragraphs (1) to (3), the sponsor may fulfil his obligations to report or provide information to the licensing authority and the competent authorities of any EEA State, other than the United Kingdom, by entering the report or information in the European database established in accordance with Article 11 of the Directive.

(5) A sponsor shall ensure that, in relation to each clinical trial in the United Kingdom for which he is the sponsor, the investigators responsible for the conduct of a trial are informed of any suspected unexpected serious adverse reaction which occurs in relation to an investigational medicinal product used in that trial, whether that reaction occurs during the course of that trial or another trial for which the sponsor is responsible.

(6) The licensing authority shall—

- (a) keep a record of all suspected unexpected serious adverse reactions relating to an investigational medicinal product which are brought to its attention, whether pursuant to paragraphs (1) or (3) or otherwise; and
- (b) ensure that the details of those reactions are entered in the European database established in accordance with Article 11 of the Directive, whether by the sponsor or the authority.

### **Clinical trials conducted in third countries**

**34.** If a clinical trial is being conducted at a trial site in a third country in addition to sites in the United Kingdom, the sponsor of that trial shall ensure that all suspected unexpected serious adverse reactions occurring at that site are entered into the European database established in accordance with Article 11 of the Directive.

### **Annual list of suspected serious adverse reactions and safety report**

**35.—(1)** As soon as practicable after the end of the reporting year, a sponsor shall, in relation to each investigational medicinal product tested in clinical trials in the United Kingdom for which he is the sponsor furnish the licensing authority and the relevant ethics committees with—

- (a) a list of all the suspected serious adverse reactions which have occurred during that year in relation to—
  - (i) those trials, whether at trial sites in the United Kingdom or elsewhere, or
  - (ii) any other trials relating to that product which are conducted outside the United Kingdom and for which he is the sponsor,

including those reactions relating to any investigational medicinal product used as a placebo or as a reference in those trials; and

- (b) a report on the safety of the subjects of those trials.

(2) In paragraph (1), “reporting year”, in relation to an investigational medicinal product, means the year ending on the anniversary of—

- (a) in the case of a product which has a marketing authorization, the earliest date on which any such authorization relating to that product was granted or issued; or

- (b) in any other case, the earliest date on which any clinical trial—
  - (i) relating to that product, and
  - (ii) for which the person responsible for making the report was the sponsor, was authorised in an EEA State.
- (3) For the purposes of paragraph (2)(b), the date on which a clinical trial was authorised in an EEA State is—
  - (a) in the case of the United Kingdom, the date on which the trial was authorised by the licensing authority in accordance with these Regulations, or
  - (b) in the case of any other EEA State, the date on which the trial was authorised by the competent authority of that EEA State in accordance with the Directive.

## 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(41).

(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—

- (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<sup>(42)</sup>.

(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—

<sup>(42)</sup> 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.



- (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,
    - (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(43); 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;
  - (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.

## PART 7

### LABELLING OF INVESTIGATIONAL MEDICINAL PRODUCTS

#### Labelling

**46.**—(1) An investigational medicinal product shall be labelled in accordance with Article 15 of Commission Directive [2003/94/EC](#)(**44**).

(2) Paragraph (1) shall not apply where the investigational medicinal product is—

- (a) for use in a clinical trial with the characteristics specified in the second paragraph of Article 14 of the Directive;
- (b) dispensed to a subject in accordance with a prescription given by an authorised health care professional; and
- (c) labelled in accordance with the requirements of Schedule 5 to the Medicines for Human Use (Marketing Authorisations Etc.) Regulations 1994(**45**) that apply in relation to dispensed relevant medicinal products.

## PART 8

### ENFORCEMENT AND RELATED PROVISIONS

#### Application of enforcement provisions of the Act

**47.**—(1) Sections 107 to 116, 118, 119, 121 to 125, 127, 129, 131 and 132(1) of, and Schedule 3 to, the Act shall apply for the purposes of these Regulations, but with the modifications specified in Schedule 9.

(2) In those provisions as applying by virtue of paragraph (1), a reference to any part of those provisions or a part of any of them is a reference to the provision or part as so applying.

#### Infringement notices

**48.**—(1) If an enforcement authority have objective grounds for considering that any person has contravened any provision to which this regulation applies, they may serve upon that person a notice in writing (in these Regulations referred to as an “infringement notice”)—

- (a) informing him of the authority’s grounds for considering that the person has contravened one or more of those provisions;
- (b) specifying the relevant provision of these Regulations;
- (c) specifying the measures which the person must take in order to ensure that the contravention does not continue or, as the case may be, does not recur;
- (d) requiring the person to take those measures, within such period as may be specified in the notice;
- (e) warning the person that unless the requirements of sub-paragraph (d) are met, further action may be taken in respect of the contravention.

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(44) OJ No. L262, 14.10.2003, p.22.

(45) S.I. 1994/3144; Schedule 5 was amended by S.I. 1998/3105, 2000/292 and 2002/542; “dispensed relevant medicinal product” is defined in paragraph 1 of Schedule 5.

(2) An infringement notice may include directions as to the measures to be taken by the person on whom the notice is served to ensure that the contravention does not continue or, as the case may be, does not recur, including the different ways of securing compliance.

(3) If an enforcement authority serves an infringement notice in accordance with paragraph (1), they shall forthwith inform—

- (a) the competent authorities of each EEA State, other than the United Kingdom;
- (b) the relevant ethics committee; and
- (c) the European Commission.

(4) This regulation applies to regulations 22(b), 27, 28(1) to (3), 29, 30(2) and 32 to 35.

(5) In this regulation, “enforcement authority” means any Minister or body on whom a duty or power to enforce any provisions of these Regulations is imposed or conferred by or under sections 108 to 110 of the Act as applied by regulation 47.

## **Offences**

**49.**—(1) Any person who contravenes any of the following provisions—

- (a) regulation 12(1) and (2);
- (b) regulation 13(1);
- (c) regulation 27;
- (d) regulation 28(1) to (3);
- (e) regulation 29;
- (f) regulation 30(2);
- (g) regulation 32(1), (3), and (5) to (9)
- (h) regulation 33(1) to (5)
- (i) regulation 34
- (j) regulation 35(1);
- (k) regulation 36(1);
- (l) regulation 42; and
- (m) regulation 43(1) and (6),

shall be guilty of an offence.

(2) Any person who has in his possession a medicinal product for the purpose of selling or supplying it in contravention of regulation 13(1) shall be guilty of an offence.

(3) Any person who fails to comply with a notice of suspension or termination served on him under regulation 31, unless that notice has been withdrawn or revoked by the licensing authority, shall be guilty of an offence.

(4) Where an investigational medicinal product is manufactured, assembled or imported in contravention of regulation 36(1), any person who sells or supplies the product for the purposes of a clinical trial knowing or having reasonable cause to suspect that it was so manufactured, assembled or imported shall be guilty of offence.

(5) Where an investigational medicinal product is imported in contravention of regulation 36(1), any person who, otherwise than for the purpose of performing or exercising a duty or power imposed or conferred by or under these Regulations, the Act or any other enactment, is in possession of the product knowing or having reasonable cause to suspect that it was so imported shall be guilty of offence.

(6) Any sponsor who sells or supplies, or procures the sale or supply, of an investigational medicinal product—

- (a) to a subject for the purposes of a clinical trial; or
- (b) to a person for the purpose of administering the product to such a subject,

the labelling of which does not comply with regulation 46, shall be guilty of an offence.

(7) Any person who sells or supplies an investigational medicinal product—

- (a) to a subject for the purposes of a clinical trial; or
- (b) to a person for the purpose of administering the product to such a subject,

the labelling of which does not comply with regulation 46, knowing, or having reasonable cause to believe, that the labelling does not so comply, shall be guilty of an offence.

### **False or misleading information**

**50.**—(1) Any person who in the course of—

- (a) making an application for an ethics committee opinion;
- (b) making a request for authorisation to conduct a clinical trial; or
- (c) making an application for the grant or variation of a manufacturing authorisation,

provides to the licensing authority or an ethics committee any relevant information which is false or misleading in a material particular shall be guilty of an offence.

(2) Any person who—

- (a) is conducting a clinical trial authorised in accordance with these Regulations;
- (b) is a sponsor of such a clinical trial;
- (c) while acting under arrangements made with a sponsor of such a clinical trial, performs the functions of that sponsor; or
- (d) holds a manufacturing authorisation,

and who, for the purposes of these Regulations, provides to the licensing authority or an ethics committee any relevant information which is false or misleading in a material particular shall be guilty of an offence.

(3) Any person who, for the purpose of being engaged as a qualified person in accordance with regulation 43, provides to the licensing authority or to the holder of a manufacturing authorisation any information which is false or misleading in a material particular shall be guilty of an offence.

(4) In this regulation, “relevant information” means any information which is relevant to an evaluation of—

- (a) the safety, quality or efficacy of an investigational medicinal product;
- (b) the safety or scientific validity of a clinical trial; or
- (c) whether, with regard to a clinical trial, the conditions and principles of good clinical practice are being satisfied or adhered to.

### **Defence of due diligence**

**51.**—(1) A person does not commit an offence under these Regulations if he took all reasonable precautions and exercised all due diligence to avoid the commission of that offence.

(2) Where evidence is adduced which is sufficient to raise an issue with respect to that defence, the court or jury shall assume that the defence is satisfied unless the prosecution proves beyond reasonable doubt that it is not.

## **Penalties**

- 52.** A person guilty of an offence under these Regulations shall be liable—
- (a) on summary conviction to a fine not exceeding the statutory maximum or to imprisonment for a term not exceeding three months or to both;
  - (b) on conviction on indictment to a fine or to imprisonment for a term not exceeding two years or to both.

## **PART 9**

### **MISCELLANEOUS PROVISIONS**

#### **Construction of references to specified publications**

**53.—**(1) Where any authorisation granted under these Regulations refers to a specified publication, but not to any particular edition of that publication, then, for the purpose of determining whether anything done, at a time when the authorisation is in force, is done in accordance with the authorisation, the reference shall, unless the authorisation otherwise expressly provides, be construed as a reference to the current edition of that publication as in force at that time.

(2) In this regulation any reference to the current edition of a specified publication as in force at a particular time is a reference to the edition of that publication in force, under whatever title, at that time together with any amendments, additions and deletions made to it up to that time.

(3) In this regulation, “specified publication” has the meaning given by section 103(1) of the Act<sup>(46)</sup>.

#### **Consequential and other amendments to enactments**

- 54.** The provisions of the enactments specified in Schedule 10 are amended as there specified.

#### **Revocations**

**55.** The enactments specified in column (1) of Schedule 11 are revoked to the extent specified in column (3) of that Schedule.

#### **Transitional provisions**

- 56.** The transitional provisions set out in Schedule 12 shall have effect.

Signed by authority of the Secretary of State for Health

31st March 2004

*Warner*  
Parliamentary Under Secretary of State,  
Department of Health

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<sup>(46)</sup> Section 103 was amended by section 22(1) of the Health and Medicines Act 1988 (c. 49).

SCHEDULE 1

Regulation 2(1)

CONDITIONS AND PRINCIPLES OF GOOD CLINICAL PRACTICE  
AND FOR THE PROTECTION OF CLINICAL TRIAL SUBJECTS

PART 1

APPLICATION AND INTERPRETATION

1.—(1) The conditions and principles specified in Part 2 apply to all clinical trials.

(2) If any subject of a clinical trial is—

- (a) an adult able to give informed consent, or
- (b) an adult who has given informed consent to taking part in the clinical trial prior to the onset of incapacity,

the conditions and principles specified in Part 3 apply in relation to that subject.

(3) If any subject of a clinical trial is a minor, the conditions and principles specified in Part 4 apply in relation to that subject.

(4) If any subject—

- (a) is an adult unable by virtue of physical or mental incapacity to give informed consent, and
- (b) did not, prior to the onset of incapacity, give or refuse to give informed consent to taking part in the clinical trial,

the conditions and principles specified in Part 5 apply in relation to that subject.

(5) If any person—

- (a) is an adult unable by virtue of physical or mental incapacity to give informed consent, and
- (b) has, prior to the onset of incapacity, refused to give informed consent to taking part in the clinical trial,

that person cannot be included as a subject in the clinical trial.

2. In this Schedule—

“Declaration of Helsinki” means the Declaration of Helsinki adopted by the World Medical Assembly in June 1964, as amended by the General Assembly of the Association in October 1975, October 1983, September 1989 and October 1996;

“guardian” shall be construed in accordance with section 51(8) of the Adults with Incapacity (Scotland) Act 2000<sup>(47)</sup>;

“legal representative” means, in relation to a minor or to an adult unable by virtue of physical or mental incapacity to give informed consent, and who is, or is being considered as, a subject for a clinical trial—

- (a) in relation to adults and minors in England, Wales and Northern Ireland, and minors in Scotland—
  - (i) a person, other than a person involved in the conduct of the trial, who—
    - (aa) by virtue of their relationship with that adult or that minor, is suitable to act as their legal representative for the purposes of that trial, and
    - (bb) is available and willing to so act for those purposes, or

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<sup>(47)</sup> 2000 asp 4.

*Status: This is the original version (as it was originally made).*

- (ii) if there is no such person, a person, other than a person connected with the conduct of the clinical trial, who is—
  - (aa) the doctor primarily responsible for the medical treatment provided to that adult, or
  - (bb) a person nominated by the relevant health care provider; and
- (b) in relation to adults in Scotland—
  - (i) any guardian or welfare attorney who has power to consent to the adult’s participation in research, or
  - (ii) if there is no such guardian or welfare attorney, the adult’s nearest relative, or
  - (iii) if it is not reasonably practicable to contact a guardian or welfare attorney or the adult’s nearest relative before the decision to enter the adult as a subject of the clinical trial is made, a person, other than a person connected with the conduct of the clinical trial, who is—
    - (aa) the doctor primarily responsible for the medical treatment provided to that adult, or
    - (bb) a person nominated by the relevant health care provider;

“nearest relative” has the meaning given by section 87(1) of the Adults with Incapacity (Scotland) Act 2000;

“parental responsibility”—

- (a) in relation to England and Wales, has the same meaning as in the Children Act 1989<sup>(48)</sup>,
- (b) in relation to Scotland, has the same meaning as in the Children (Scotland) Act 1985<sup>(49)</sup>, and
- (c) in relation to Northern Ireland, has the same meaning as in the Children (Northern Ireland) Order 1995<sup>(50)</sup>;

“person connected with the conduct of the trial” means—

- (a) the sponsor of the trial,
- (b) a person employed or engaged by, or acting under arrangements made with, the sponsor and who undertakes activities in connection with the management of the trial,
- (c) an investigator for the trial,
- (d) a health care professional who is a member of an investigator’s team for the purposes of the trial, or
- (e) a person who provides health care under the direction or control of a person referred to in paragraphs (c) and (d) above, whether in the course of the trial or otherwise;

“relevant health care provider” means—

- (a) in relation to a person receiving services in pursuance of the National Health Service Act 1977<sup>(51)</sup>, the National Health Service (Scotland) Act 1978<sup>(52)</sup>, or the Health and Personal Social Services (Northern Ireland) Order 1972<sup>(53)</sup>—
  - (i) in a case where a health service body is providing those services, that body, or

<sup>(48)</sup> 1989 c. 41; *see*, in particular, sections 3(1) and 5(6).

<sup>(49)</sup> 1995 c. 36; *see*, in particular, sections 1(3) and 7(5).

<sup>(50)</sup> S.I. 1995/755 (N.I.2); *see*, in particular, article 6.

<sup>(51)</sup> 1977 c. 49.

<sup>(52)</sup> 1978 c. 29.

<sup>(53)</sup> S.I. 1972/1265 (N.I. 14).



- (ii) in any other case, the health service body which entered the arrangements under which those services are provided, or
  - (b) in relation to any other person receiving health care, the person primarily responsible for providing that health care; and
- “welfare attorney” shall be construed in accordance with section 51(8) of the Adults with Incapacity (Scotland) Act 2000.

**3.—(1)** For the purposes of this Schedule, a person gives informed consent to take part, or that a subject is to take part, in a clinical trial only if his decision—

- (a) is given freely after that person is informed of the nature, significance, implications and risks of the trial; and
  - (b) either—
    - (i) is evidenced in writing, dated and signed, or otherwise marked, by that person so as to indicate his consent, or
    - (ii) if the person is unable to sign or to mark a document so as to indicate his consent, is given orally in the presence of at least one witness and recorded in writing.
- (2) For the purposes of this Schedule, references to informed consent—
- (a) shall be construed in accordance with paragraph (1); and
  - (b) include references to informed consent given or refused by an adult unable by virtue of physical or mental incapacity to give informed consent, prior to the onset of that incapacity.

## PART 2

### CONDITIONS AND PRINCIPLES WHICH APPLY TO ALL CLINICAL TRIALS

#### **Principles based on International Conference on Harmonisation GCP Guideline(54)**

**1.** Clinical trials shall be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with good clinical practice and the requirements of these Regulations.

**2.** Before the trial is initiated, foreseeable risks and inconveniences have been weighed against the anticipated benefit for the individual trial subject and other present and future patients. A trial should be initiated and continued only if the anticipated benefits justify the risks.

**3.** The rights, safety, and well-being of the trial subjects are the most important considerations and shall prevail over interests of science and society .

**4.** The available non-clinical and clinical information on an investigational medicinal product shall be adequate to support the clinical trial.

**5.** Clinical trials shall be scientifically sound, and described in a clear, detailed protocol.

**6.** A trial shall be conducted in compliance with the protocol that has a favourable opinion from an ethics committee.

**7.** The medical care given to, and medical decisions made on behalf of, subjects shall always be the responsibility of an appropriately qualified doctor or, when appropriate, of a qualified dentist.

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(54) See Section 2 of the Note for Guideline on Good Clinical Practice (CPMP/ICH/135/95) published by the European Agency for the Evaluation of Medicinal Products in July 2002.

*Status: This is the original version (as it was originally made).*

8. Each individual involved in conducting a trial shall be qualified by education, training, and experience to perform his or her respective task(s).
9. Subject to the other provisions of this Schedule relating to consent, freely given informed consent shall be obtained from every subject prior to clinical trial participation.
10. All clinical trial information shall be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.
11. The confidentiality of records that could identify subjects shall be protected, respecting the privacy and confidentiality rules in accordance with the requirements of the Data Protection Act 1998 and the law relating to confidentiality.
12. Investigational medicinal products used in the trial shall be—
  - (a) manufactured or imported, and handled and stored, in accordance with the principles and guidelines of good manufacturing practice, and
  - (b) used in accordance with the approved protocol.
13. Systems with procedures that assure the quality of every aspect of the trial shall be implemented.

**Conditions based on Article 3 of the Directive**

14. A trial shall be initiated only if an ethics committee and the licensing authority comes to the conclusion that the anticipated therapeutic and public health benefits justify the risks and may be continued only if compliance with this requirement is permanently monitored.
15. The rights of each subject to physical and mental integrity, to privacy and to the protection of the data concerning him in accordance with the Data Protection Act 1998 are safeguarded.
16. Provision has been made for insurance or indemnity to cover the liability of the investigator and sponsor which may arise in relation to the clinical trial.

**PART 3**

**CONDITIONS WHICH APPLY IN RELATION TO AN  
ADULT ABLE TO CONSENT OR WHO HAS GIVEN  
CONSENT PRIOR TO THE ONSET OF INCAPACITY**

1. The subject has had an interview with the investigator, or another member of the investigating team, in which he has been given the opportunity to understand the objectives, risks and inconveniences of the trial and the conditions under which it is to be conducted.
2. The subject has been informed of his right to withdraw from the trial at any time.
3. The subject has given his informed consent to taking part in the trial.
4. The subject may, without being subject to any resulting detriment, withdraw from the clinical trial at any time by revoking his informed consent.
5. The subject has been provided with a contact point where he may obtain further information about the trial.

## PART 4

### CONDITIONS AND PRINCIPLES WHICH APPLY IN RELATION TO A MINOR

#### Conditions

1. Subject to paragraph 6, a person with parental responsibility for the minor or, if by reason of the emergency nature of the treatment provided as part of the trial no such person can be contacted prior to the proposed inclusion of the subject in the trial, a legal representative for the minor has had an interview with the investigator, or another member of the investigating team, in which he has been given the opportunity to understand the objectives, risks and inconveniences of the trial and the conditions under which it is to be conducted.

2. That person or legal representative has been provided with a contact point where he may obtain further information about the trial.

3. That person or legal representative has been informed of the right to withdraw the minor from the trial at any time.

4. That person or legal representative has given his informed consent to the minor taking part in the trial.

5. That person with parental responsibility or the legal representative may, without the minor being subject to any resulting detriment, withdraw the minor from the trial at any time by revoking his informed consent.

6. The minor has received information according to his capacity of understanding, from staff with experience with minors, regarding the trial, its risks and its benefits.

7. The explicit wish of a minor who is capable of forming an opinion and assessing the information referred to in the previous paragraph to refuse participation in, or to be withdrawn from, the clinical trial at any time is considered by the investigator.

8. No incentives or financial inducements are given—

(a) to the minor; or

(b) to a person with parental responsibility for that minor or, as the case may be, the minor's legal representative,

except provision for compensation in the event of injury or loss.

9. The clinical trial relates directly to a clinical condition from which the minor suffers or is of such a nature that it can only be carried out on minors.

10. Some direct benefit for the group of patients involved in the clinical trial is to be obtained from that trial.

11. The clinical trial is necessary to validate data obtained—

(a) in other clinical trials involving persons able to give informed consent, or

(b) by other research methods.

12. The corresponding scientific guidelines of the European Medicines Agency are followed.

#### Principles

13. Informed consent given by a person with parental responsibility or a legal representative to a minor taking part in a clinical trial shall represent the minor's presumed will.

*Status: This is the original version (as it was originally made).*

14. The clinical trial has been designed to minimise pain, discomfort, fear and any other foreseeable risk in relation to the disease and the minor's stage of development.

15. The risk threshold and the degree of distress have to be specially defined and constantly monitored.

16. The interests of the patient always prevail over those of science and society.

## PART 5

### CONDITIONS AND PRINCIPLES WHICH APPLY IN RELATION TO AN INCAPACITATED ADULT

#### Conditions

1. The subject's legal representative has had an interview with the investigator, or another member of the investigating team, in which he has been given the opportunity to understand the objectives, risks and inconveniences of the trial and the conditions under which it is to be conducted.

2. The legal representative has been provided with a contact point where he may obtain further information about the trial.

3. The legal representative has been informed of the right to withdraw the subject from the trial at any time.

4. The legal representative has given his informed consent to the subject taking part in the trial.

5. The legal representative may, without the subject being subject to any resulting detriment, withdraw the subject from the trial at any time by revoking his informed consent.

6. The subject has received information according to his capacity of understanding regarding the trial, its risks and its benefits.

7. The explicit wish of a subject who is capable of forming an opinion and assessing the information referred to in the previous paragraph to refuse participation in, or to be withdrawn from, the clinical trial at any time is considered by the investigator.

8. No incentives or financial inducements are given to the subject or their legal representative, except provision for compensation in the event of injury or loss.

9. There are grounds for expecting that administering the medicinal product to be tested in the trial will produce a benefit to the subject outweighing the risks or produce no risk at all.

10. The clinical trial is essential to validate data obtained—

(a) in other clinical trials involving persons able to give informed consent, or

(b) by other research methods.

11. The clinical trial relates directly to a life-threatening or debilitating clinical condition from which the subject suffers.

#### Principles

12. Informed consent given by a legal representative to an incapacitated adult in a clinical trial shall represent that adult's presumed will.

13. The clinical trial has been designed to minimise pain, discomfort, fear and any other foreseeable risk in relation to the disease and the cognitive abilities of the patient.

14. The risk threshold and the degree of distress have to be specially defined and constantly monitored.

15. The interests of the patient always prevail over those of science and society.

## SCHEDULE 2

Regulations 7(1)(b), 8(a) and 9

### ADDITIONAL PROVISIONS RELATING TO ETHICS COMMITTEES

#### Interpretation

1. In this Schedule—

“appointing authority” means—

- (a) in relation to an ethics committee established under regulation 6, the Authority,
- (b) in relation to an ethics committee recognised by the Authority after an application in accordance with regulation 7(1), the person who applied for recognition, or
- (c) in relation to an ethics committee recognised without an application for recognition being submitted in accordance with regulation 7(3), the Authority;

“expert member” means a member of an ethics committee who—

- (a) is a health care professional,
- (b) has professional qualifications or experience relating to the conduct of, or use of statistics in clinical trials, unless those professional qualifications or experience relate only to the ethics of clinical research or medical treatment, or
- (c) is not a health care professional, but has been a registered medical practitioner or a person registered in the dentists register under the Dentists Act 1984;

“financial year” means the twelve months ending with 31st March; and

“lay member” means a member of an ethics committee, other than an expert member.

#### Application of provisions of the Schedule

2.—(1) The provisions of this Schedule shall not apply in relation to the Ethics Committee constituted by regulations made by the Scottish Ministers under section 51(6) of the Adults with Incapacity (Scotland) Act 2000.

(2) The provisions of this Schedule, other than paragraph 13, shall not apply before 1st May 2005 in relation to an ethics committee established or recognised solely for the purpose of considering Phase I trials.

#### Membership

3.—(1) An ethics committee shall consist of—

- (a) expert members; and
- (b) lay members.

(2) An ethics committee shall have no more than 18 members.

(3) Subject to paragraph 7, the members of an ethics committee shall be appointed by the appointing authority.

*Status: This is the original version (as it was originally made).*

(4) A person shall not be eligible for appointment as a lay member of an ethics committee if, in the course of his employment or business, he—

- (a) provides medical, dental or nursing care, or
- (b) conducts clinical research.

(5) An appointing authority shall, in relation to an ethics committee, exercise their power under sub-paragraph (3) so as to ensure that—

- (a) at least one third of the total membership shall be lay members; and
- (b) at least half of the lay members must be persons who are not, or who never have been—
  - (i) health care professionals,
  - (ii) persons involved in the conduct of clinical research, other than as a subject of such research, or
  - (iii) a chairman, member or director of—
    - (aa) a health service body, or
    - (bb) a body, other than a health service body, which provides health care.

4. A member of an ethics committee shall hold and vacate office as a member in accordance with the terms of the instrument appointing him as a member.

#### **Chairman, vice-chairman and alternate vice-chairman**

5.—(1) The appointing authority shall appoint—

- (a) one of the members of each ethics committee to be chairman of the committee;
- (b) another member to be vice-chairman; and
- (c) another member to be alternate vice-chairman.

(2) The members appointed as chairman, vice-chairman and alternate vice-chairman shall each be appointed for such period, not exceeding the remainder of his term as a member, as the appointing authority may specify on appointing him.

(3) Any member so appointed may at any time resign from the office of chairman, vice-chairman or alternate vice-chairman.

(4) Where the chairman has died or has ceased to hold office, or where he is unable to perform his duties as chairman owing to illness, absence or any other cause, references to the chairman in this Schedule shall, so long as there is no chairman available to perform his duties, be taken to include references to—

- (a) the vice-chairman;
- (b) if the vice-chairman is also is unable to perform his duties, the alternate vice-chairman; or
- (c) if all three individuals are unavailable, a member appointed by the appointing authority for the purposes of acting as chairman until one of those individuals is available to perform his duties.

#### **Committees, meetings and proceedings**

6.—(1) An ethics committee may—

- (a) appoint sub-committees consisting of members of the committee; and
- (b) make arrangements for the exercise, on behalf of the committee, of any of its functions by such a sub-committee,

in accordance with the standing orders and operating procedures adopted under sub-paragraph (3).

(2) Subject to sub-paragraph (4), the meetings and proceedings of an ethics committee and its sub-committees shall be conducted in accordance with the standing orders made, and standing operating procedures adopted, under sub-paragraph (3).

(3) An ethics committee—

(a) shall, subject to approval by the Authority, make standing orders, and adopt standing operating procedures, for the regulation of its proceedings and business; and

(b) may, subject to approval by the Authority, vary or revoke such orders or procedures, including provision for the suspension of the standing orders or operating procedures or any of them.

(4) No business shall be transacted at a meeting of an ethics committee, or a sub-committee of an ethics committee, to determine, in accordance with regulation 15, the opinion of an ethics committee in relation to a clinical trial, unless at least seven members of the committee (including any members co-opted under paragraph 8) are present, including at least—

(a) one lay member who is not and never has been—

(i) a health care professional, or

(ii) a chairman, member, director, officer or employee of a health service body; and

(b) one expert member.

#### **Deputies and co-opted members**

7.—(1) An ethics committee may appoint a person to act as the deputy of an expert member or a lay member provided that the person would be eligible for appointment as an expert member or, as the case may be, a lay member.

(2) A deputy shall hold and vacate office as a deputy member in accordance with the terms of the instrument appointing him as a deputy.

(3) A deputy may vote as a member of the committee only if the member for which he acts as deputy is absent.

(4) A deputy member and the member for which he is deputy shall count as one member for the purposes of paragraphs 3(2) and (4) and 6(4).

8.—(1) At any meeting of an ethics committee, the committee may co-opt up to 2 additional members for the purposes of that meeting.

(2) At any meeting of a sub-committee of an ethics committee, the sub-committee may co-opt an additional member for the purposes of that meeting.

(3) Subject to sub-paragraph (4), a person shall be eligible to be co-opted as a member only if he is or has been a member of an ethics committee.

(4) Paragraph (3) shall not apply in relation to the Gene Therapy Advisory Committee.

(5) A co-opted member shall hold office only in relation to the meeting for which he is co-opted.

(6) A member co-opted under this paragraph shall not count as a member for the purposes of paragraphs 3(2) and (4).

#### **Staff, premises and facilities**

9.—(1) The appointing authority shall make arrangements for the appointment of such administrative and other staff for an ethics committee as they consider necessary to enable the committee to perform its functions.

(2) The appointing authority shall—

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- (a) secure the provision to an ethics committee of such accommodation and facilities as they consider necessary to enable the committee to perform its functions; and
  - (b) secure that arrangements are made for such administration, maintenance, cleaning and other services as may, in their opinion, be necessary for such accommodation and facilities.
- (3) To enable an ethics committee to perform its functions, a health service body may make staff, premises and facilities available to an ethics committee under arrangements made with the appointing authority.

### **Expenses**

**10.**—(1) The appointing authority shall, in respect of each financial year, pay to an ethics committee sums equal to the amount approved as the amounts of expenditure which they consider may be reasonably incurred by the committee in that year for the purpose of performing its functions.

(2) An ethics committee shall not incur expenses in excess of the amounts approved for that committee by the appointing authority under this paragraph.

**11.** The appointing authority may pay to members of ethics committees such travelling and other allowances as the authority may determine.

### **Annual report**

**12.**—(1) Within the period six months from the end of each financial year, every ethics committee shall prepare a report on the committee's activities during that year, which shall include a list of—

- (a) the applications made to the committee in accordance with regulation 14; and
- (b) the decisions made by the committee in relation to those applications.

(2) The ethics committee shall send a copy of the report to the Authority and, if the Authority is not the appointing authority for that committee, to its appointing authority.

### **Transfer of functions**

**13.**—(1) This paragraph applies where—

- (a) recognition of an ethics committee is revoked in accordance with regulation 8; or
- (b) an ethics committee is abolished or ceases operation.

(2) If the person who was the appointing authority before revocation, abolition or the ceasing of operation of the committee ("the old committee") is the Authority, that person may nominate another ethics committee as responsible for the work of the committee.

(3) If the person referred to in sub-paragraph (2) was not the Authority, that person may only nominate an ethics committee with the approval of the Authority.

(4) If the person referred to in sub-paragraph (2) no longer exists or if that person fails to nominate another ethics committee, the Authority shall nominate such a committee.

(5) Where an ethics committee is nominated in accordance with the preceding sub-paragraphs—

- (a) that committee shall consider any applications made to the old committee in accordance with regulation 14, if the old committee had not given an opinion before the date of revocation, abolition or ceasing of operation;
- (b) that committee shall be the relevant ethics committee for any clinical trial in relation to which the old committee had given a favourable opinion in accordance with regulation 15.



### SCHEDULE 3

Regulation 14(6), 17(2), 24(9) and 27(3)

## PARTICULARS AND DOCUMENTS THAT MUST ACCOMPANY AN APPLICATION FOR AN ETHICS COMMITTEE OPINION, A REQUEST FOR AUTHORISATION, A NOTICE OF AMENDMENT AND A NOTIFICATION OF THE CONCLUSION OF A TRIAL

### PART 1

#### APPLICATION FOR ETHICS COMMITTEE OPINION

1. An application document including the following information or, in each case, an explanation of why that information is not being provided—
  - (a) the reference number of the ethics committee to which the application is made;
  - (b) particulars identifying the trial including—
    - (i) the number allocated to the trial on the European database referred to in Article 11 of the Directive, and
    - (ii) full and short titles of the trial;
  - (c) the following particulars relating to the trial design—
    - (i) a summary of the trial, including justification and relevance, and the methodology to be used,
    - (ii) the primary, and any secondary, research hypothesis,
    - (iii) statistical analysis and justification for the numbers of subjects to be recruited for the trial, and
    - (iv) details of the process for peer review of the scientific value of the trial;
  - (d) brief details of any plans to conduct the trial outside the UK and any authorisation given in relation to the trial by a competent authority of an EEA State in accordance with Article 9 of the Directive;
  - (e) the name and address of the sponsor;
  - (f) details of any arrangements under which the sponsor has delegated any of his responsibilities in relation to the proposed trial;
  - (g) the financial arrangements for the trial, in particular—
    - (i) sources of funding for the trial and information on financial or other interests of the applicant relevant to the trial,
    - (ii) the arrangements for remuneration of, or re-imbursment of expenses incurred by, subjects,
    - (iii) any provision for compensation in the event of injury or death attributable to the trial,
    - (iv) details of any insurance or indemnity to cover the liability of the sponsor and investigator, and
    - (v) summary details of any financial arrangements between—
      - (aa) the sponsor or person funding the trial and the investigator, and
      - (bb) the sponsor or person funding the trial and the owner or occupier of the trial site;
  - (h) arrangements for the recruitment of subjects, including the materials to be used;
  - (i) the criteria for inclusion and exclusion of patients, including justification for recruiting from vulnerable groups;

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- (j) in the case of Phase I trials, methods for recording and verifying health status for healthy volunteers;
  - (k) procedures for checking simultaneous or recent involvement of potential subjects in other trials;
  - (l) details of any relationship between subject and investigator which may be relevant for the purposes of an ethical opinion;
  - (m) details of—
    - (i) any proposed additional investigational procedures or other interventions over and above those required for normal clinical care, and
    - (ii) any aspect of normal clinical care to be withheld or other deviation from normal treatment, and
    - (iii) the plan for treatment or care of subjects once their participation in the trial has ended;
  - (n) the procedures for—
    - (i) providing information to potential subjects, including a contact point where additional information can be obtained about the trial and the rights of trial subjects,
    - (ii) providing subjects with updated information during and (where relevant) after the trial, and
    - (iii) obtaining informed consent;
  - (o) details of the arrangements for access to confidential data about the subjects and the arrangements to protect subjects' privacy;
  - (p) the rules for terminating or concluding the trial before—
    - (i) the date for the conclusion of the trial specified in the protocol, or
    - (ii) the event specified in the protocol as the event which indicates that the end of the trial has occurred;
  - (q) any agreement on—
    - (i) the access by the investigator or his team to the data produced by the trial, and
    - (ii) the policy for publication of that data;
  - (r) an assessment of the ethical issues relating to the trial, including—
    - (i) the importance of the trial and of the new knowledge to be gained,
    - (ii) an assessment of the potential benefits, and
    - (iii) an assessment of the possible risks for the subjects;
  - (s) details relating to the chief investigator and each investigator, including—
    - (i) experience in conducting research, and
    - (ii) any potential conflicts of interest; and
  - (t) details of any proposed trial site and its suitability for conducting the trial.
2. A document containing the particulars specified in paragraphs 1 to 4 and 6 to 9 of Part 2 of this Schedule.
3. The following documents or, in each case, an explanation of why that document is not being provided—
- (a) the protocol;

- (b) the investigator's brochure for the proposed trial or, where the investigational medicinal product has a marketing authorisation and the product is to be used in accordance with the terms of that authorisation, the summary of product characteristics relating to that product;
- (c) any document providing evidence of any insurance to cover the liability of the sponsor and investigator;
- (d) copies of the advertisement material for recruitment of research participants;
- (e) in the case of advertising contained on video or audio cassettes, a copy of the script for that advertising;
- (f) a copy of any letter inviting a subject to participate in the trial;
- (g) a copy of any questionnaire, diary or sample card to be completed by the subject in writing;
- (h) a copy of all written information to be given to a potential subject or their legal representative prior to seeking informed consent;
- (i) a copy of the form to be used to record the consent of a subject or their legal representative;
- (j) a copy of any letters or other written information to be sent to any person who normally provides a subject's clinical care;
- (k) a summary curriculum vitae for the chief investigator and each investigator.

## PART 2

### REQUEST FOR AUTHORISATION

1. The name and address of—
  - (a) the sponsor,
  - (b) if the sponsor is not established in the European Community, his legal representative,
  - (c) if any person has been authorised by the sponsor to make the request on his behalf, that person,
  - (d) if the persons taking responsibility for the initiation, management and financing (or arranging the financing) of the clinical trial have allocated responsibility in accordance with regulation 3(4), any person responsible for carrying out the functions of the sponsor under Part 4 or 5 of these Regulations, and
  - (e) any other person to whom the sponsor has delegated any of his responsibilities in relation to the proposed trial.
2. If any person is specified as a person responsible for the duties of the sponsor under regulation 28(2) and (3) in relation to the trial—
  - (a) the name and address of that person; and
  - (b) the trial sites in relation to which they are so responsible.
3. The address of each trial site and the names and address of the investigator responsible for the conduct of the trial at each site.
4. Where the trial is to be conducted at trial sites in another EEA State, a list of the competent authorities to which a request for authorisation has been made.
5. A copy of the ethics committee opinion in relation to that trial, if available.
6. A description of any investigational medicinal product to be used in the trial.

*Status: This is the original version (as it was originally made).*

7. The name and address of the person responsible for the manufacture or importation of any finished investigational medicinal product to be used in the trial and the details of any authorisation referred to in Article 13 of the Directive held by that person.

8.—(1) The address of any premises at which any batch of finished investigational medicinal products to be used in the clinical trial has been, or is to be, checked in accordance with Article 13(3) of the Directive.

(2) If an investigational medicinal product to be used in the clinical trial has been, or is to be, imported from a third country, a statement from the qualified person at the disposal of the person holding the authorisation referred to in Article 13 of the Directive in relation to that importation specifying—

- (a) the address of any premises outside the European Economic Area at which the product was manufactured or assembled; and
- (b) the manufacturing or assembling operations performed at those premises.

9. A description of the proposed clinical trial.

10. The protocol for the proposed trial.

11.—(1) Subject to sub-paragraph (7), a dossier on each investigational medicinal product to be used in the trial (“investigational medicinal product dossier”), compiled in accordance with the following sub-paragraphs.

(2) In all cases the dossier must contain a summary assessment of the potential risks and benefits of the use of the product in the proposed trial.

(3) In the case of an investigational medicinal product, other than a product referred to in sub-paragraphs (4) to (7), the dossier must contain—

- (a) summaries of the chemical, pharmaceutical and biological data on the active substance and the finished product;
- (b) summaries of the non-clinical pharmacology and toxicology data on that product, if available; and
- (c) summaries of the available data from previous clinical trials of, and human experience with, that product.

(4) In the case of an investigational medicinal product which has a marketing authorization, the dossier must contain—

- (a) a copy of the summary of product characteristics;
- (b) if there has been a change—
  - (i) to the process of manufacture of the product or its active substance, or
  - (ii) of manufacturer of that product or substance,
 the summaries referred to in sub-paragraph (3)(a);
- (c) if the product is to be used in the trial after it has been blinded, the summaries referred to in sub-paragraph (3)(a), in so far as they relate to the blinded product; and
- (d) if the product is to be used other than in accordance with the terms of the summary of product characteristics under that authorization, the summaries referred to in sub-paragraphs (3)(b) and (c), in so far as that data relates to such use.

(5) In the case of an investigational medicinal product which does not have a marketing authorization, but where—

- (a) another pharmaceutical form or strength of that product has a marketing authorization; and

(b) the investigational medicinal product is supplied by the holder of that authorization, the dossier must contain the summaries referred to in sub-paragraph (3)(a), in so far as they relate to the finished product to be used in the trial, and the summaries referred to in sub-paragraph (3)(b) and (c), in so far as they relate to the product to be used in the trial.

(6) In the case of an investigational medicinal product which does not have a marketing authorization, but where—

(a) another medicinal product containing the same active substance has a marketing authorization; and

(b) the investigational medicinal product is supplied by the manufacturer of that other product, the dossier must contain the summaries referred to in sub-paragraph (3)(a), in so far as they relate to that other product, and the summaries referred to in sub-paragraph (3)(b) and (c), in so far as they relate to the product to be used in the trial.

(7) Where the investigational medicinal product is a placebo, the dossier must contain the summaries referred to in sub-paragraph (3)(a), in so far as they relate to that product.

(8) A dossier relating to an investigational medicinal product is not required if—

(a) the product has been used in a clinical trial that has been authorised, or is to be treated as having been authorised, by the licensing authority for the purposes of these Regulations; and

(b) the sponsor of that trial authorises the licensing authority to refer to the dossier submitted in relation to that trial.

**12.** A description or sample of the labelling which is to appear on each investigational medicinal product when supplied to a subject in the trial.

## PART 3

### NOTICE OF AMENDMENT

**1.** The name and address of—

(a) the sponsor,

(b) if the sponsor is not established in the European Community, his legal representative, and

(c) if any person has been authorised by the sponsor to send the notice on his behalf, that person.

**2.** Particulars identifying the trial, including—

(a) the title of the trial; and

(b) the number allocated to the trial on the European database referred to in Article 11 of the Directive.

**3.** A description of the proposed amendment.

**4.** A statement of the reasons for proposing that amendment.

**5.** A copy of the proposed changes to—

(a) the clinical trial protocol; or

(b) any other particulars or documents accompanying the request for authorisation or the application for an ethics committee opinion.

**6.** Summaries of—

(a) any data submitted in support of the proposed amendment; and

- (b) any change to the assessment referred to in paragraph 11(2) of Part 2.

## PART 4

### NOTIFICATION OF CONCLUSION OF A CLINICAL TRIAL

1. The name and address of—
  - (a) the sponsor, and
  - (b) if the sponsor is not established in the European Community, his legal representative.
2. Particulars identifying the trial, including—
  - (a) the title of the trial; and
  - (b) the number allocated to the trial on the European database referred to in Article 11 of the Directive.
3. The investigational medicinal product tested in the trial.
- 4.—(1) The date on which the trial ended in the United Kingdom.
  - (2) If the trial was conducted at more than one trial site in the United Kingdom, the dates on which the trial was ended at those sites, if different from the date referred to in sub-paragraph (1).
  - (3) If the trial was conducted at any trial sites outside the United Kingdom, a statement as to whether the trial has ended at any of those sites and, if so, the date on which the trial was so ended.
5. If the trial is terminated as specified in regulation 27(2), the reasons for terminating the trial early.

## SCHEDULE 4

Regulation 16(6)

### APPEAL AGAINST UNFAVOURABLE ETHICS COMMITTEE OPINION

- 1.—(1) Subject to the following sub-paragraphs, where the United Kingdom Ethics Committee Authority (“the Authority”) receive a notice pursuant to regulation 16(3) or (7) that a chief investigator wishes to appeal against an ethics committee opinion which is not favourable, the Authority shall, subject to sub-paragraph (2)—
  - (a) direct that the application for that opinion may be considered by another ethics committee specified in the direction; or
  - (b) appoint a panel in accordance with paragraph 3 (“an appeal panel”) and refer the opinion to that panel.
  - (2) Subject to sub-paragraph (4), the Authority may refuse to give a direction or appoint a panel pursuant to sub-paragraph (1) where it considers that the grounds for appealing against the opinion are unfounded.
  - (3) Where the Authority refuse to give a direction or appoint a panel pursuant to sub-paragraph (1), the Authority shall send a notice to the chief investigator setting out their reasons for refusal.
  - (4) Where the opinion was given by the Gene Therapy Advisory Committee, the Authority must appoint a panel in accordance with paragraph 3 and refer the opinion to that panel.
2. Where a direction is given in accordance with paragraph 1(1)(a)—

- (a) the ethics committee which gave the unfavourable opinion shall—
  - (i) send the application for that opinion, and
  - (ii) any additional information provided by the chief investigator, to the ethics committee specified in the direction; and
- (b) that committee shall consider the application in accordance with regulation 15.

**3.—**(1) An appeal panel appointed pursuant to paragraph 1(1)(b) shall consist of a chairman and at least 6 other members.

- (2) One of the members shall be a person who is not—
  - (a) a health care professional,
  - (b) a person having professional qualifications or experience relating to the conduct of, or use of statistics in, clinical trials, unless those professional qualifications or experience relate only to the ethics of clinical research or medical treatment, or
  - (c) a person who, although not a health care professional, has been a registered medical practitioner or a person registered in the dentists register under the Dentists Act 1984.

**4.—**(1) An appeal panel shall consider an ethics committee opinion referred to it in accordance with the following sub-paragraphs.

- (2) The appeal panel shall consider—
  - (a) the opinion;
  - (b) the application for that opinion;
  - (c) the particulars and documents accompanying that application;
  - (d) the matters specified in regulation 15(6);
  - (e) any representations set out in the notice to the Authority; and
  - (f) in a case where the opinion has been confirmed by the Gene Therapy Advisory Committee on a review pursuant to regulation 16(5), the reasons given by the Committee for that confirmation.

(3) The panel may, if the chief investigator so requests, hold a hearing to consider the opinion, at which the chief investigator may make oral representations.

(4) The panel shall within 30 days of the opinion being referred to the panel, or such extended period as the Authority may in any particular case allow, either confirm the opinion or give a favourable opinion.

**5.** If an appeal panel gives a favourable opinion, the condition specified in regulation 11(3)(a) shall be deemed to have been satisfied.

**6.** The Authority may pay to members of an appeal panel such travelling and other allowances as the Authority may determine.

## SCHEDULE 5

Regulations 26(2) and 31(8)

PROCEDURAL PROVISIONS RELATING TO THE REFUSAL OR AMENDMENT  
OF, OR IMPOSITION OF CONDITIONS RELATING TO, CLINICAL TRIAL  
AUTHORISATION AND THE SUSPENSION OR TERMINATION OF CLINICAL TRIALS

1.—(1) Where the licensing authority are notified of the sponsor's wish to make representations in accordance with regulation 26(1) or 31(7) the authority shall afford an opportunity for the sponsor to make written or oral representations to the appropriate committee or, if for the time being there is no such committee, the Medicines Commission.

(2) After considering the representations, the appropriate committee or the Medicines Commission shall report their findings and advice, and the reasons for their advice, to the licensing authority.

(3) In the case of a decision not to accept a request for authorisation or an amendment to the clinical trial authorisation, the licensing authority shall, after considering the report of the appropriate committee or the Commission—

- (a) confirm that they have grounds for not accepting the request or amendment; or
- (b) accept the request for authorisation or amendment to the clinical trial authorisation, subject to such conditions as the licensing authority may consider appropriate.

(4) In the case of a decision to impose a condition following a request for authorisation or notice of amendment, the licensing authority shall, after considering the report of the appropriate committee or the Commission—

- (a) confirm their decision; or
- (b) remove or alter the condition in question.

(5) In the case of a notice to suspend or terminate a trial, the licensing authority shall, after considering the report of the appropriate committee or the Commission, confirm or revoke the notice.

(6) The licensing authority shall give notice to the sponsor of—

- (a) the findings and advice of the appropriate committee or the Medicines Commission and the reasons for it; and
- (b) their decision in accordance with sub-paragraphs (3), (4) or (5).

2.—(1) If a person to whom a notice is given under paragraph 1(6) is dissatisfied and he has not made representations to the Medicines Commission under paragraph 1(1), he may give notice in writing to the licensing authority within 28 days, or such extended period as the licensing authority may in any particular case allow, of the notice being given of his wish to make written or oral representations to the Medicines Commission.

(2) On receipt of a notice under sub-paragraph (1) the licensing authority shall afford an opportunity for the sponsor to be heard by the Medicines Commission or, as the case may be, for his written representations to be considered by them.

(3) After considering the representations the Medicines Commission shall report their findings and advice, and the reasons for their advice, to the licensing authority.

(4) After considering the report of the Medicines Commission, the licensing authority shall—

- (a) confirm or alter their decision under paragraph 1(3), (4) or (5); and
- (b) give notice to the person of—
  - (i) the findings and advice of the Medicines Commission and the reasons for it, and
  - (ii) the licensing authority's confirmation or alteration of their decision under paragraph 1(3) to (5).



3.—(1) If a decision notified in accordance with paragraphs 1(6) or 2(4) is a decision to which this paragraph applies, the sponsor may within the time allowed after the notification was given, give notice of his wish to appear before and be heard by a person appointed for the purpose by the licensing authority, or of making representations in writing to the licensing authority with respect to the decision referred to in the notification.

(2) Where the sponsor gives notice under sub-paragraph (1) of his wish to appear before and be heard by a person appointed for the purpose by the licensing authority, the licensing authority shall make that appointment and—

- (a) the person so appointed shall not, except with the consent of the applicant or holder, be an officer or servant of any of the Ministers specified in paragraphs (a) and (b) of section 1(1) of the Act;
- (b) if the applicant or holder so requests, the hearing shall be in public; and
- (c) if the applicant or holder so requests, the licensing authority shall furnish to him a copy of the report of the person so appointed.

(3) The licensing authority shall take into account the report of the person appointed and decide whether to confirm or alter their decision.

(4) The decisions to which this paragraph applies are decisions of the licensing authority—

- (a) to confirm—
  - (i) that they have grounds for not accepting a request for authorisation or an amendment to the clinical trial authorisation,
  - (ii) their decision to impose a condition, or
  - (iii) the notice to suspend or terminate the trial,against the advice of the Medicines Commission under paragraph 1(2);
- (b) to impose conditions in accordance with paragraph 1(3)(b) or alter a condition in accordance with paragraph 1(4)(b), in a way which differs from the advice given by the Medicines Commission under paragraph 1(2); or
- (c) to confirm a decision under paragraph 1(3), (4) or (5) against the advice of the Medicines Commission under paragraph 2(3);
- (d) to alter a decision under paragraph 1(3), (4) or (5) in a way which differs from the advice of the Medicines Commission under paragraph 2(3).

## SCHEDULE 6

Regulation 38(3)

### PARTICULARS THAT MUST ACCOMPANY AN APPLICATION FOR A MANUFACTURING AUTHORISATION

1. The name and address of the applicant, and, where the applicant is not the proposed holder of the authorisation, the name and address of the proposed holder.

2. A statement of the types of investigational medicinal products in respect of which the authorisation is required.

3. A statement of the manufacturing, assembling or importation operations to which the authorisation is to relate, including a statement whether they include one or more of the following—

- (a) the manufacture of investigational medicinal products;
- (b) the assembly of investigational medicinal products; or
- (c) the importation of investigational medicinal products.

*Status: This is the original version (as it was originally made).*

**4.—(1)** The address of each of the premises where the manufacturing, assembling or importation operations to which the application relates, including any testing associated with manufacture, assembly or import, are or are to be carried out.

(2) The address of each of the premises where the proposed holder of the authorisation proposes to store investigational medicinal products or from which he proposes to distribute them.

(3) A statement indicating the facilities and equipment available at each of the premises referred to in sub-paragraphs (1) and (2), for storing the investigational medicinal products on, and distributing them from or between, such premises.

(4) A separate statement in respect of each of the premises referred to in sub-paragraphs (1) and (2), of the manufacturing, assembling or importation operations capable of being carried out at those premises with their existing facilities. Each statement shall specify the classes of investigational medicinal products to which the operations are relevant.

(5) A separate statement in respect of each of the premises referred to in sub-paragraphs (1) and (2), of the facilities and equipment available at those premises for carrying out each stage of the manufacturing, assembling or importation operations described in sub-paragraph (4) of this paragraph.

**5.** A statement of any manufacturing operations, other than those to which the manufacturing authorisation is to relate, that are carried on by the proposed authorisation holder on or near each of the premises referred to in paragraph 4, and of the substances or articles which are the subject of any such operation.

**6.—(1)** The name and address and qualifications and experience of the qualified person who is to carry out the duties referred to in regulation 43(2).

(2) In the case of an authorisation relating to manufacture or assembly, the name and qualifications and experience of the production manager or other person whose duty it will be to supervise the production operations at each of the premises referred to in paragraph 4 of this Schedule, and the name and function of the person to whom he is responsible.

(3) In the case of an authorisation relating to manufacture or assembly—

- (a) the name and degrees, diplomas or other qualifications and experience of the person to be in charge of quality control over all the premises referred to in paragraph 4 of this Schedule;
- (b) the extent of the authority to be delegated to him to reject unsatisfactory batches of investigational medicinal products, and
- (c) the name and function of the person to whom he is responsible.

**7.** A description of the arrangements for the identification and storage of materials and ingredients before and during manufacture and for the storage of investigational medicinal products after manufacture, assembly or importation.

**8.** A description of the arrangements at each of the premises where the holder of the authorisation stores or proposes to store investigational medicinal products for ensuring, so far as practicable, whether by maintaining records or other means, a satisfactory turn-over of stocks of investigational medicinal products.

**9.** A description of the arrangements—

- (a) for maintaining production or importation records;
- (b) for maintaining records of analytical and other testing procedures applied in the course of manufacture, assembly or importation for ensuring compliance of materials used in the manufacture of any investigational medicinal products with the specification of such materials or medicinal products; and

- (c) for keeping reference samples of materials used in the manufacture of any investigational medicinal products and of the investigational medicinal products.

## SCHEDULE 7

Regulation 40(4)

### STANDARD PROVISIONS FOR MANUFACTURING AUTHORISATIONS

#### PART 1

##### INTERPRETATION

In this Schedule, “product specification” means—

- (a) in the case of an investigational medicinal product 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 that product provided by the person who is to act as the sponsor of the proposed clinical trial,
- (b) in the case of an investigational medicinal product manufactured for the purpose of export, the specification for that product provided by the person to whose order the products are manufactured, or
- (c) in any other case, the specification for an investigational medicinal product contained in the investigational medicinal product dossier for that product.

#### PART 2

##### PROVISIONS WHICH MAY BE INCORPORATED IN AN AUTHORISATION RELATING TO THE MANUFACTURE OR ASSEMBLY OF INVESTIGATIONAL MEDICINAL PRODUCTS

1. The holder of the authorisation shall—
  - (a) provide and maintain such staff, premises and plant (including technical equipment) as are necessary for the carrying out, in accordance with his authorisation and the product specification, of such stages of the manufacture and assembly of the investigational medicinal products as are undertaken by him; and
  - (b) not carry out any such manufacture or assembly except at the premises specified in his manufacturing authorisation.
2. The holder of the authorisation shall—
  - (a) provide and maintain such staff, premises, equipment and facilities for the handling, storage and distribution of the investigational medicinal products which he handles, stores or distributes under his authorisation as are necessary to maintain the quality of the investigational medicinal products;
  - (b) not use for such purposes premises other than those specified in the authorisation or which may be approved from time to time by the licensing authority; and
  - (c) ensure that any arrangements he makes with a person for the storage and distribution of the investigational medicinal products are adequate to maintain the quality of those products.

*Status: This is the original version (as it was originally made).*

**3.** The holder of the authorisation shall place the quality control system referred to in Article 11(1) of Commission Directive [2003/94/EC](#) under the authority of the person notified to the licensing authority in accordance with paragraph 6(3) of Schedule 6 as being responsible for quality control.

**4.** The holder of the authorisation may use a contract laboratory pursuant to Article 11(2) of Commission Directive [2003/94/EC](#) if operated by a person approved by the licensing authority.

**5.** The holder of the authorisation shall provide such information as may be requested by the licensing authority for the purposes of these Regulations or the Act—

- (a) about the products currently being manufactured or assembled under his authorisation; and
- (b) of the operations being carried out in relation to such manufacture or assembly.

**6.** The holder of the authorisation shall—

- (a) inform the licensing authority before making any material alteration in the premises or plant used under his authorisation, or in the operations for which they are used; and
- (b) inform the licensing authority of any change that he proposes to make in any personnel named in his authorisation as respectively—
  - (i) responsible for supervising the production operations, or
  - (ii) responsible for quality control of the investigational medicinal products being manufactured or assembled including the person named as the qualified person for the purposes of regulation 43 and paragraph 14.

**7.** The holder of the authorisation shall—

- (a) keep readily available for inspection by a person authorised by the licensing authority the batch documentation referred to in Article 9(1) of Commission Directive [2003/94/EC](#); and
- (b) permit the person authorised to take copies or make extracts from such documentation.

**8.** The holder of the authorisation shall keep readily available for examination by a person authorised by the licensing authority the samples of each batch of bulk formulated products referred to in Article 11(4) of Commission Directive [2003/94/EC](#).

**9.** Where the holder of the authorisation has been informed by the licensing authority that any batch of any investigational medicinal product to which his authorisation relates has been found not to conform as regards strength, quality or purity with—

- (a) the specification of the relevant product; or
- (b) the provisions of these Regulations, the Act or any regulations under the Act that are applicable to the investigational medicinal product,

he shall, if so directed, withhold such batch from distribution for use in clinical trials, so far as may be reasonably practicable, for such a period not exceeding six weeks as may be specified by the licensing authority.

**10.** The holder of the authorisation shall ensure that any tests for determining conformity with the standards and specifications applying to any particular product used in the manufacture shall, except so far as the conditions of the product specification for that product otherwise provide, be applied to samples taken from the investigational medicinal product after all manufacturing processes have been completed, or at such earlier stage in the manufacture as may be approved by the licensing authority.

**11.** Where the authorisation relates to the assembly of an investigational medicinal product, and the holder of the authorisation supplies that investigational medicinal product at such a stage of assembly that does not fully comply with the provisions of the product specification that relate to labelling, that holder of the authorisation shall communicate the particulars of those provisions to the person to whom that investigational medicinal product has been so supplied.

**12.** Where—

- (a) the manufacturing authorisation relates to the assembly of an investigational medicinal product;
- (b) that investigational medicinal product is not manufactured by the holder of the authorisation; and
- (c) particulars as to the name and address of the manufacturer of, or of the person who imports, that investigational medicinal product had been given by the holder of the authorisation to the licensing authority,

the holder of the authorisation shall forthwith notify the licensing authority in writing of any changes in such particulars.

**13.** The holder of the authorisation, for the purpose of enabling the licensing authority to ascertain whether there are any grounds—

- (a) for suspending, revoking or varying any authorisation or licence granted under these Regulations or Part II of the Act;
- (b) amending the clinical trial authorisation in accordance with regulation 23 or 24; or
- (c) suspending or terminating any clinical trial in accordance with regulation 31,

shall permit, and provide all necessary facilities to enable, any person duly authorised in writing by the licensing authority, on production if required of his credentials, to carry out such inspection or to take such samples or copies, in relation to things belonging to, or any business carried on by, the holder of the authorisation, as such person would have the right to carry out or take under the Act for the purpose of verifying any statement contained in an application for an authorisation or licence.

**14.** The holder of the authorisation shall at all times provide and maintain such staff, premises, equipment and facilities as will enable the qualified person who is at his disposal pursuant to regulation 43(1) to carry out the duties referred to in regulation 43(2).

## PART 3

### PROVISIONS WHICH MAY BE INCORPORATED IN AN AUTHORISATION RELATING TO THE IMPORTATION OF INVESTIGATIONAL MEDICINAL PRODUCTS

**1.** The holder of the authorisation shall—

- (a) provide and maintain such staff, premises, equipment and facilities for the handling, storage and distribution of the investigational medicinal products which he handles, stores or distributes under his authorisation as are necessary to avoid deterioration of the investigational medicinal products;
- (b) not use for such purposes premises other than those specified in the authorisation or which may be approved from time to time by the licensing authority; and
- (c) ensure that any arrangements he makes with a person for the storage and distribution of the investigational medicinal products are adequate to maintain the quality of those products.

**2.** The holder of the authorisation may use a contract laboratory pursuant to Article 11(2) of Commission Directive [2003/94/EC](#) if operated by a person approved by the licensing authority.

**3.** The holder of the authorisation shall provide such information as may be requested by the licensing authority concerning the type and quantity of any investigational medicinal products which he imports.

*Status: This is the original version (as it was originally made).*

4. The holder of the authorisation shall—
  - (a) inform the licensing authority before making any structural alterations to, or discontinuance of the use of, premises to which his authorisation relates; and
  - (b) inform the licensing authority if he changes the person named as the qualified person for the purposes of regulation 43 and paragraph 9.
5. The holder of the authorisation shall—
  - (a) keep readily available for inspection by a person authorised by the licensing authority the batch documentation referred to in Article 9(1) of Commission Directive 2003/94/EC; and
  - (b) permit the person authorised to take copies or make extracts from such documentation.
6. Where the holder of the authorisation has been informed by the licensing authority that any batch of any investigational medicinal product to which his authorisation relates has been found not to conform as regards strength, quality or purity with—
  - (a) the specification of the relevant product; or
  - (b) the provisions of these Regulations, the Act or any regulations under the Act that are applicable to the investigational medicinal product,

he shall, if so directed, withhold such batch from distribution for use in clinical trials, so far as may be reasonably practicable, for such a period not exceeding six weeks as may be specified by the licensing authority.

7. If the holder of the authorisation is not the sponsor of the clinical trial for which the investigational medicinal product is manufactured or assembled, he shall comply with the provisions of the product specification that relates to the supply of that investigational medicinal product for use in the trial.

8. The holder of the authorisation, for the purpose of enabling the licensing authority to ascertain whether there are any grounds—
  - (a) for suspending, revoking or varying any authorisation or licence granted under these Regulations or Part II of the Act;
  - (b) amending the conduct of a clinical trial in accordance with regulation 23 or 24; or
  - (c) suspending or terminating any clinical trial in accordance with regulation 31,

shall permit, and provide all necessary facilities to enable, any person duly authorised in writing by the licensing authority, on production if required of his credentials, to carry out such inspection or to take such samples or copies, in relation to things belonging to, or any business carried on by, the holder of the authorisation, as such person would have the right to carry out or take under the Act for the purpose of verifying any statement contained in an application for an authorisation or licence.

9. The holder of the authorisation shall at all times provide and maintain such staff, premises, equipment and facilities as will enable the qualified person who is at his disposal pursuant to regulation 43(1) to carry out the duties referred to in regulation 43(2).

## SCHEDULE 8

Regulations 40(5) and 44(6)

### PROCEDURAL PROVISIONS RELATING TO PROPOSALS TO GRANT, REFUSE TO GRANT, VARY, SUSPEND OR REVOKE MANUFACTURING AUTHORISATIONS

1. In this Schedule—

“authorisation” means a manufacturing authorisation; and

“time allowed” means the period of 28 days or such extended period as the licensing authority may in any particular case allow.

2. Subject to paragraph 6, if the licensing authority propose—
  - (a) not to grant an authorisation;
  - (b) to grant an authorisation other than in accordance with the application; or
  - (c) to revoke, vary or suspend an authorisation,

the licensing authority shall notify the applicant or holder accordingly.

3. Any notification given under paragraph 2 shall include a statement of the proposals of the licensing authority and of the reasons for them.

4. A person to whom notification has been given under paragraph 2 may, within the time allowed after the notification was given, give notice of his wish to appear before and be heard by a person appointed for the purpose by the licensing authority, or of making representations in writing to the licensing authority with respect to the decision or proposal referred to in the notification.

5.—(1) Where an applicant or the holder gives notice under paragraph 4 of his wish to appear before and be heard by a person appointed for the purpose by the licensing authority, the licensing authority shall make that appointment and—

- (a) the person so appointed shall not, except with the consent of the applicant or holder, be an officer or servant of any of the Ministers specified in paragraphs (a) and (b) of section 1(1) of the Act;
- (b) if the applicant or holder so requests, the hearing shall be in public; and
- (c) if the applicant or holder so requests, the licensing authority shall furnish to him a copy of the report of the person so appointed.

(2) The licensing authority shall take into account the report of the person appointed and decide whether to grant the authorisation, revoke, vary or suspend the authorisation or confirm or alter their decision, as the case may be.

6.—(1) Paragraph 2 shall not apply to the suspension of an authorisation where it appears to the licensing authority that, in the interests of safety, it is necessary to suspend the authorisation with immediate effect for a period not exceeding 3 months.

(2) If, after the suspension has taken effect, it appears to the licensing authority that the authorisation should be further suspended or revoked, the licensing authority shall proceed in accordance with the provisions of paragraphs 2 to 5.

## SCHEDULE 9

Regulation 47(1)

### MODIFICATIONS OF THE ENFORCEMENT PROVISIONS OF THE ACT SUBJECT TO WHICH THOSE PROVISIONS ARE APPLIED FOR THE PURPOSES OF THESE REGULATIONS

1. The modifications of the Act mentioned in regulation 47 are as follows.

2.—(1) Amendments in section 107 (validity of decisions and related proceedings) as follows.

(2) In subsection (1), for “Part II of this or of a Minister under section 75 of this Act, and the validity of any licence or certificate” substitute “the Clinical Trials Regulations, and the validity of any authorisation”.

*Status: This is the original version (as it was originally made).*

- (3) In subsections (2)(a) and (3)(b), for “this Act” substitute “the Clinical Trials Regulations”.
- (4) In subsection (2)(b), for “this Act or of any regulations made under this Act” substitute “the Clinical Trials Regulations”.
- (5) In subsection (4) (effect of quashing a decisions) substitute—
- “ (4) Subsections (4A) and (4B) of this section apply where a decision—
- (a) to grant or issue an authorisation, or
- (b) to give notice accepting a request for an authorisation, is quashed under this section.
- (4A) Any authorisation granted or issued, or notice given, in pursuance of the decision shall be void.
- (4B) Any proceedings on the application, or request, for the authorisation may be continued as if not such decision had been made.”.
3. For section 108 (enforcement in England and Wales) substitute—
- “(1) It shall be the duty of the Secretary of State to enforce in England, or to secure the enforcement in England of, the provisions of the Clinical Trials Regulations.
- (2) It shall be the duty of the National Assembly for Wales to enforce in Wales, or to secure the enforcement in Wales of, the provisions of the Clinical Trials Regulations”.
4. In section 109 (enforcement in Scotland), for subsections (1) to (3), substitute—
- “(1) It shall be the duty of the Scottish Ministers to enforce in Scotland, or to secure the enforcement in Scotland of, the provisions of the Clinical Trials Regulations.”.
5. For section 110 (enforcement in Northern Ireland) substitute—
- “It shall be the duty of the Department for Health, Social Services and Public Safety to enforce in Northern Ireland, or to secure the enforcement in England and Wales of, the provisions of the Clinical Trials Regulations.”.
- 6.—(1) Amendments in section 111 (rights of entry) as follows.
- (2) In subsection (1)(a) (entry to ascertain whether Act etc. contravened), for the words after “contravention” substitute “of any provisions of the Clinical Trials Regulations, or”.
- (3) In subsection (1)(b) (entry for purposes of functions under the Act etc.), for “this Act or any such regulations or order” substitute “those Regulations or any of the provisions of this Act applied by regulation 47 or those Regulations”.
- (4) In subsection (2)(a) (right to enter craft), for the words from “this Act or of any regulations” onwards substitute “the Clinical Trials Regulations;”.
- (5) In subsection (3) (rights to enter premises conferred on persons authorised by licensing authority)—
- (a) for “an applicant for a licence under Part II of this Act” substitute “a person applying for or requesting an authorisation under the Clinical Trials Regulations”, and
- (b) for “application for the licence or certificate” substitute “application or request for the authorisation”.
- 7.—(1) Amendments in section 112 (power to inspect, take samples and seize goods and documents) as follows.
- (2) In subsection (1) (inspection for purpose of ascertaining whether Act etc. contravened), for the words before paragraph (a) substitute—



“For the purposes of ascertaining whether there is or has been a contravention of the Clinical Trials Regulations, any person duly authorised in writing by an enforcement authority shall have a right to inspect—”.

(3) In subsection (2) (items of which samples may be taken), before the word “or” at the end of paragraph (a) insert—

“(aa) a medicinal product used or intended to be used in a clinical trial.”.

(4) In subsection (3) (right to require production etc. of books and documents), after paragraph (a) insert—

“(a) to require—

(i) the sponsor of a clinical trial,

(ii) any person who, under arrangements made with the sponsor of a clinical trial, carries out functions of the sponsor of the trial,

(iii) an investigator for a trial,

(iv) any person, other than an investigator, who conducts a trial,

(v) any person occupying premises at which a clinical trial is being conducted, or

(vi) any person who, in the course of their employment with a person of a description specified in any of sub-paragraphs (i) to (v) of this paragraph, undertakes activities in connection with a clinical trial,

to produce any books or documents relating to the clinical trial which are in his possession or under his control;”.

(5) In subsection (3)(b) (powers to take copies of documents produced), for “the preceding paragraph” substitute “paragraph (a) or (aa) of this subsection;”.

(6) In subsection (3), after paragraph (b) insert—

“(c) to take possession of any book or document produced under paragraph (a) or (aa) of this subsection.”.

(7) In subsection (4) (right to seize items and documents), for “offence under this Act is” substitute—

“offence—

(a) under the Clinical Trials Regulations, or

(b) under section 114, 118 or 123 of this Act,

is.”

(8) In that subsection, for “under this Act” (in the second place) substitute “under those Regulations or under any of the provisions of this Act applied by regulation 47 of those Regulations”.

(9) In subsection (5) (opening of containers), for “this Act and any regulations or order made thereunder” substitute “the Clinical Trials Regulations”.

(10) In subsection (7) (rights of persons authorised by licensing authority)—

(a) for “a licence or certificate under Part II of this Act” substitute “an authorisation under the Clinical Trials Regulations”, and

(b) for “the application for the licence or certificate” substitute “the application or request for the authorisation”.

(11) In subsection (9) (Schedule 3 to have effect in relation to samples obtained for purposes of the Act), for “this Act” (in the second place) substitute “the Clinical Trials Regulations”.

(12) After subsection (9) insert—

*Status: This is the original version (as it was originally made).*

“(10) In this section “clinical trial”, and “investigator” and “sponsor” in relation to a clinical trial, have the meaning given by the Clinical Trials Regulations.”

**8.—**(1) Amendments in section 115 (analysis of samples) as follows.

(2) In subsection (7) (certificate to be in prescribed form and signed), for “form prescribed by the Ministers” substitute “prescribed form”.

(3) Omit subsection (9) (regulations under subsection (5) to be made by the Ministers).

**9.—**(1) Amendments in section 116 (liability to forfeiture under the Customs and Excise Management Act 1979) as follows.

(2) For “this Act” (in both places) substitute “the Clinical Trials Regulations”.

(3) After subsection (3) insert—

“(4) In this section “the Ministers” means the Secretary of State and the Department for Health, Social Services and Public Safety, acting jointly.”

**10.** In section 118(1)(b) (restrictions on disclosing of information obtained in pursuance of the Act), for “this Act” substitute “the Clinical Trials Regulations or any provision of this Act applied by regulation 47 of those Regulations”.

**11.—**(1) Amendments in section 119 (protection for officers of enforcement authorities) as follows.

(2) In each of subsections (1) and (2) (relief from personal liability and power of authority to indemnify officer)—

(a) for “this Act” (in the first place) substitute “relevant legislation”, and

(b) for “this Act” (in the second place) substitute “that legislation”.

(3) In subsection (3) (meaning of “officer”), for “this Act” substitute “relevant legislation”.

(4) After subsection (3) insert—

“(4) In this section “relevant legislation” means—

(a) the Clinical Trials Regulations, or

(b) any provision of this Act applied by regulation 47 of those Regulations.”

**12.—**(1) Amendments in section 121 (contravention due to fault of other person) as follows.

(2) In subsection (1) (where a person is guilty of an offence due to act or default of another, the other is also guilty of the offence), for “to which this section applies constitutes an offence under this Act” substitute “of the Clinical Trials Regulations constitutes an offence under those Regulations”.

(3) In subsection (2) (defence of due diligence where contravention due to act or default of another), for “this Act in respect of a contravention of a provision to which this section applies” substitute “the Clinical Trials Regulations in respect of a contravention of a provision of those Regulations”.

(4) Omit subsection (4) (provisions to which section applies).

**13.—**(1) Amendments in section 122 (warranty as defence) as follows.

(2) In subsection (1), for “this Act in respect of a contravention of a provision to which this section applies” substitute “the Clinical Trials Regulations in respect of a contravention of regulation 46 of those Regulations”.

(3) Omit subsection (2) (provisions to which section applies).

**14.—**(1) Amendments in section 124 (offences by bodies corporate) as follows.

(2) In subsection (1), for “this Act” substitute “the Clinical Trials Regulations, or under section 114, 118 or 123 of this Act,”.

(3) After subsection (2) insert—

“(2A) In subsections (1) and (2) of this section “body corporate” includes a Scottish partnership and “director”, in relation to such a partnership, includes any of its partners.”

**15.—**(1) Amendments in section 125 (prosecutions) as follows.

(2) In each of subsections (1) and (2) (time limits in England and Wales, and in Scotland), for “under this Act” substitute “under the Clinical Trials Regulations, or for an offence under section 114, 118 or 123 of this Act,”.

(3) Omit subsections (3) to (7).

**16.** In section 127 (service of documents)—

(a) for “any provision of this Act” substitute “relevant legislation”, and

(b) at the end add—

“In this section “relevant legislation” means any provision of the Clinical Trials Regulations or any provision of this Act applied by regulation 47 of those Regulations.”

**17.—**(1) Amendments in section 129 (orders and regulations) as follows.

(2) Omit subsection (1) (powers to make regulations exercisable by the Ministers where not expressed to be otherwise exercisable).

(3) In subsection (2) (powers to make orders and regulations under the Act exercisable by statutory instrument), for the words from “this Act (other” to “section 120 of this Act)” substitute “any provision of this Act applied by regulation 47 of the Clinical Trials Regulations”.

(4) In subsection (3) (instruments which are subject to negative procedure), for paragraphs (a) to (c) substitute “an order or regulations made under any provision of this Act applied by regulation 46 of the Clinical Trials Regulations”.

(5) In subsection (4) (powers to make orders that include power to revoke or vary), for the words from “, other than” to “69(3), of this Act” substitute “of this Act applied by regulation 47 of the Clinical Trials Regulations”.

(6) In subsection (5) (powers to make regulations include power to make differential provision etc.), for “this Act” substitute “any provision of this Act applied by regulation 47 of the Clinical Trials Regulations”.

(7) In subsection (6) (duty to consult), for the words from the beginning to “effect) the Ministers” substitute—

“Before making any regulations or order under any provision of this Act applied by regulation 47 of the Clinical Trials Regulations, the persons.”

(8) Omit subsections (6A) and (7) (which apply only in relation to veterinary products or instruments made otherwise than under Part 8 of the Act).

**18.—**(1) Amendments in section 131 (meaning of “wholesale dealing” and “retail sale” etc).

(2) Omit subsection (1) (meaning of “wholesale dealing”).

(3) In subsection (2) (purposes referred to in subsections (1) and (3)), for “the preceding subsection” substitute “subsection (3) of this section”.

*Status: This is the original version (as it was originally made).*

(4) In subsection (3) (meaning of “retail sale”), for “In this Act” substitute “In the provisions of this Act applied by regulation 47 of the Clinical Trials Regulations,”.

(5) Omit subsection (4) (meaning of “supply in circumstances corresponding to retail sale”).

**19.**—(1) Amendments in section 132(1) (interpretation) as follows.

(2) At the beginning, for “In this Act,” substitute “In the provisions of this Act applied by regulation 47 of the Clinical Trials Regulations,”.

(3) In the definition of “enforcement authority”, for the words from “power” to “or under” substitute “to enforce the provisions of the Clinical Trials Regulations is imposed by”.

(4) After the definition of “manufacture” insert—

““medicinal product” means—

(a) anything that is a medicinal product within the meaning given by Article 1 of Directive [2001/83/EC](#), and

(b) anything that is an investigational medical product for the purposes of the Clinical Trials Regulations;”.

(5) Omit the definition of “offence under this Act”.

(6) For the definition of “prescribed” substitute—

““prescribed” means prescribed by regulations made by the Secretary of State and the Department for Health, Social Services and Public Safety, acting jointly;”.

**20.**—(1) Amendments in Schedule 3 (sampling) as follows.

(2) In paragraph 1(1)(a), for the words from “this Act or of any regulations” onwards substitute “the Clinical Trials Regulations, or”.

(3) In paragraph 1(1)(b), for the words from “of their functions” onwards substitute “(in this Schedule referred to as “the relevant enforcement authority”) of their functions under those Regulations or under any provision of this Act applied by regulation 47 of those Regulations,”.

(4) In paragraph 16, omit “the relevant enforcement officer is a Minister or the Pharmaceutical Society, and”.

(5) Omit paragraph 17.

(6) In paragraph 19(3), for “form prescribed by the Ministers” substitute “prescribed form”.

(7) Omit paragraph 20(2).

(8) In each of paragraphs 21 and 22, for “under this Act” substitute “under the Clinical Trials Regulations, or under section 114, 118 or 123 of this Act,”.

(9) In paragraph 24(1), for “under this Act,” substitute “under the Clinical Trials Regulations or under section 114, 118 or 123 of this Act,”.

(10) In paragraph 27 (power to apply Schedule with modifications), for “Ministers” substitute “Secretary of State and the Department for Health, Social Services and Public Safety, acting jointly,”.

SCHEDULE 10

Regulation 54

CONSEQUENTIAL AND OTHER AMENDMENTS OF ENACTMENTS

PART 1

ACTS OF PARLIAMENT

**The Act**

1.—(1) Section 3 of the Act (general functions of the Medicines Commission)(55) is amended as follows—

(2) In subsection (1), for the words from “advice” to “products, where” substitute—

“advice on matters—

- (a) relating to the execution of this Act,
- (b) relating to the exercise of any power conferred by this Act,
- (c) relating to the execution of the Clinical Trials Regulations,
- (d) relating to the exercise of any power conferred by those regulations, or
- (e) otherwise relating to medicinal products,

where.”

(3) In subsection (2), after “by or under this Act” insert “or the Clinical Trials Regulations”.

(4) For subsection (2)(d) substitute—

“(d) to advise the licensing authority in cases where the authority—

- (i) are required by the provisions of Part II of this Act, or by the provisions of the Clinical Trial Regulations, to consult the Commission with respect to any matter arising under those provisions; or
- (ii) without being required to do so, elect to consult the Commission with respect to any matter arising under any of those provisions.”

2. In section 4 of the Act (establishment of committees)(56), in subsection (2), for the words from “connected with” onwards substitute—

“connected with—

- (a) the execution of this Act or the Clinical Trials Regulations, or
  - (b) the exercise of any power conferred by this Act or those regulations,
- either generally or in relation to any particular class of substances or articles to which any provision of this Act or those regulations applies.”

3. In section 7 of the Act (restrictions as to dealings with medicinal products)(57), after subsection (3), insert the following subsection—

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(55) Section 3 has effect as if any reference to the Act included a reference to the Medicines for Human Use (Marketing Authorisations Etc) Regulations 1994 (S.I. 1994/3144) (“the 1994 Regulations”); see regulation 9(1) of the 1994 Regulations.

(56) Section 4 has effect as if any reference to the Act included a reference to the Medicines for Human Use (Marketing Authorisations Etc) Regulations 1994 (S.I. 1994/3144) (“the 1994 Regulations”); see regulation 9(1) of the 1994 Regulations

(57) Section 7 does not apply to “relevant medicinal products” within the meaning of regulation 1(2) of the 1994 Regulations; see regulation 9(2) of the 1994 Regulations.

*Status: This is the original version (as it was originally made).*

“(3A) The restrictions imposed by subsections (2) and (3) of this section shall not apply where the medicinal product concerned is an investigational medicinal product within the meaning of the Clinical Trials Regulations.”.

4.—(1) Section 8 of the Act (provisions as to manufacture and wholesale dealing) shall be amended as follows.

(2) At the beginning of subsection (2), insert “Subject to subsection (2A) of this section”.

(3) After subsection (2) insert the following subsections—

“(2A) In the case of a medicinal product that is an investigational medicinal product, the restrictions imposed by subsection (2) of this section only apply—

- (a) if the product has a product licence or marketing authorization, and
- (b) to the extent that the manufacture or assembly of the product is in accordance with the terms and conditions of that licence or authorization.

(2B) In subsection (2A) of this section—

“investigational medicinal product” has the meaning given by the Clinical Trials Regulations; and

“marketing authorization” means—

- (a) a marketing authorization issued by a competent authority in accordance with Directive [2001/83/EC](#), or
- (c) a marketing authorization granted by the European Commission under Council Regulation ([EEC](#)) [2309/93](#)(**58**).

(4) In subsections (3) and (3A)(**59**), for “subsection (3C)”, in both places those words appear, substitute “subsections (3C) and (3D)”.

(5) After subsection (3C), insert the following subsection—

“(3D) The restrictions imposed by subsections (3) and (3A) of this section do not apply where the product concerned is an investigational medicinal product within the meaning given by the Clinical Trials Regulations.”.

5.—(1) Section 23 of the Act (special provisions as to the effect of manufacturer’s licence)(**60**) shall be amended as follows.

(2) In subsection (1)—

- (a) omit “clinical trials and”;
- (b) for paragraph (b), substitute the following paragraph—
  - “(b) the products are manufactured or assembled to the order of—
    - (i) a person who is the holder of such a product licence, or
    - (ii) if the products are to be used for the purposes of a clinical trial, the sponsor of that trial.”.

(3) After subsection (5), insert the following subsection—

“(6) In this section, “clinical trial” and “sponsor”, in relation to a clinical trial, have the meaning given by Clinical Trials Regulations.”.

6. Section 31 of the Act shall be omitted

(58) OJ No. L214, 24.8.1993, p.1.

(59) Subsections (3A) to (3C) of section 8 were inserted by regulation 2(4) of [S.I. 1993/834](#)

(60) Section 23 of the Act has effect as if any reference in subsection (1) to a product licence included a reference to a marketing authorization; *see* regulation 9(1) of the 1994 Regulations.

**7.—(1)** Section 35 of the Act (supplementary provisions as to clinical trials and medicinal test on animals) shall be amended as follows.

(2) In subsection (1), omit “a clinical trial certificate or”.

(3) In subsection (2), omit paragraph (a).

(4) In subsection (4), omit the words from the beginning to “; and”.

(5) In subsection (5)—

(a) omit “a clinical trial or”;

(b) for paragraph (a), substitute the following paragraph—

“(a) an animal test certificate has been issued and is for the time being in force in respect of that test, and the test is to be carried out in accordance with that certificate, and;”

(c) in paragraph (b), omit “trial or”.

(6) In subsection (7)—

(a) for “sections 31 and 32” substitute “section 32”;

(b) omit “of a clinical trial or”; and

(c) in paragraph (a), omit “trial or”.

(7) In subsection (8), omit paragraph (a).

(8) In subsection (10), omit “any of the provisions of subsections (5) to (8) of section 31 of this Act, or”.

**8.** In section 36 of the Act (application for, and issue of, certificate)—

(a) in subsection (1), omit “a clinical trial certificate or”;

(b) in subsection (2), omit “clinical trial or”;

(c) in subsection (3), omit “clinical trial certificates or”.

**9.—(1)** Section 37 of the Act (transitional provisions as to clinical trials and medicinal tests on animals) shall be amended as follows.

(2) In subsection (1), omit “31, ”.

(3) In subsection (2), for “sections 31 and 32” substitute “section 32”.

(4) In subsection (3)—

(a) omit paragraph (a);

(b) for “section 31 or section 32 of this Act do not apply to anything done in relation to medicinal products of that description or (as the case may be)” substitute “section 32 of the Act do not apply to anything done”.

(5) In subsection (4)—

(a) omit “a clinical trial certificate or”;

(b) in paragraph (a), for the words from the beginning to “so specified” substitute “substances or articles specified in the application”.

**10.** In section 38 of the Act (duration and renewal of certificate)—

(a) in subsections (1) and (4), omit “clinical trial certificate or”;

(b) in subsections (5) and (6), for “a clinical trial certificate or animal test certificate” substitute “an animal test certificate”.

**11.** In section 39 of the Act (suspension, revocation or variation of certificate)—

*Status: This is the original version (as it was originally made).*

- (a) in subsections (1), (3) and (4), for “a clinical trial certificate or animal test certificate” substitute “an animal test certificate”;
  - (b) in subsection (2)(c) and (e), omit “clinical trial or”.
- 12.** In section 44 of the Act (provision of information to licensing authority), in subsections (1) and (2), for “a clinical trial certificate or animal test certificate” substitute “an animal test certificate”.
- 13.** In section 45 of the Act (offences under Part II)—
- (a) in subsections (1) and (2), omit “section 31,”;
  - (b) in subsection (3), for “a clinical trial certificate or animal test certificate” substitute “an animal test certificate”.
- 14.** In section 46 of the Act (special defences under section 45), for “a clinical trial certificate or animal test certificate” (in each place) substitute “an animal test certificate”.
- 15.** In section 47 of the Act (standard provisions for licences or certificates), in subsection (2) and (4), omit “clinical trial certificate or”.
- 16.** In section 50 of the Act (certificates for exporters of medicinal products), after paragraph (b) insert
- “, and
- (c) to the provisions of the Clinical Trials Regulations and to any authorisation granted or other thing done by virtue of those regulations.”.
- 17.** In section 104 of the Act (application of Act to certain articles and substances), in subsection (1), after “such provisions of this Act” insert “, or the Clinical Trials Regulations,”.
- 18.** In section 105 of the Act (application of Act to certain other substances which are not medicinal products), in subsection (1), after “such provisions of this Act” insert “, or the Clinical Trials Regulations,”.
- 19.** In section 132 of the Act (general interpretation provisions)—
- (a) in subsection (1)—
    - (i) omit the entry defining “clinical trial” and “clinical trial certificate”, and
    - (ii) before the definition of “the Commission” insert the following definition—
 

““the Clinical Trials Regulations” means the Medicines for Human Use (Clinical Trials) Regulations 2004;”;
- in subsection (3), omit “a clinical trial certificate or”.

### **The Medicines Act 1971**

**20.** In section 1 of the Medicines Act 1971 (fees payable for the purposes of Part II of the Act)(**61**) after subsection (2) insert the following subsection—

“(2A) In subsections (1) and (2)(b) above, any reference to a licence under Part II of the principal Act shall be taken to include a reference to a manufacturing authorisation under the Medicines for Human Use (Clinical Trials) Regulations 2004.”.

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(61) Section 1 of the Medicines Act 1971 has effect as if any reference in subsection (1) to any application in pursuance of the Act for a licence under Part II of the Act (or for the variation or renewal of such a licence) included a reference to any application under the Medicines for Human Use (Marketing Authorisations Etc) Regulations 1994 (S.I. 1994/3144) for a marketing authorization (or for the variation or renewal of such an authorization) and any reference in subsection (2)(b) to a licence under Part II of the Act included a reference to a marketing authorization; *see* regulation 9(12) of the those Regulations.



## **The Adults with Incapacity (Scotland) Act 2000**

**21.** Section 51 of the Adults with Incapacity (Scotland) Act 2000<sup>(62)</sup> (authority for research) shall be amended as follows—

- (a) in subsection (2), at the beginning of paragraph (b) insert “Subject to subsection (3A),”;
- (b) after subsection (3), insert the following subsection—

“(3A) Where the research consists of a clinical trial of a medicinal product, the research may be carried out—

- (a) without being approved by the Ethics Committee, if a favourable opinion on the trial has been given by an ethics committee, other than the Ethics Committee, in accordance with regulation 15 of the Medicines for Human Use (Clinical Trials) Regulations 2004; and
- (b) without the consent of any guardian or welfare attorney, or the adult’s nearest relative, if—
  - (i) it has not been practicable to contact any such person before the decision to enter the adult as a subject of the clinical trial is made, and
  - (ii) consent has been obtained from a person, other than a person connected with the conduct of the clinical trial, who is—
    - (A) the doctor primarily responsible for the medical treatment provided to that adult, or
    - (B) a person nominated by the relevant health care provider.”; and

- (c) at the end insert the following subsection—

“(9) In this section—

“clinical trial on a medicinal product” means a clinical trial as defined by regulation 2(1) of the Medicines for Human Use (Clinical Trials) Regulations 2004;

“an ethics committee” has the meaning given by that regulation;

“person connected with the conduct of the trial” and “relevant health care provider” have the meanings given by Schedule 1 to those regulations.”.

## **PART 2**

### **ORDERS AND REGULATIONS**

**1.** In the Medicines (Standard Provisions for Licences and Certificates) Regulations 1971<sup>(63)</sup>—

- (a) in regulation 2 (interpretation), in the definition of “clinical trial certificate of right” and “animal test certificate of right”, omit ““clinical trial certificate of right” and”;
- (b) in regulation 3 (standard provisions for licences and certificates), omit paragraph (2); and
- (c) in Schedule 1, omit Part II (standard provisions for clinical trial certificates and clinical trial certificates of right).

**2.** In the Medicines (Surgical Materials) Order 1971<sup>(64)</sup>, in article 3, for the words from “, the provisions contained in Parts I and II of the Act” to the end substitute—

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<sup>(62)</sup> 2000 asp 4.

<sup>(63)</sup> S.I. 1971/972; regulation 3(3) and Part III of Schedule 1 are revoked insofar as they apply to animal test certificates by S.I. 2003/3309.

<sup>(64)</sup> S.I. 1971/1267, as amended by S.I. 1994/3119.

*Status: This is the original version (as it was originally made).*

- “(a) the provisions contained in Parts I and II of the Act, sections 62, 64, 65 and 67 of Part III of the Act, and the provisions contained in Parts V, VI and VIII of the Act shall have effect in relation to the said articles or substances described in the Schedule to this Order, as those provisions have effect in relation to medicinal products; and
- (b) the provisions of the Clinical Trials Regulations shall have effect in relation to the said articles or substances.”.

**3.—(1)** In the Medicines (Exemption from Licences) (Special Cases and Miscellaneous Provisions) Order 1972(**65**), article 4 shall be amended as follows.

(2) In paragraph (1)—

- (a) for “sections 7, 31(2) and 32” substitute “sections 7 and 32”;
- (b) in subparagraph (a), omit “a clinical trial, or, as the case may be,”.

(3) In paragraph (2)—

- (a) in subparagraph (i)—
  - (i) in paragraph (a), omit “a clinical trial, or, as the case may be,”;
  - (ii) in paragraph (b), omit “clinical trial or”;
- (b) in subparagraph (iii)—
  - (i) omit “the clinical trial or, as the case may be,”;
  - (ii) omit the words from “the doctor or dentist” to “as the case may be,”;
- (c) in subparagraph (iv)—
  - (i) omit the words from “that the doctor or dentist” to “as the case may be,”;
  - (ii) omit the words “the trial, or, as the case may be”.

(4) Omit paragraph (3).

**4.** In the Medicines (Dental Filling Substances) Order 1975(**66**), in article 2, in paragraph (1), for the words from “the following provisions of the Act” to the end substitute—

- “(a) the provisions contained in Parts I, II, III, V, VI and VIII of the Act shall have effect in relation to dental filling substances as those provisions have effect in relation to medicinal products; and
- (b) the provisions of the Clinical Trials Regulations shall have effect in relation to those substances.”.

**5.** In the Medicines (Specified Articles and Substances) Order 1976(**67**), in article 2, in paragraph (1), for the words from “the provisions of the Act” to the end substitute—

- “(a) the provisions of the Act set out in Part I of the said Schedule 2 shall have effect in relation to such articles or substances as those provisions have effect in relation to medicinal products; and
- (b) the provisions of the Clinical Trials Regulations shall have effect in relation to those articles or substances.”.

**6.—(1)** The Medicines (Labelling) Regulations 1976(**68**) shall be amended as follows.

(65) S.I. 1972/1200.

(66) S.I. 1975/533, as amended by S.I. 1994/3119.

(67) S.I. 1976/968, as amended by S.I. 1994/3119.

(68) S.I. 1976/1726; the Regulations were revoked in so far as they relate to the labelling of containers and packages of medicinal products for administration in certain medicinal tests on animals by S.I. 1996/2194.

(2) In regulation 1 (citation and scope)(**69**), after “apply”, insert “or a medicinal product which is an investigational medicinal product within the meaning of the Medicines for Human Use (Clinical Trials) Regulations 2003”.

(3) In regulation 2 (commencement), in paragraph (b), in sub-paragraph (i), omit “, clinical trial certificate”.

(4) Omit regulation 6 (clinical trials).

(5) In regulation 10 (surgical materials), omit the words from “, except that” to the end.

(6) In regulation 16 (provisions in licences, clinical trial certificates and animal test certificates)—

(a) in paragraph (1), for “a clinical trial certificate or animal test certificate ” substitute “an animal test certificate”;

(b) in paragraph (2), omit “, clinical trial certificate”.

(7) Omit Schedule 2 (particulars required in the labelling of containers and packages of medicinal products for clinical trials).

7. In the Medicines (Fluted Bottles) Regulations 1978(**70**), in regulation 3 (exceptions)—

(a) after paragraph (e), insert the following paragraph—

“(ee) where medicinal products are investigational medicinal products within the meaning given by the Medicines for Human Use (Clinical Trials) Regulations 2004;” and

(b) in paragraph (g), omit “clinical trial certificate or”.

8. In Schedule 1 to the Medicines (Fixing of Fees Relating to Medicinal Products for Human Use) Order 1989(**71**), after paragraph 9A(**72**) insert the following paragraph—

“**9B.** Functions of the licensing authority which are functions of theirs by virtue of the Medicines for Human Use (Clinical Trials) Regulations 2004 and the functions of any person appointed under Schedule 5 or 8 to those Regulations.”.

9. In the Medicines Act 1968 (Application to Radiopharmaceutical-Associated Products) Regulations 1992(**73**), in the Schedule—

(a) in the entry relating to section 44 of the Act, for ““, or of a clinical trial certificate or animal test certificate,”” substitute ““, or of an animal test certificate,””;

(b) in the entry relating to section 45 of the Act, omit “section 31,” in both places those words appear;

(c) in the entry relating to section 46 of the Act, for ““or of a clinical trial certificate or animal test certificate”” substitute ““or of an animal test certificate””; and

(d) in the entry relating to section 47 of the Act—

(i) for ““any clinical trial certificate or animal test certificate”” substitute ““any animal test certificate””, and

(ii) for ““, or any clinical trial certificate or animal test certificate,”” substitute ““, or any animal test certificate,””.

10. In the Medicines (Homoeopathic Medicinal Products for Human Use) Regulations 1994(**74**), in Schedule 4 (application of the provisions of the Act)—

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(69) As amended by [S.I. 1994/3144](#).

(70) [S.I. 1978/40](#); regulation 3 was amended by [S.I. 1994/3142](#) and [3144](#).

(71) [S.I. 1989/684](#).

(72) Paragraph 9A was inserted by [S.I. 1995/871](#).

(73) [S.I. 1992/605](#).

(74) [S.I. 1994/105](#).

*Status: This is the original version (as it was originally made).*

- (a) in the entry relating to section 23 of the Act, omit “clinical trials and”;
- (b) in the entry relating to section 44 of the Act, for “a clinical trial certificate or animal test certificate”, in both places those words appear, substitute “an animal test certificate”;
- (c) in the entry relating to section 45 of the Act—
  - (i) omit “section 31,”, and
  - (ii) for ““or of a clinical trial certificate or animal test certificate”” substitute ““or of an animal test certificate””; and
- (d) in the entry relating to section 46 of the Act, for ““or of a clinical trial certificate or animal test certificate”” substitute ““or of an animal test certificate””.

**11.** In the Dangerous Substances and Preparations (Safety) (Consolidation) Regulations 1994(75), in regulation 1 (citation, commencement and interpretation), in paragraph (2), in the definition of “medicinal product”—

- (a) for sub-paragraph (ii), substitute the following sub-paragraph—
  - “(ii) which is an “investigational medicinal product” within the meaning of regulation 2(1) of the Medicines for Human Use (Clinical Trials) Regulations 2003, or”; and
- (b) omit sub-paragraph (iii).

**12.** In the Medicines for Human Use (Marketing Authorisations Etc.) Regulations 1994(76)—

- (a) in regulation 1—
  - (i) in paragraph (2), after the definition of “the Act” insert the following definition—
    - ““the Clinical Trials Directive” means Directive 2001/20/EC of the European Parliament and of the Council on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use;”,
  - (ii) in paragraph (5), omit “and except in the case of “clinical trial,””; and
- (b) in Schedule 1, in paragraph 2, for sub-paragraph (e)(77) substitute the following sub-paragraph—
  - “(e) the relevant medicinal product—
    - (i) is manufactured, assembled or imported by the holder of an authorization referred to in Article 40 of the 2001 Directive which relates specifically to the manufacture, assembly or import of relevant medicinal products to which paragraph 1 applies; or
    - (ii) has been manufactured, assembled or imported as an investigational medicinal product by the holder of an authorization referred to in Article 13 of the Clinical Trials Directive”; and.

**13.** In the Prescription Only Medicines (Human Use) Order 1997(78)—

- (a) in article 1 (citation, commencement and interpretation), in paragraph (2), for the definition of “clinical trial exemption” substitute the following definition—
  - ““clinical trial” has the meaning given by regulation 2(1) of the Medicines for Human Use (Clinical Trials) Regulations 2003;”; and

(75) S.I. 1994/2844; regulation 1(2) was substituted by S.I. 1996/2635.

(76) S.I. 1994/3144.

(77) Paragraph 2(e) of Schedule 1 was amended by SI 2002/236.

(78) S.I. 1997/1830; the relevant amending instrument is S.I. 2003/696.

- (b) in article 3B (prescribing and administration by supplementary prescribers), in paragraph (3), in sub-paragraph (b), in head (ii), for the words from “and—” to the end substitute “which has been authorised, or is to be treated as having been authorised, by the licensing authority in accordance with the Medicines for Human Use (Clinical Trials) Regulations 2003”.

**14.** In the Ionising Radiation (Medical Exposure) Regulations 2000(**79**), in regulation 2 (interpretation), in paragraph (1), after the definition of “ionising radiation”, insert the following definition—

““Local Research Ethics Committee” means—

- (a) an ethics committee established or recognised in accordance with Part 2 of the Medicines for Human Use (Clinical Trials) Regulations 2004,
- (b) the Ethics Committee constituted by regulations made by the Scottish Ministers under section 51(6) of the Adults with Incapacity (Scotland) Act 2000, or
- (c) any other committee established to advise on the ethics of research investigations in human beings, and recognised for that purpose by or on behalf of the Secretary of State, the National Assembly for Wales or Scottish Ministers;”.

**15.** In the Private and Voluntary Health Care (England) Regulations 2001(**80**), in regulation 24 (research), for paragraph (2) substitute the following paragraph—

“(2) For the purposes of paragraph (1)(a), “appropriate Research Ethics Committee” means—

- (a) an ethics committee established or recognised in accordance with Part 2 of the Medicines for Human Use (Clinical Trials) Regulations 2004; or
- (b) any other committee established to advise on the ethics of research investigations in human beings, and recognised for that purpose by or on behalf of the Secretary of State;”.

**16.** In the Misuse of Drugs Regulations 2001(**81**), in regulation 18 (marking of bottles and other containers), for paragraph (3) substitute the following paragraph—

“(3) In this regulation—

“clinical trial” has the same meaning as in the Medicines for Human Use (Clinical Trials) Regulations 2003;

“medicinal test on animals” has the same meaning as in the Medicines Act 1968.”.

**17.** In the Health Service (Control of Patient Information) Regulations 2002(**82**), in regulation 1 (citation, commencement, interpretation and extent), in paragraph (2), for the definition of “research ethics committee” substitute the following definition—

““research ethics committee” means—

- (a) an ethics committee established or recognised in accordance with Part 2 of the Medicines for Human Use (Clinical Trials) Regulations 2004, or
- (b) any other committee established to advise on the ethics of research investigations in human beings, and recognised for that purpose by or on behalf of the Secretary of State or the National Assembly for Wales;”.

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(79) S.I. 2000/1059.

(80) S.I. 2001/3968.

(81) S.I. 2001/3998.

(82) S.I. 2002/1438.

*Status: This is the original version (as it was originally made).*

**18.** In the National Health Service (Functions of Strategic Health Authorities and Primary Care Trusts and Administration Arrangements) (England) Regulations 2002(**83**), in regulation 2 (interpretation), in paragraph (1), for the definition of “research ethics committee” substitute the following definition—

““research ethics committee” means—

- (a) an ethics committee established or recognised in accordance with Part 2 of the Medicines for Human Use (Clinical Trials) Regulations 2004, or
- (b) any other committee established to advise on the ethics of research investigations on human beings and recognised for that purpose by or on behalf of the Secretary of State;”.

## SCHEDULE 11

Regulation 55

### REVOCATIONS

<i>Regulations and orders</i>	<i>S.I. number</i>	<i>Extent of revocation</i>
The Medicines (Standard Provisions for Licence and Certificates) Regulations 1971	<a href="#">S.I. 1971/972</a>	The whole Regulations in so far as they relate to clinical trial certificates
The Medicines (Applications for Product Licences and Clinical Trial and Animal Test Certificates) Regulations 1971	<a href="#">S.I. 1971/973</a>	The whole Regulations in so far as they relate to applications for clinical trial certificates
The Medicines (Exemption from Licences) (Clinical Trials) Order 1974	<a href="#">S.I. 1974/498</a>	The whole Order
The Medicines (Renewal Applications for Licences and Certificates) Regulations 1974	<a href="#">S.I. 1974/832</a>	The whole Regulations in so far as they relate to renewal applications for clinical trial certificates
The Medicines (Exemption from Licences) (Clinical Trials) Order 1995	<a href="#">S.I. 1995/2808</a>	The whole Order
The Medicines (Exemption from Licences and Certificates) (Clinical Trials) Order 1995	<a href="#">S.I. 1995/2809</a>	The whole Order
The National Health Service Reform and Health Care Professions Act 2002 (Supplementary, Consequential Etc Provisions) Regulations 2002	<a href="#">S.I. 2002/2469</a>	Schedule 1, Part 2, paragraph 67.

(83) [S.I. 2002/2375](#).

SCHEDULE 12

Regulation 56

TRANSITIONAL PROVISIONS

**Ethical approval given before 1st May 2004**

- 1.—(1) This sub-paragraph applies where—
  - (a) a clinical trial is conducted after 30th April 2004;
  - (b) no ethics committee has given a favourable opinion in relation to that trial in accordance with regulation 15; and
  - (c) a committee established or recognised for the purpose of advising on the ethics of research investigations on human beings has before 1st May 2004 given a favourable ethical opinion in relation to that trial.
- (2) Subject to the following sub-paragraphs, where sub-paragraph (1) applies—
  - (a) the trial shall be treated for the purposes of these Regulations as if an ethics committee has given a favourable opinion in relation to that trial in accordance with regulation 15;
  - (b) regulations 12, 24(3) and 29 shall apply in relation to the trial with the modification that references to the application for an ethics committee opinion shall be read as references to the application for approval made to the committee referred to in sub-paragraph (1)(c); and
  - (c) regulations 24, 25, 27, 30 to 35 and 48 shall apply in relation to the trial with the modification that references to the relevant ethics committee shall be read as references to the committee referred to in sub-paragraph (1)(c).
- (3) This sub-paragraph applies where the committee referred to in sub-paragraph (1)(c) has not been recognised by the Authority in accordance with regulation 7—
  - (a) for the area in which the trial sites are situated, or
  - (b) for the description or class of clinical trial into which the trial falls,before 1st September 2004.
- (4) Where sub-paragraph (3) applies—
  - (a) the sponsor of the clinical trial may make an application to an ethics committee established or recognised by the Authority in accordance with Part 2—
    - (i) for the area in which the trial sites are situated, or
    - (ii) for the description or class of clinical trial into which the trial falls,for an amendment to the protocol for the trial within the meaning of Part 3 of these Regulations; or
  - (b) the chief investigator may make an application to an ethics committee in accordance with regulation 14.
- (5) Where an ethics committee receives an application for an amendment in accordance with sub-paragraph (4)(a), it shall consider the amendment as if it was a valid notice of amendment under regulation 24.
- (6) Where an ethics committee gives a favourable opinion in relation an application for amendment made pursuant to sub-paragraph (4)(a)—
  - (a) sub-paragraph (2)(c) shall cease to apply; and
  - (b) regulations 24, 25, 27, 30 to 35 and 48 shall apply in relation to the trial with the modification that references to the relevant ethics committee shall be read as references to the committee which gave that favourable opinion.

*Status: This is the original version (as it was originally made).*

(7) Where an ethics committee gives a favourable opinion in relation to an application pursuant to sub-paragraph (4)(a), sub-paragraph (2) shall cease to apply in relation to that trial

(8) Where sub-paragraph (3) applies and before 1st May 2006 no favourable opinion has been given as specified in sub-paragraphs (6) and (7), sub-paragraph (2) and (4) shall cease to apply from that date.

(9) If the committee referred to in sub-paragraph (1)(b) is abolished or ceases operation before 1st May 2006—

- (a) the Authority shall nominate an ethics committee as responsible for the work of the committee which is abolished or which ceases operation; and
- (b) regulations 24, 25, 27, 30 to 35 and 48 shall apply in relation to the trial with the modification that references to the relevant ethics committee shall be read as references to the committee so nominated.

#### **Applications for ethical approval prior to 1st May 2004**

2.—(1) This sub-paragraph applies where a person has made an application for an ethical opinion in relation to a clinical trial before 1st May 2004 to a committee established or recognised for the purpose of advising on the ethics of research investigations on human beings.

(2) Where—

- (a) sub-paragraph (1) applies;
- (b) the committee has not given its opinion before 1st May 2004; and
- (c) the committee has been recognised by the Authority in accordance with regulation 7 for the area in which the trial sites are situated, or for the description or class of clinical trial into which the trial falls,

the committee shall consider the application as if it had been made in accordance with regulation 14.

#### **Clinical trial exemptions or notifications prior to 1st May 2004**

3.—(1) This sub-paragraph applies where—

- (a) a clinical trial is conducted after 30th April 2004; and
- (b) immediately before 1st May 2004, a clinical trial certificate was in force and the trial was being conducted in accordance with that certificate.

(2) Where sub-paragraph (1) applies—

- (a) the trial shall be treated for the purposes of these Regulations as having been authorised by the licensing authority;
- (b) regulations 17 to 21 shall not apply in relation to the trial; and
- (c) regulations 11, 24(2), 29, 31 and 45(1), and Schedule 7, shall apply in relation to the trial with the modification that references to the request for authorisation shall be read as references to the application for the clinical trial certificate.

4.—(1) This sub-paragraph applies where—

- (a) a clinical trial is conducted after 30th April 2004; and
- (b) immediately before 1st May 2004, the exemption conferred by article 3 of the Medicines (Exemption from Licences) (Clinical Trials) Order 1995<sup>(84)</sup> applied in respect of the sale or supply of medicinal products for the purposes of that trial.

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(84) S.I. 1995/2808.



- (2) Where sub-paragraph (1) applies—
- (a) the trial shall be treated for the purposes of these Regulations as having been authorised by the licensing authority;
  - (b) regulations 17 to 21 shall not apply in relation to the trial; and
  - (c) regulations 11, 24(2), 29, 31 and 45(1), and Schedule 7, shall apply in relation to the trial with the modification that references to the request for authorisation shall be read as references to the notice to the licensing authority specified in article 4(1)(a) of the Medicines (Exemption from Licences) (Clinical Trials) Order 1995 .
- 5.—(1) This sub-paragraph applies where—
- (a) a clinical trial is conducted after 30th April 2004;
  - (b) the investigational medicinal product used in the trial is a product with a marketing authorization;
  - (c) the trial has before 1st May 2004 been notified to the licensing authority by the person supplying the product for the purposes of that trial; and
  - (d) the licensing authority has before 1st May 2004 notified that person that—
    - (i) the trial appeared to fall within the terms of the Medicines (Exemption from Licences) (Clinical Trials) Order 1974(85), and
    - (ii) the authority agreed to the trial proceeding.
- (2) Where sub-paragraph (1) applies—
- (a) the trial shall be treated for the purposes of these Regulations as having been authorised by the licensing authority;
  - (b) regulations 17 to 21 shall not apply in relation to the trial; and
  - (c) regulations 11, 24(2), 29, 31 and 45(1), and Schedule 7, shall apply in relation to the trial with the modification that references to the request for authorisation shall be read as references to the notification referred to in sub-paragraph (1)(c).
- 6.—(1) This sub-paragraph applies where—
- (a) a clinical trial is conducted 30th April 2004; and
  - (b) immediately before 1st May 2004, the exemption conferred by article 2(2) of the Medicines (Exemption from Licences) (Special Cases and Miscellaneous Provisions) Order 1972(86) applied in respect of the sale or supply of medicinal products for the purposes of that trial.
- (2) Where sub-paragraph (1) applies—
- (a) the trial shall be treated for the purposes of these Regulations as having been authorised by the licensing authority;
  - (b) regulations 17 to 21 shall not apply in relation to the trial; and
  - (c) regulations 11, 24(2), 29, 31 and 45(1), and Schedule 7, shall apply in relation to the trial with the modification that references to the request for authorisation shall be read as references to the notification to the licensing authority specified in article 2(3)(c) or (4)(a) of the Medicines (Exemption from Licences) (Special Cases and Miscellaneous Provisions) Order 1972.

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(85) S.I. 1974/498.

(86) S.I. 1972/1200.

**Applications for clinical trial exemptions or notifications prior to 1st May 2004**

7.—(1) This sub-paragraph applies where—

- (a) an application for a clinical trial certificate has been made in accordance with section 36 of the Act and the licensing authority has not before 1st May 2004 determined whether to issue a certificate;
- (b) the licensing authority has received a notice pursuant to article 4(1)(a) of the Medicines (Exemption from Licences) (Clinical Trials) Order 1995 and on 1st May 2004—
  - (i) the specified period within the meaning of article 4(2) of that Order has not expired, and
  - (ii) the authority has not given or sent a notice pursuant to article 4(1)(b); or
- (c) the licensing authority has received a notice pursuant to article 4(2)(iv) of the Medicines (Exemption from Licences) (Special Cases and Miscellaneous Provisions) Order 1972 and on 1st May 2004—
  - (i) the period specified in article (2)(v) of that Order has not expired, and
  - (ii) the authority has not given a direction pursuant to that article.

(2) Where sub-paragraph (1) applies the licensing authority shall treat the application or notice as a valid request for authorisation to conduct the clinical trial to which the application or notice relates under regulation 17.

**EXPLANATORY NOTE**

*(This note is not part of the Regulations)*

These Regulations implement Directive [2001/20/EC](#) on the approximation of laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use (“the Directive”).

The Regulations provide that the licensing authority established in accordance with the Medicines Act 1968 for the purpose of Part II of that Act (licences and certificates relating to medicinal products) shall exercise the functions of the competent authority under the Directive and certain functions falling to be performed by Member States under that Directive (regulation 4), unless those functions are conferred on any other person or body (for example, enforcement functions are conferred on the Secretary of State for Health, the National Assembly for Wales, the Scottish Ministers and the Department for Health, Social Services and Public Safety in Northern Ireland).

Regulations 5 to 10, and Schedule 2, make provision for ethics committees in the United Kingdom, which are to be responsible, amongst other things, for giving opinions on the ethics of clinical trials involving medicinal products. Regulation 5 provides for the United Kingdom Ethics Committees Authority, which is to be responsible for establishing, recognising, and monitoring ethics committees.

Regulations 11 to 27, and Schedules 3 to 5, make provision for clinical trial authorisations by the licensing authority and for ethics committee opinions. In particular: regulation 12 provides that a clinical trial may be conducted only if it has been authorised by the licensing authority and an ethics committee has given a favourable opinion; regulation restricts the supply of medicinal products for the purposes of clinical trials; regulations 14 to 16 and Schedules 3 and 4 make

provision for applications for ethics committee opinions; and regulations 17 to 21 and Schedule 3 deal with requests to the licensing authority for authorisation. Regulations 22 to 25 make provision for amendments to clinical trial authorisations; and regulation 26 and Schedule 5 make provision for the reference to the appropriate committee or the Medicines Commission of decisions to refuse authorisations, amendments etc. Regulation 27 makes provision for the conclusion of a trial.

Regulations 28 to 31, and Schedules 1 and 5, make provision for: the conduct of a clinical trial, including the requirement to adhere to the principles of Good Clinical Practice; urgent safety measures to protect trial subjects from immediate hazards; and the suspension and termination of a trial. Schedule 5 includes provisions for referral to the appropriate committee or the Medicines Commission where a trial is suspended or terminated by the licensing authority.

Regulations 32 to 35 make provision for pharmacovigilance; i.e. the recording and reporting of adverse events and reactions to medicinal products being used in a clinical trial.

Regulations 36 to 45, and Schedules 6 to 8, make provision for the manufacture and importation of medicinal products to be used in clinical trials. In particular they make provision for: authorisations for manufacture, assembly and importation (regulations 36 and 37); the applications for, consideration of and grant or refusal of such authorisations (regulations 38 to 40 and Schedules 6 to 8); the application and effect of authorisations (regulations 41 and 42); the qualified persons responsible for checking the quality of products being manufactured, assembled or imported (regulation 43); and the variation, suspension and revocation of authorisations (regulations 44 and 45 and Schedule 8).

Regulation 46 concerns the labelling of such medicinal products.

Regulations 47 to 52, and Schedule 9, make provision for enforcement and related matters, including powers of inspection, infringement notices, offences and penalties for breaches of the Regulations.

Regulations 53 to 56, and Schedules 10 to 12, contain miscellaneous provisions for the construction of references in authorisations to pharmacopoeias and other publications, for the consequential amendment and revocation of legislation, and for transitional arrangements.

A full regulatory impact assessment of the effect that this instrument will have on the costs of business is available from the Medicines and Healthcare products Regulatory Agency, Room 10-202, Market Towers, 1 Nine Elms Lane, London SW8 5NQ. A copy of that assessment, and a Transposition Note in relation to the implementation of Directive [2001/20/EC](#), have been placed in the libraries of both Houses of Parliament.