2003 No.

MEDICINES

The Medicines for Human Use (Clinical Trials) Regulations 2003

Made - - - - 2003
Laid before Parliament 2003
Coming into force - - 2003

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The Secretary of State, being a Minister designated(a) for the purposes of section 2(2) of the European Communities Act 1972(b) 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 I
INTRODUCTORY PROVISIONS

Citation and commencement
1. These Regulations may be cited as the Medicines for Human Use (Clinical Trials) Regulations 2003 and shall come into force on [   ].

Interpretation
2.—(1) In these Regulations—
“the Act” means the Medicines Act 1968(c);
“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;
“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 registered nurse,

(a) S.I. 1972/1811.
(b) 1972 c.68.
(c) 1968 c.67.
(d) a pharmacist;

“the EMEA” means the European Agency for the Evaluation of Medicinal Products established by Council Regulation (EEC) No. 2309/93(a);

“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” and “assembly”, in relation to an investigational medicinal product, have the meaning given by section 132(1) of the Act;

“business”, unless the context otherwise requires, has the meaning given by section 132(1) of the Act;

“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;

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


“conditions and principles of good clinical practice” means—

(a) the Principles of Good Clinical Practice set out in [Commission Directive xxx/2003(d) on good clinical practice in the conduct of clinical trials on medicinal products for human use], and

(b) the conditions and principles for the protection of clinical trial subjects 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,

(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—


(b) OJ No. L193, 17.7.91, p.30.

(c) Amended by...[amending directive]

(d) OJ No. L.........
(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, has the meaning given by section 132(1) of the Act;
“dentist” has the meaning given by section 132(1) of the Act(a);
“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(b);
“doctor” means a registered medical practitioner(d);
“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(e) as adjusted by the Protocol signed at Brussels on 17th March 1993(f);
“European Economic Area” means the European Economic Area created by the EEA Agreement;
“ethics committee” means, unless the context otherwise requires—
(a) a committee established or recognised in accordance with Part 2 of these Regulations, or
(b) the Ethics Committee constituted by regulations made by the Scottish Ministers under section 51(6) of the Adults with Incapacity (Scotland) Act 2000(g);
“export”, unless the context otherwise requires, means export to a third country from the United Kingdom, whether by land, sea or air;
“Health and Social Services Board” means a Health and Social Services Board established under the Health and Personal Social Services (Northern Ireland) Order 1972(h);
“Health Authority” means a Health Authority established under the National Health Service Act 1977(i);
“Health Board” means a Health Board established under the National Health Service (Scotland) Act 1978(j);
“health care” means services for or in connection with the prevention, diagnosis or treatment of illness;
“health care professional” means—
(a) a doctor,

(a) The definition of “dentist” was amended by paragraph 2 of Schedule 5 to the Dentists Act 1984 (c.24).
(b) OJ No. L121, 1.5.2001, p.34.
(c) OJ No. L311, 28.11.2001, p.67.
(d) 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).
(e) OJ No. L1, 3.1.1994, p.3.
(f) OJ No. L1, 3.1.1994, p.572.
(g) 2000 asp. 4; see S.S.I. 2002/190.
(h) S.I. 1972/1265 (N.I. 14).
(i) 1977 c.49; 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).
(j) 1978 c. 29.
(b) a dentist,
(c) a registered nurse,
(d) a pharmacist,
(e) a person registered in a register of ophthalmic opticians maintained under section 7 of the Opticians Act 1989(a),
(f) a person registered in—
   (i) a register maintained pursuant to paragraph 11 of Schedule 2 to the Health Professions Order 2001(b), or
   (ii) a register established and maintained under article 5 of that Order,
(g) a registered osteopath as defined by section 41 of the Osteopaths Act 1993(c), or
(h) a registered chiropractor as defined by section 43 of the Chiropractors Act 1994(d);
“health centre” has the meaning given by section 132(1) of the Act(e);
“health service body” means—
   (a) a Strategic Health Authority, 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) the Public Health Laboratory Service Board continued in being by section 5(4) and (5) of, and Schedule 3 to, the National Health Service Act 1977,
   (d) the Dental Practice Board constituted under section 37(1) of the National Health Service Act 1977,
   (e) a Special Health Board established under the National Health Service (Scotland) Act 1978,
   (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) a National Health Service trust established under the National Health Service and Community Care Act 1990(f) or the National Health Service (Scotland) Act 1978, or
   (h) a Health and Social Services trust established under the Health and Personal Social Services (Northern Ireland) Order 1991(g);
“hospital” has the meaning given by section 132(1) of the Act;
“import”, unless the context otherwise requires, means import to the United Kingdom, whether by land, sea or air, from a third country;
“informed consent” shall be construed in accordance with paragraph 3 of Part 1 of Schedule 1;
“insurance or indemnity” includes arrangements—
   (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)(h),
(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)(a), 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)(b), 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 accepting financial liability for clinical negligence (known as NHS Indemnity);

“investigational medicinal product” means, subject to regulation 34(4), 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;

“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” and “label”, in relation to an investigational medicinal product, have the meanings given by section 132(1) of the Act;

“legal representative” has the meaning given in Part 1 of Schedule 1 to these Regulations;

“manufacturing authority” has the meaning given by regulation 35(1) of these Regulations;

“marketing authorization” shall be construed in accordance with regulation 1(4)(a) of the Medicines for Human Use (Marketing Authorisations Etc.) Regulations 1994(c);

“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—

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(a) 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).

(b) S.I. 1991/194 (N.I. 1).

(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 clinical trial 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;

“package”, in relation to an investigational medicinal product, has the meaning given by section 132(1) of the Act;

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

(a) any container in which the product is or is to be contained, and

(b) any package in which such a container is or is to be contained;

“Pharmaceutical Society” has the meaning given by section 132(1) of the Act;

“pharmacist” has the meaning given by section 132(1) of the Act;


“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 42(2) in respect of investigational medicinal products for a period of at least one year prior to the date the manufacturing authorisation in respect of which the person is to act as qualified person was granted or 1st May 2004, whichever is earlier,

(ii) has, in accordance with paragraph 5 of Schedule 4, been named as a qualified person in a valid application for a manufacturing authorisation made prior to 1st May 2006, and

(iii) is—

(a) 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

(b) the holder of a diploma, certificate or other evidence of formal qualifications awarded on completion of a university course in pharmacy, medicine, chemistry, pharmaceutical chemistry, or biology;

“registered nurse” means a person who is registered in the register maintained by the Nursing and Midwifery Council pursuant to paragraph 10 of Schedule 2 to the Nursing and Midwifery Order 2001;

“registered pharmacy” means premises for the time being entered in the register required to be kept under section 75 of the Act;

(a) The definition of “pharmacist” was amended by paragraph 7 of Schedule 5 to S.I. 1976/1213 (N.I. 22).

(b) See article 3 of the Nursing and Midwifery Order 2001, S.I. 2002/253.

(c) S.I. 2002/253.

(d) Section 75 was amended by articles 2 and 5(4)(a) of S.I. 1968/1699.
“relevant ethics committee”, in relation to a clinical trial, means the ethics committee which has given a favourable opinion in relation to that trial;

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

(a) removing the product from its packaging and placing or enclosing it in different packaging,

(b) affixing to or displaying on such packaging a different label, whether or not the original label is removed;

“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” means, in relation to a clinical trial, the person who takes on ultimate responsibility for the initiation and management (or arranging the initiation and management) of, and the financing (or arranging the financing) for, that trial;

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

“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;

“treatment” has the meaning given by section 132(1) of the Act;

“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—

(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.

Responsibility for functions under the Directive

3.—(1) For the purposes of the Directive, the competent authority 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

(a) 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).
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

4.—(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

5.—(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 considers appropriate.

(2) The Authority may—

(a) vary the area for which any committee it has 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

6.—(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) it is 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, for the purpose of advising on the ethics of research investigations on human beings, a committee has been established or recognised as a research ethics committee by—

(a) the Secretary of State;

(b) the Scottish Ministers;

(c) the National Assembly for Wales;

(d) the Department of Health and Social Services for Northern Ireland;

(e) a Strategic Health Authority, Health Authority, Health Board or Health and Social Services Board,

and that committee was in existence on 1st February 2004, the Authority may recognise the 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

7. The Authority may revoke a recognition of an ethics committee if it is 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

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

Other functions of the Authority

9.—(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

10. 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 clinical trial 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 13; 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 16, and “valid amended request” shall be construed accordingly.

Requirement for authorisation and ethics committee opinion

11.—(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 has issued a favourable opinion in relation to the clinical trial;
(b) the clinical trial has been authorised by the licensing authority;
(c) the sponsor of the trial, or a person authorised to act on his behalf in relation to the trial, is established in the Community.

(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 17 relates—
   (i) the trial is to be treated as authorised by virtue of regulation 17, or
   (ii) the authority has accepted the request for authorisation in accordance with the procedure specified in Schedule 3; or
(b) in the case of a clinical trial to which regulation 18 or 19 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 3.

Supply of investigational medicinal products for the purpose of clinical trials

12.—(1) 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 purposes of such a trial, other than in accordance with the terms of any marketing authorization relating to that product, 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 any EEA State, other than in accordance with a marketing authorization relating to that product, the product has been manufactured or assembled by a person holding, in relation to that product—
   (i) a manufacturing authorisation, or
   (ii) an authorisation referred to in Article 13 of the Directive granted by a competent authority of an EEA State other than the United Kingdom;
(c) in the case of an imported investigational medicinal product, the product has been imported by a person holding a manufacturing authorisation relating to the importation of that product; and
(d) 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.
Application for ethics committee opinion

13.—(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) Subject to regulation 15, a chief investigator for a trial shall make only one application for an ethics committee opinion in relation to that trial, regardless of the number of trial sites at which the trial is to be conducted.

(3) Subject to paragraph (4), 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(a).

(5) An application shall be—

(a) in writing;
(b) signed by the chief investigator making the application, whether in ink or by means of an electronic signature; and
(c) accompanied by—
   (i) the particulars and documents set out in Section 5.1.2 of the detailed guidance on the application format and documentation to be submitted in an application for an ethics committee opinion on a clinical trial on a medicinal product for human use dated [ ] and published by the Commission under Article 8 of the Directive(b); and
   (ii) any fee which may be payable in connection with that application.

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

(7) 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

14.—(1) Subject to paragraphs (2) and (3), 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.

(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.

(a) 2000 asp. 4; see S.S.I. 2002/190.
(b) OJ ……
(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) In the case of a clinical trial involving—
   (a) medicinal products for gene therapy and somatic cell therapy, including xenogenic cell therapy; or
   (b) medicinal products containing genetically modified organisms,
the ethics committee may consult a specialist committee before giving its opinion.

(5) 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.

(6) 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 1 of Part 2 of Schedule 1 is satisfactory and whether the conclusions are justified;
   (c) the clinical trial 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 4 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);
   (m) the arrangements for the recruitment of subjects.

(7) 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.

(8) 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.
(9) 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.

(10) Where an ethics committee gives an opinion in accordance with this regulation, it shall publish a summary of that opinion, including a summary of the details contained in the valid application to which the opinion relates.

(11) In this regulation—

“the specified period” means—

(a) in the case of a clinical trial involving a medicinal product for gene therapy and somatic cell therapy or a medicinal product containing a genetically modified organism—
   (i) where the relevant committee is consulted in accordance with paragraph (4), 180 days, or
   (ii) where there is no such consultation, 90 days; or
(b) in any other case, 60 days;

“specialist committee” means a committee whose functions include the provision of advice on the ethical and 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.

Second ethics committee opinion

15.—(1) If a chief investigator for a trial has been notified by the ethics committee to which he made an application for an ethics committee opinion in accordance with regulation 13 that the committee’s opinion in relation to that trial is not favourable, he may within 90 days of being so notified, or such extended period as the Authority may in any particular case allow, give notice to the Authority of his wish to have a second ethics committee opinion.

(2) On receipt of a notice pursuant to paragraph (1), the Authority may direct that the application in relation to that trial shall be considered by another ethics committee specified in the direction.

(3) Where a direction is given in accordance with paragraph (2), the chief investigator shall send the application to the ethics committee specified in the direction and that committee shall consider the application in accordance with regulation 14.

Request for authorisation to conduct a clinical trial

16.—(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 applicant, whether in ink or by means of an electronic signature; and
(b) be accompanied by—
   (i) the particulars and documents set out in Section 3.1 of the [detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities in the European Union, notification of substantial
amendments and declaration of the end of the trial, dated [????] and published by the
Commission under Article 9.8 of the Directive(a), and
(ii) any fee which may be payable in connection with that application.

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

Authorisation procedure for clinical trials involving general medicinal products

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

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

(a) medicinal products for gene therapy and somatic cell therapy, including xenogenic cell therapy; and

(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, it 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(a); 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

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

(a) involving medicinal products—

(a) 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.
(i) which do not have a marketing authorization and are referred to in Part A of the Annex to Regulation (EEC) No. 2309/93(a),

(ii) involving medicinal products which have an active ingredient—
(a) that is a biological product of human or animal origin,
(b) containing biological components of human or animal origin, or
(c) the manufacturing of which requires such components,

other than products falling within regulation 18; 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—

(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

20.—(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 17 to 19.

Amendments to clinical trial authorisation

21. Subject to regulation 28, an amendment to a clinical trial authorisation may be made—

(a) by the licensing authority, in accordance with regulation 22; or
by the sponsor, in accordance with regulation 23 or 24.

Amendments by the licensing authority

22.—(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

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

(2) 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 (3).

(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 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 (2).

(4) 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.

(5) 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.

(6) Subject to paragraph (7), if the sponsor has sent a notice in accordance with paragraph (2), he may make the amendment only if—

(a) the licensing authority have given him a notice in accordance with paragraph (4)(b); or

(b) no notice has been given by the licensing authority in accordance with paragraph (4).

(7) If the sponsor has been given a notice in accordance with paragraph (4)(b), he may make the amendment subject to the conditions, if any, specified in the notice.
If the sponsor has sent a notice in accordance with paragraph (3), he may make the amendment only if the relevant ethics committee has given a favourable opinion.

In this regulation—

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

(a) in writing; and
(b) accompanied by—

(i) the particulars and documents set out in [Section 3.2.8] of the [detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities in the European Union, notification of substantial amendments and declaration of the end of the trial, dated [???] and published by the Commission under Article 9(8) of the Directive(a)], and
(ii) any fee which may be payable in connection with that notice.

Modifying or adapting rejected proposals for amendment

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

(a) the ethics committee opinion on a proposed amendment to the clinical trial 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 clinical trial 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 clinical trial 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

25.—(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 17(2) or (8), 18(8) or 19(5), the trial is authorised subject to specified conditions;
(b) the licensing authority has amended a clinical trial authorisation under regulation 22; or
(c) the sponsor who has been notified by the licensing authority in accordance with regulation 23(3) or 24(3) that—
(i) the authority does not accept a proposed, modified or adapted amendment to the clinical trial authorisation, or
(ii) that 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 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(a).

(2) Schedule 3 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).

PART 4
GOOD CLINICAL PRACTICE AND THE CONDUCT OF CLINICAL TRIALS

Good clinical practice and protection of clinical trial subjects

26.—(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) 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 paragraph (4), 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(b);
(b) the National Health Service (Scotland) Act 1978(c); or
(c) the Health and Personal Social Services (Northern Ireland) Order 1972(d),
in respect of any medicinal products or devices provided in pursuance of those Acts or that Order.

Conduct of trial in accordance with clinical trial authorisation etc.

27. Subject to regulation 28, no person shall conduct a clinical trial otherwise than in accordance with—
(a) the clinical trial protocol relating to that trial, as may be amended from time to time in accordance with regulations 21 to 24;
(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

(a) See section 2 of the Act.
(b) 1977 c.49.
(c) 1978 c.29.
(d) S.I. 1972/1265 (N.I. 14).
(iii) any particulars or documents, other than the clinical protocol, accompanying that request or that application, as may be amended from time to time in accordance with regulations 21 to 24; and

(c) any conditions imposed by the licensing authority under regulation 17(2) or (8), 18(8), 19(5), 23(3) or Schedule 3.

Urgent safety measures

28.—(1) The sponsor and investigator may take appropriate urgent safety measures in order to protect the subjects of the 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

29.—(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 17(2) or (8), 18(8), 19(5), 23(3) or Schedule 3, 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;

(c) if the notice requires suspension—

(i) whether the suspension applies until further notice from the authority or for such period as may be specified in the notice,

(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;

(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) the competent authorities of each EEA State, other than the United Kingdom;
(b) the relevant ethics committee;
(c) the EMEA;
(d) 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;
(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 3 shall have effect to regulate the procedure for reference to the appropriate committee or, as the case may be, the Medicines Commission(a) 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 3.

**Conclusion of clinical trial**

30.—(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 clinical trial 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 information specified in Section 3.3.2 of the detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities in the European Union, notification of substantial amendments and declaration of the end of a clinical trial, dated [??????] and published by the Commission under Article 9.8 of the Directive.

(4) A notification made in accordance with paragraph (2) shall include an explanation of the reasons for the terminating the trial early.

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(a) See section 2 of the Act.
PART 5
PHARMACOVIGILANCE

Notification of adverse events

31.—(1) Subject to paragraph (7), 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 clinical trial 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 clinical trial 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 clinical trial protocol for the trial.

(7) The number assigned to a subject in accordance with the clinical trial 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

32.—(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 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,

(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, 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 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

33. 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 for 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

34.—(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; and

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

(2) In this regulation, “reporting year”, in relation to an investigational medicinal product, means the year ending on the anniversary of the earliest date on which any clinical trial—

(a) relating to that product, and

(b) 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), 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—
(i) the trial was authorised by the licensing authority in accordance with these Regulations, or
(ii) a clinical trial certificate in respect of that trial was issued by the licensing authority or a clinical trial exemption in respect of that trial took effect, whichever is earlier; and
(b) in the case of any other EEA State, the date on which the trial was—
(i) authorised by the competent authority of that EEA State in accordance with the Directive, or
(ii) authorised, approved or consented to by any public body in accordance with any provision of the law of that State relating to the regulation or control of clinical trials on medicinal products, whichever is earlier.

(4) For the purposes of this regulation—
“clinical trial certificate” means a certificate issued by the licensing authority under section 31 of the Act;
“clinical trial exemption” means an exemption—
(a) conferred by article 3 of the Medicines (Exemption from Licences) (Clinical Trials) Order 1995(a), or
(b) conferred by article 4 of the Medicines (Exemption from Licences) (Special Cases and Miscellaneous Provisions) Order 1972(b);
“investigational medicinal product” does not include a placebo or a product used only as a reference in a clinical trial.

PART 6
MANUFACTURE AND IMPORTATION OF INVESTIGATIONAL MEDICINAL PRODUCTS

Requirement for authorisation to manufacture or import investigational medicinal products

35.—(1) Subject to paragraph (2) and regulation 36, 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 that has a marketing authorization, to the extent that such manufacture or assembly is in accordance with the terms and conditions of that authorization.

Exemption for hospitals and health centres

36.—(1) Subject to paragraph (3), the restriction imposed by regulation 35(1) shall not apply to the repackaging, or the making of other changes to the packaging 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 repackaging, or other changes to the packaging, is done—
   (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

(a) S.I. 1995/2808
(b) S.I. 1972/1200.
(b) the investigational medicinal product is intended for use only in that hospital or health centre.

(3) The licensing authority may, by a notice in writing given or sent to the hospital or health centre in question, terminate the exemption conferred by paragraph (1) in so far as it relates to that hospital or health centre if it appears to them that—

(a) the hospital or health centre does not have the staff, premises, equipment or facilities necessary to carry out properly the processes of repackaging, or making other changes to the packaging of, the product; or

(b) as a result of the repackaging, or other changes to the packaging, the product can no longer be regarded either as a product which can be safely administered to subjects or as a product which is of satisfactory quality for such administration.

(4) Where the licensing authority terminate the exemption in relation to a particular hospital or health centre pursuant to paragraph (3), that termination shall have effect until the notice is revoked or withdrawn.

Application for manufacturing authorisation

37.—(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, whether in ink or by means of an electronic signature.

(2) Every application for the grant of a manufacturing authorisation shall specify—

(a) the—

(i) descriptions of investigational medicinal products, and

(ii) manufacturing, assembling or importation operations, in respect of which the authorisation is required;

(b) in the case of an authorisation in respect of manufacturing, the manufacturing processes for the products in respect of which the authorisation is required;

(c) the premises at which those products are to be manufactured, assembled or controlled;

(d) which, if any, of the standard provisions referred to in regulation 39(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 4 to these regulations; and

(b) any fee which may be payable in connection with that application.

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

Consideration of application for manufacturing authorisation

38.—(1) Subject to paragraph (2) and regulation 39, 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 37(2) and (3); or

(b) the qualified person referred to in regulation 42.

(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 37.

Grant or refusal of manufacturing authorisation

39.——(1) The licensing authority shall grant a manufacturing authorisation only if—
   (a) the applicant—
      (i) has complied with the requirements of regulation 37,
      (ii) has at his disposal suitable and sufficient premises, technical equipment and control facilities complying with the requirements of Commission Directive 91/356/EEC, as regards the manufacture or import, and control, of the products specified in accordance with regulation 37(2)(a) 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 38(2), has provided the information requested by the licensing authority; and
   (b) they have established that the particulars supplied pursuant to regulation 37(2) and (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;
   (c) in respect of manufacturing, the manufacturing processes; or
   (d) the premises,
specified in the application made pursuant to regulation 37.

(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 5; and
   (b) in the case of a manufacturing authorisation relating to the importation of investigational medicinal products, in Part 3 of Schedule 5,
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 6 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

40. A manufacturing authorisation shall apply only in relation to—
   (a) the descriptions of investigational medicinal products;
   (b) the manufacturing, assembling or importation operations;
   (c) in respect of manufacturing, the manufacturing processes; and
   (d) the premises,

specified in the application made pursuant to regulation 37 and in respect of which the authorisation is granted.

Obligations of manufacturing authorisation holder

41. 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 39(3).

Qualified persons

42.—(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 (2001), published jointly by the Institute of Biology, the Pharmaceutical Society of Great Britain and the Royal Society of Chemistry(a).

(4) If the holder of the authorisation is a person who as respects qualifications and experience satisfies the requirements of Article 49 or 50 of Directive 2001/83/EC, 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, or paragraph (b) of the definition of “qualified person” in regulation 2(1), 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.

(a) A copy of the Code of Practice may be obtained by writing to......................
(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

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

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

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

(i) descriptions of investigational medicinal products,

(ii) the manufacturing, assembling or importation operations,

(iii) in the case of an authorisation in respect of manufacturing, the manufacturing processes,

(iv) the premises,

(v) 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 6 shall have effect where the licensing authority propose to vary a manufacturing authorisation in accordance with this regulation.

(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, whether in ink or by means of an electronic signature;
(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; and
(e) where the application, and any accompanying material, is in the English language.

Suspension and revocation of manufacturing authorisation

44.—(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 matters specified in the application in accordance with regulation 37(2), or the particulars accompanying the application in accordance with regulation 37(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 41 or 42(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 16 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 for 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 accompanying the request for authorisation of the clinical trial in which the products are or are to be used;
(g) the qualified person has failed to carry out the duties referred to in regulation 42(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 processes of manufacture or assembly 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 processes or operations.

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

(a) total; or
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 6 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
45. An investigational medicinal product shall be labelled and packaged in compliance with the obligations which relate to that product by virtue of Article 14 of the Directive(a).

PART 8
ENFORCEMENT AND RELATED PROVISIONS

Application of enforcement provisions of the Act
46.—(1) Subject to paragraph (2) below, the following provisions of Part VIII of the Act (which provide for enforcement of the Act)—
  (a) sections 107 to 109;
  (b) section 110 except subsection (4);
  (c) sections 111 to 116;
  (d) section 118;
  (e) section 119;
  (f) sections 121 to 125
  (g) section 127;
  (h) Schedule 3,
shall apply for the purposes of these Regulations as they apply for the purposes of the Act.

(2) Those provisions as so applied shall have effect—
  (a) with the modifications specified in Schedule 7 to these Regulations; and
  (b) as if all investigational medicinal products were medicinal products for the purposes of the Act (whether or not they would otherwise be so).

Infringement notices
47.—(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.

(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 21(b), 26(1) to (3), 27, 28(2) and 30 to 34.

(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 46.

Offences

48.—(1) Any person who contravenes any of the following provisions of these Regulations—

   (a) regulation 11(1) and (2);
   (b) regulation 12(1);
   (c) regulation 21(b);
   (d) regulation 26(1) to (3);
   (e) regulation 27;
   (f) regulation 28(2);
   (g) regulations 30 to 34;
   (h) regulation 35(1);
   (i) regulation 41; and
   (j) regulation 42(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 12(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 29(1), 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 35(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 an offence.

(5) Where an investigational medicinal product is imported in contravention of regulation 35(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 45(1), 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 45(1), knowing, or having reasonable cause to believe, that the labelling does not so comply, shall be guilty of an offence.

False or misleading information

49.—(1) Any person who in the course of—
   (a) an application for an ethics committee opinion;
   (b) a request for authorisation to conduct a clinical trial;
   (c) giving notice of amendment to the clinical trial authorisation under regulation 23(1);
   (d) giving notice of a proposal to modify or adapt such an amendment under regulation 24(2); or
   (e) 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 42, provides 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

50. In any proceedings for an offence under any of the preceding provisions of these Regulations, it shall be a defence for the person charged to prove that he took all reasonable precautions and exercised all due diligence to avoid the commission of the offence.
Penalties

51. 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

FEES

[ Fees for clinical trial and manufacturing authorisations, and inspections ]

52. —(1) ....

PART 10

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(a).

Consequential and other amendments to enactments


(2) The provisions of the orders and regulations specified in Schedule 10 shall be amended as there specified.

Revocations

55. The regulations and orders specified in column (1) of Schedule 11 are hereby revoked to the extent specified in column (3) of that Schedule.

[ Transitional provisions ]

56.

(a) Section 103 was amended by section 22(1) of the Health and Medicines Act 1988 (c.49).
Signed by authority of the Secretary of State for Health

Name
Parliamentary Under Secretary of State
Department of Health

Date
SCHEDULE 1

CONDITIONS AND PRINCIPLES 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 an adult able to give informed consent, 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 their incapacity, give or refuse to give informed consent to the treatment to be provided as part of the clinical trial,

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

2. In this Schedule—

“guardian” shall be construed in accordance with section 51(8) of the Adults with Incapacity (Scotland) Act 2000;[a]

“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—

(a) 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

(b) is available and willing to so act for those purposes, or

(ii) if there is no such person, a person, other than a person connected with the conduct of the clinical trial, who is—

(a) the doctor responsible for the health care provided to that adult, or

(b) 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—

(a) the doctor responsible for the health care provided to that adult, or

(a) 2000 asp 4.
(b) 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(a),
(b) in relation to Scotland, has the same meaning as in the Children (Scotland) Act 1985(b), and
(c) in relation to Northern Ireland, has the same meaning as in the Children (Northern Ireland) Order 1995(e);
“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(d), the National Health Service (Scotland) Act 1978(e), or the Health and Personal Social Services (Northern Ireland) Order 1972(f)—
(i) in a case where a health service body is providing those services, that body, or
(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 if his decision to take part, or that a subject is to take part, in a clinical trial—
(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

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(a) 1989 c.41; see, in particular, sections 3(1) and 5(6).
(b) 1995 c.36; see, in particular, sections 1(3) and 7(5).
(c) S.I. 1995/755 (N.I.2); see, in particular, article 6.
(d) 1977 c.49.
(e) 1978 c. 29.
(f) S.I. 1972/1265 (N.I. 14).
(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.

4. For the purposes of this Schedule, if a court in the United Kingdom has made a ruling or makes an order to the effect that the treatment provided or to be provided to a minor in the course of the clinical trial may be provided despite the absence of consent on the part of a person with parental responsibility—

(a) the conditions specified in paragraphs 1 to 4 of Part 4 shall be deemed to have been satisfied; and

(b) in relation to the condition specified in paragraph 5 of that Part, the minor shall be withdrawn from the trial if the court makes a subsequent ruling or order to the effect that the treatment should not continue.

PART 2

CONDITIONS AND PRINCIPLES WHICH APPLY TO ALL CLINICAL TRIALS

Conditions

1. The foreseeable risks and inconveniences have been weighed against the anticipated benefit for each subject of the clinical trial and other present and future patients.

2. 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.

Principles

3. 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.

PART 3

CONDITIONS WHICH APPLY IN RELATION TO A SUBJECT ABLE TO CONSENT

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 EMEA are followed.

Principles

13. 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.

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.

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. 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.

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

14. The interests of the patient always prevail over those of science and society.
SCHEDULE 2 Regulations 6(1)(b), 7(a) and 8

ADDITIONAL PROVISIONS RELATING TO ETHICS COMMITTEES

Interpretation

1. In this Schedule—
   “appointing authority” means—
   (a) in relation to an ethics committee established under regulation 5, the Authority, or
   (b) in relation to an ethics committee recognised under regulation 6—
       (i) in the case of an ethics committee recognised without an application for
           recognition being submitted accordance with regulation 6(3), the Authority, or
       (ii) in any other case, the person who applied for recognition in accordance with
           regulation 6(1);
   “expert member” means a member of an ethics committee who—
       (a) is a health care professional, or
       (b) has professional qualifications or experience relating to the conduct of, or use of
           statistics in, clinical research, unless those professional qualifications or experience
           relate only to the ethics of clinical research or medical treatment;
   “financial year” means the twelve months ending with 31st March;
   “lay member” means a member of an ethics committee, other than an expert member, who—
       (a) is not, and never has been, a doctor or dentist,
       (b) is not a chairman, member or director of—
           (i) a health service body,
           (ii) a body, other than a health service body, which provides health care, or
           (iii) a university or other body involved in the conduct of clinical research, and
       (c) does not, in the course of their employment or business—
           (i) provide medical, dental or nursing care, or
           (ii) conduct clinical research.

Application of provisions of the Schedule

2. 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.

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 6, the members of an ethics committee shall be appointed by the
       appointing authority.
   (4) 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; or
   (ii) persons involved in the conduct of clinical research, other than as a subject of such research.

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; or
   (b) if the vice-chairman is also is unable to perform his duties, the alternate vice-chairman.

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 to determine, in accordance with regulation 14, the opinion of an ethics committee in relation to a clinical trial, unless the chairman and at least six other members (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 attend meetings and 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) 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) A co-opted member shall hold office only in relation to the meeting for which he is co-opted.

(5) 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—

(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 13; 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.
PROCEDURAL PROVISIONS RELATING TO THE REFUSAL OR AMENDMENT OF, OR IMPOSITION OF CONDITIONS RELATING TO, CLINICAL TRIALS AUTHORISATIONS AND THE SUSPENSION OR TERMINATION OF CLINICAL TRIALS

1.—(1) Where the licensing authority is notified of the sponsor’s wish to make representations in accordance with regulation 25(1) or 29(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 it has 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 its decision;
   (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) its 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 its 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 its 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 it has grounds for not accepting a request for authorisation or an amendment to the clinical trial authorisation,

(ii) its 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).
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 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.

3.—(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 if different from those referred to in the proceeding subparagraph—
      (a) on which are to be kept any living animals; or
      (b) on which are to be kept or from which are to be obtained any materials of animal origin, from which, in either case, are to be derived any substance or substances used in the production of the investigational medicinal product to which the application relates.

   (3) 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.

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

   (5) A separate statement in respect of each of the premises referred to in subparagraphs (1) to (3), 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.

   (6) A separate statement in respect of each of the premises referred to in subparagraphs (1) to (3), of equipment available at those premises for carrying out each stage of the manufacturing, assembling or importation operations described in sub-paragraph (5) of this paragraph.

4. 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 3 of this Schedule, and of the substances or articles which are the subject of any such operation.

5.—(1) The name and address and degrees, diplomas or qualifications and experience of the qualified person who is to carry out the duties referred to in regulation 42(2).

   (2) In the case of an authorisation relating to manufacture or assembly, the name and address 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 3 of this Schedule, and the name and function of the person to whom he is responsible.

   (3) The name and address 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 3 of this Schedule and the extent of the authority to be delegated to him to reject unsatisfactory batches of
investigational medicinal products, and the name and function of the person to whom he is responsible.

(4) The name and address and degrees, diplomas or other qualifications of the person in charge of the animals referred to in paragraph 3(2) of this Schedule.

(5) The name and address and degrees, diplomas or other qualifications of the person to be responsible for the culture of any living tissue to be used in the manufacture of investigational medicinal products.

6. An outline 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.

7. An outline 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.

8. An outline 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.

9. Where the application relates to the importation of investigational medicinal products from a third country—
   (a) the address of each of premises where the investigational products are or are to be manufactured;
   (b) evidence to demonstrate that the products have been manufactured in conformity with good manufacturing standards at least equivalent to those laid down in the principles and guidelines of good manufacturing practice.
SCHEDULE 5

STANDARD PROVISIONS FOR MANUFACTURING AUTHORISATIONS

PART 1

INTERPRETATION

In this Schedule—

“relevant period” means the five years from the date on which the clinical trial for which the relevant batch referred to in paragraphs 10(a) of Part 2 of, or paragraph 8(a) of Part 3 of, this Schedule was manufactured, assembled or imported was completed, terminated or discontinued; and

“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 16 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 for 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 accompanying the request for authorisation of the clinical trial in which the product is or is to be used.

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 avoid 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.

3. The holder of the authorisation shall—
(a) conduct all manufacture and assembly operations in such a way as to ensure that the investigational medicinal products conform with the standards of strength, quality and purity applicable to them in accordance with their product specification; and

(b) conduct all such operations in accordance with the principles and guidelines of good manufacturing practice.

4. The holder of the authorisation shall use, establish and implement an effective pharmaceutical quality assurance system involving the active participation of the management and personnel of the different services involved.

5. The holder of the authorisation, where animals are used in the production of any investigational medicinal products and the product specification for those products contains provisions relating to them, shall arrange for the animals to be housed in premises of such a nature and to be managed in such a way as will facilitate compliance with such provisions.

6.—(1) The holder of the authorisation shall—

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

(b) place the quality control department or unit under the authority of the person notified to the licensing authority in accordance with paragraph 5(3) of Schedule 4 being responsible for quality control.

(2) Subject to paragraph 7, the holder of the authorisation shall, in order to support the quality control department or unit, provide and maintain such staff, premises and plant as are necessary for carrying out—

(a) such tests of the strength, quality and purity of the investigational medicinal products which he manufactures under the manufacturing authorisation as are required by the product specification for those products; and

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

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

(4) The holder of the authorisation shall ensure that the quality control department or unit, in determining whether finished investigational medicinal products are to be released for use in clinical trials takes into account, in addition to analytical results—

(a) the conditions of production;

(b) the result of in-process controls;

(c) the examination of manufacturing documents; and

(d) the conformity of products to their product specification.

7. A holder of an authorisation need not himself provide and maintain such staff, premises and plant as are necessary for carrying out such tests as are specified in paragraph 6(2) provided that he makes arrangements with a person approved by the licensing authority to carry out of such tests on his behalf in accordance with paragraph 6(2) and (3).

8. 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.

9. 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 42 and paragraph 20, or
(iii) in charge of the animals from which are derived any substances used in the production of the investigational medicinal products being manufactured or assembled, or
(iv) responsible for the culture of any living tissues used in the manufacture of the investigational medicinal products being manufactured or assembled.

10. The holder of the authorisation shall—

(a) keep readily available for inspection by a person authorised by the licensing authority durable records of—

(i) the details of manufacture and assembly of each batch of every investigational medicinal product being manufactured or assembled under his authorisation, and
(ii) the tests carried out thereon including any register or other document referred to in Article 13(4) of the Directive, in such a form that the records will be easily identifiable from the number of the batch as shown on each container in which the investigational medicinal product is sold, supplied or exported; and

(b) permit the person authorised to take copies or make extracts from such records.

Such records shall not be destroyed without the consent of the licensing authority for the relevant period.

11. The holder of the authorisation shall keep readily available for examination by a person authorised by the licensing authority samples of—

(a) each batch of finished investigational medicinal products manufactured or assembled under his authorisation for at least a period of one year from their expiry date; and
(b) each batch of bulk formulated products and of the packaging components used for each finished product for at least a period of two years from the date on which the clinical trial for which the relevant batch was manufactured or assembled was completed, terminated or discontinued.

12. The holder of the authorisation shall make suitable arrangements to ensure that any record or sample referred to in paragraph 10 or 11 is retained for the periods specified in those paragraphs.

13.—(1) The holder of the authorisation shall implement a system for recording and reviewing complaints in relation to investigational medicinal products manufactured or assembled under his authorisation, together with an effective system for recalling promptly and at any time any such investigational medicinal product distributed for use in clinical trials.

(2) The holder of the authorisation shall—

(a) record and investigate all complaints described in sub-paragraph (1) of this paragraph; and
(b) shall immediately inform the licensing authority of any defect which could result in a recall from distribution for use in clinical trials.

14. 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.

15. 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.

16.—(1) The holder of the authorisation shall comply with the provisions of the product specification that relate to the supply of that investigational medicinal product for the purposes of the trial.

(2) 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.

17. Where in his application for a manufacturing authorisation the holder of the authorisation—

(a) had specified a general classification of investigational medicinal products in respect of which that authorisation was required; or

(b) had given particulars of manufacturing operations and of substances or articles in accordance with paragraph 4 of Schedule 4,

and there has been, or it is proposed that there shall be, a change in such general classification or such particulars, the holder of the authorisation shall forthwith notify the licensing authority in writing of such change or proposed change.

18. 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.

19. 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 22 or 23

(c) suspending or terminating any clinical trial in accordance with regulation 29,

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.
20.—(1) Subject to regulation 42, the holder of the authorisation shall at all times, and in accordance with that regulation, have a qualified person to carry out duties referred to in regulation 42(2).

(2) 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 to carry out the said duties.

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 shall ensure that—
   (a) all manufacture and assembly operations have been carried out by a duly authorised manufacturer or assembler; and
   (b) the investigational medicinal products have been manufactured and assembled, and are imported, in accordance with the principles and guidelines of good manufacturing practice.

3. The holder of the authorisation shall use, establish and implement an effective quality assurance system involving the active participation of the management and personnel of the different services involved.

4. 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.

5. 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 of any change that he proposes to make in any personnel named in his authorisation as responsible for quality control of the investigational medicinal products being imported including the person named as the qualified person for the purposes of regulation 42 and paragraph 14.

6. The holder of the authorisation shall—
   (a) keep readily available for inspection by a person authorised by the licensing authority durable records of—
      (i) the details of importation of each batch of every investigational medicinal product being imported under his authorisation, and
      (ii) the tests carried out thereon including any register or other document referred to in Article 13(4) of the Directive,
in such a form that the records will be easily identifiable from the number of the batch as shown on each container in which the investigational medicinal product is sold, supplied or exported; and

(b) permit the person authorised to take copies or make extracts from such records.

Such records shall not be destroyed without the consent of the licensing authority for the relevant period.

7. The holder of the authorisation shall keep readily available for examination by a person authorised by the licensing authority samples of—

(a) each batch of finished investigational medicinal products imported under his authorisation for at least a period of one year from their expiry date; and

(b) each batch of bulk formulated products and of the packaging components used for each finished product for at least a period of two years from the date on which the clinical trial for which the relevant batch was manufactured or assembled was completed, terminated or discontinued.

8. The holder of the authorisation shall make suitable arrangements to ensure that any record or sample referred to in paragraph 6 or 7 is retained for the periods specified in those paragraphs.

9.—(1) The holder of the authorisation shall implement a system for recording and reviewing complaints in relation to investigational medicinal products imported under his authorisation, together with an effective system for recalling promptly and at any time any such investigational medicinal product distributed for use in clinical trials.

(2) The holder of the authorisation shall—

(a) record and investigate all complaints described in sub-paragraph (1) of this paragraph; and

(b) shall immediately inform the licensing authority of any defect which could result in a recall from distribution for use in clinical trials.

10. 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.

11. 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.

12. Where—

(a) in his application for a manufacturing authorisation the holder of the authorisation had given particulars of manufacturing operations and of substances or articles in accordance with paragraph 4 of Schedule 4; and

(b) there has been, or it is proposed that there shall be, a change in such particulars,

the holder of the authorisation shall forthwith notify the licensing authority in writing of such change or proposed change.

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 conduct of a clinical trial in accordance with regulation 22 or 23
(c) suspending or terminating any clinical trial in accordance with regulation 29,

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.—(1) Subject to regulation 42, the holder of the authorisation shall at all times, and in accordance with that regulation, have a qualified person to carry out duties referred to in regulation 42(2).

(2) 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 to carry out the said functions.
SCHEDULE 6 Regulations 39(5) and 43(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 an 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.
MODIFICATIONS OF ENFORCEMENT PROVISIONS OF THE ACT

1. In section 107 of the Act (validity of decisions and proceedings relating thereto)—
   (a) in subsection (1)—
      (i) the reference to Part II of the Act shall include a reference to these Regulations, and
      (ii) the reference to any licence or certificate shall include a reference to any authorisation;
   (b) in subsections (2) and (3), any reference to the Act, other than the second reference in subsection (2)(b), shall include a reference to these Regulations;
   (c) in subsection (4), the reference to a decision to grant licence or certificate shall include a reference to—
      (i) a decision to authorise, or accept a request to conduct, a clinical trial, and
      (ii) a decision to grant a manufacturing authorisation.

2. In section 108 of the Act (enforcement in England and Wales), in subsection (1), the reference to the Act shall include a reference to these Regulations.

3. In section 109 of the Act (enforcement in Scotland), in subsection (1), the reference to the Act shall include a reference to these Regulations.

4. In section 110 of the Act (enforcement in Northern Ireland) in subsection (1), the reference to the Act shall include a reference to these Regulations.

5. In section 111 of the Act (rights of entry)—
   (a) in subsection (1), the first and third references to the Act shall include a reference to these Regulations;
   (b) in subsection (2), the first reference to the Act shall include a reference to these Regulations;
   (c) in subsection (3), the reference to an applicant for a licence or certificate under Part II of this Act shall include a reference to—
      (i) a person making a request for authorisation to conduct a trial under these Regulations, and
      (ii) an applicant for a manufacturing authorisation under these Regulations.

6. In section 112 of the Act (power to inspect, take samples and seize goods and documents)—
   (a) in subsection (1), the first reference to the Act shall include a reference to these Regulations;
   (b) in subsection (2), the reference to a medicinal product sold or supplied or intended to be sold or supplied shall include a reference to a medicinal product to be used or intended to be used in a clinical trial;
   (c) in subsection (3)(a)—
      (i) the reference to a person carrying on a business which consists of or includes the manufacture, assembly, sale or supply of medicinal products shall include a reference to a person—
      (a) carrying out the functions of a sponsor of a clinical trial (whether that person is the sponsor or is acting under arrangements made with that sponsor),
      (b) conducting a trial, or
      (c) occupying premises at which a clinical trial is being conducted, and
(ii) the reference to a person employed in connection with such a business includes a reference to a person who in the course of their employment with a person referred to in sub-paragraph (b)(i)(a) to (c) undertakes activities in connection with the clinical trial;

(d) in subsection (3)(b)—
   (i) the reference to taking copies shall include a reference to taking possession,
   (ii) any reference to any book or document relating to the business shall include a reference to any book or document relating to the clinical trial.

(e) in subsection (4) and (5), any reference to the Act shall include a reference to these Regulations;

(f) in subsection (7)—
   (i) the reference to an applicant for a licence or certificate under Part II of this Act shall include a reference to—
      (a) a person making a request for authorisation to conduct a trial in accordance with these Regulations, and
      (b) an applicant for a manufacturing authorisation under these Regulations, and
   (ii) the reference to the application for the licence or certificate shall include a reference to such a request or an application for such an authorisation;

(g) in subsection (9), the second reference to the Act shall include a reference to these Regulations.

7. In section 116 of the Act (liability to forfeiture under Customs and Excise Management Act 1979), any reference to the Act shall include a reference to these Regulations.

8.—(1) Subject to sub-paragraph (2), in section 118 of the Act (restrictions on disclosure of information), any reference to the Act shall include a reference to these Regulations.

   (2) The restriction in section 118 shall not apply to the disclosure by a sponsor of information provided to him by an investigator pursuant to these Regulations.

9. In section 119 of the Act (protection for officers of enforcement authorities), any reference to the Act shall include a reference to these Regulations.

10. In section 121 of the Act (contravention due to default of other person)—

   (a) in subsections (1) and (2), any reference to the Act shall include a reference to these Regulations; and

   (b) in subsection (4), the reference to sections 63 to 65, 85 to 90 and 93 to 96, shall include a reference to these Regulations.

11. In section 122 of the Act (warranty as a defence)—

   (a) in subsections (1), the reference to the Act shall include a reference to these Regulations; and

   (b) in subsection (4), the reference to sections 63(b), sections 64 and 65, sections 85 to 88 and section 90, shall include a reference to regulation 45 of these Regulations.

12. In section 124 of the Act (offences by bodies corporate), in subsection (1)—

   (a) the reference to the Act shall include a reference to these Regulations;
   (b) any reference to a body corporate shall include a reference to a Scottish partnership; and
   (c) the reference to a director, manager, secretary or other similar officer shall include a reference to a partner of a Scottish partnership.

13. In section 125 of the Act (prosecutions), in subsections (1) to (3), any reference to the Act shall include a reference to these Regulations.
14. In section 127 of the Act (service of documents), the reference to the Act shall include a reference to these Regulations.

15. In Schedule 3 of the Act (sampling), in paragraph 1(1), the first reference to the Act shall include a reference to these Regulations.
SCHEDULE 8

[FEES]
SCHEDULE 9
Regulation 54(1)

CONSEQUENTIAL AND OTHER AMENDMENTS OF THE ACT
AND THE MEDICINES ACT 1971

The Act

1.—(1) Section 3 of the Act (general functions of the Medicines Commission) 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) there is substituted—
      “(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 Comission with respect to any matter arising under any of those provisions.”

2. In section 4 of the Act (establishment of committees), 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), after subsection (3), insert the following subsection—
   “(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—

(a) 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.
(b) 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.
(c) 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.
“(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 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 authorization.

(2B) In subsection (2A) of this section—

“investigational medicinal product” has the meaning given by the Clinical Trials Regulations; and

“marketing authorization” shall be construed in accordance with regulation 1(4)(a) of the Medicines for Human Use (Marketing Authorisations Etc.) Regulations 1994.”.

(4) In subsections (3) and (3A)(a), 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 sub-sections (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)(b) shall be amended as follows.

(2) In subsection (1)—

(a) omit “to 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 for 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

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) Subsections (3A) to (3C) of section 8 were inserted by regulation 2(4) of S.I. 1993/834

(b) 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.
(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)—
(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 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 2003;”; and
(b) in subsection (3), omit “a clinical trial certificate or”.

The Medicines Act 1971

18. [In section 1 of the Medicines Act 1971 (fees payable for the purposes of Part II of the Act)(a) 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 2003.”.

(a) 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.
SCHEDULE 10

CONSEQUENTIAL AND OTHER AMENDMENTS TO REGULATIONS AND ORDERS

1. In the Medicines (Standard Provisions for Licences and Certificates) Regulations 1971(a)—
   (a) in regulation 3 (standard provisions for licences and certificates), omit paragraph (2);
   (b) in Schedule 1, omit Part II (standard provisions for clinical trial certificates and clinical trial certificates of right).

2. The Medicines (Applications for Product Licences and Clinical Trial and Animal Test Certificates) Regulations 1971(b) shall be amended as follows.
   (1) In regulation 2 (interpretation), in paragraph (1)—
      (a) in the definition of “application”, for “a clinical trial certificate or animal testing certificate”, in each place those words appear, substitute “an animal testing certificate”;
      (b) omit the definition of “clinical trial certificate”.
   (2) In regulation 3 (form and manner of application)—
      (a) in paragraph (4)—
         (i) for “a clinical trial certificate or animal testing certificate” substitute “an animal testing certificate”;
         (ii) omit subparagraph (f);
      (b) in paragraph (5), for “a clinical trial certificate or animal testing certificate” substitute “an animal testing certificate”.
   (3) In regulation 4 (material to be contained in or to accompany an application)—
      (a) in paragraph (1), for “a clinical trial certificate or animal testing certificate” substitute “an animal testing certificate”;
      (b) omit paragraph (5).
   (4) In regulation 5 (supplementary provisions as to application), in paragraphs (1) to (3), for “a clinical trial certificate or animal testing certificate”, in each place those words appear, substitute “an animal testing certificate”.
   (5) Schedule 2 shall be omitted.

3. —(1) Article 4 of the Medicines (Exemption from Licences) (Special Cases and Miscellaneous Provisions) Order 1972(c) 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,”,

(a) S.I. 1971/972, to which there are amendments not relevant to this instrument.
(b) S.I. 1971/973; as amended by S.I. 1975/681 and 1993/2538.
(c) S.I. 1972/1200.
(ii) omit the words from “the doctor or dentist” to “as the case may be,”;

(c) in subparagraph (iv)—

(i) omit the words from “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.—(1) The Medicines (Renewal Applications for Licences and Certificates) Regulations 1974(a) shall be amended as follows.

(2) In regulation 1 (citation, commencement and interpretation), in paragraph (2), in the definition of “certificate”, omit “a clinical trial certificate or”.

(3) In the Schedule, in paragraph 6, omit “the clinical trial or, as the case may be,”.

5. In Schedule 1 to the Medicines (Fixing of Fees Relating to Medicinal Products for Human Use) Order 1989(b), after paragraph 9A(c) 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 2003 and the functions of any person appointed under Schedule 3 or 6 to those Regulations.”.

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(a) S.I. 1974/832.
(b) S.I. 1989/684.
(c) Paragraph 9A was inserted by S.I. 1995/871.
### SCHEDULE 11

**Revocations**

<table>
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<th>Regulations and orders</th>
<th>S.I. number</th>
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<tr>
<td>The Medicines (Exemption from Licences) (Clinical Trials) Order 1974</td>
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<td>The entire Order</td>
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<tr>
<td>The Medicines (Exemption from Licences) (Clinical Trials) Order 1995</td>
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<td>The entire Order</td>
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<td>S.I. 1995/2809</td>
<td>The entire Order</td>
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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 3), 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 4 to 9, 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 10 to 25, and Schedule 3, make provision for clinical trial authorisations by the licensing authority and for ethics committee opinions. In particular: regulation 11 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; regulations 12 to 15 make provision for applications for ethics committee opinions; and regulations 16 to 20 deal with requests to the licensing authority for authorisation. Regulations 21 to 24 make provision for amendments to clinical trial authorisations; and regulation 25 and Schedule 3 make provision for the reference to the appropriate committee or the Medicines Commission of decisions to refuse authorisations, amendments etc.

Regulations 26 to 30, and Schedules 1 and 3, 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 conclusion of a trial. Schedule 3 includes provisions for referral to the appropriate committee or the Medicines Commission where a trial is suspended or terminated by the licensing authority.

Regulations 31 to 34 make provisions for pharmacovigilance; i.e. the recording and reporting of adverse events and reactions to medicinal products being used in a clinical trial.

Regulations 35 to 44, and Schedules 4 to 6, 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 35 and 36); the applications for, consideration of and grant or refusal of such authorisations (regulations 37 to 39 and Schedule 4 to 6); the application and effect of authorisations (regulations 40 and 41); the qualified persons responsible for checking the quality of products being manufactured, assembled or imported (regulation 42); and the variation, suspension and revocation of authorisations (regulations 43 and 44 and Schedule 6).

Regulation 45 concerns the labelling of such medicinal products.

Regulations 46 to 51, and Schedule 7, make provision for enforcement and related matters, including powers of inspection, infringement notices, offences and penalties for breaches of the Regulations.

[Regulation 52, and Schedule 8, deal with the fees for applications related to clinical trial authorisations and manufacturing authorisations, and fees for related inspections.]
Regulations 53 to 56, and Schedules 9 to 11, contain miscellaneous provisions for the construction of references in authorisations to pharmacopoeias and other publications, for the amendment and revocation of legislation, and for transitional provisions.

A Regulatory Impact Assessment in relation to these Regulations has been placed in the libraries of both Houses of Parliament, and copies can be obtained from the [Medicines Control Agency], Room 10-202, Market Towers, 1 Nine Elms Lane, London SW8 5NQ.