STATUTORY INSTRUMENTS

2025 No. 538

MEDICINES

The Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025

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Coming into force in accordance with regulation 1(2)

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The Secretary of State in relation to England and Wales and Scotland, and the Department of Health in Northern Ireland and the Secretary of State acting jointly in relation to Northern Ireland,

make the following Regulations in exercise of the powers conferred by sections 2(1), 5(1)(a) to (e), 6(1)(b) and 43(2)(a) to (d) of the Medicines and Medical Devices Act 2021(**a**).

The Secretary of State and the Department of Health in Northern Ireland have carried out a public consultation in accordance with section 45(1) of that Act.

In accordance with section 2(2) to (4) of that Act, the overarching objective of the Secretary of State and the Department of Health in Northern Ireland in making these Regulations is safeguarding public health. The Secretary of State and the Department of Health in Northern Ireland have had regard to the matters specified in section 2(3) of that Act and consider that, where these Regulations may have an impact on the safety of human medicines, the benefits of making these Regulations outweigh the risks.

In accordance with section 47(3) and (6)(c) of that Act, a draft of this instrument was laid before Parliament and the Northern Ireland Assembly and approved by a resolution of each House of Parliament and the Northern Ireland Assembly.

PART 1

General

Citation, commencement and extent

1.—(1) These Regulations may be cited as the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025.

(2) These Regulations come into force 12 months after the day on which they are made.

(3) These Regulations extend to England and Wales, Scotland and Northern Ireland.

Amendment of the Medicines for Human Use (Clinical Trials) Regulations 2004

2. The Medicines for Human Use (Clinical Trials) Regulations 2004(**b**) are amended in accordance with these Regulations.

PART 2

Amendment to Part 1 (Introductory Provisions)

Amendment to regulation 2

3.—(1) Regulation 2 (interpretation) is amended as follows.

(2) In paragraph (1)—

(a) in the definition of "adverse event" for "subject" substitute "participant";

(**a**) 2021 c. 3. The powers in section 2(1) of the Medicines and Medical Devices Act 2021, and the provisions that relate to it, are exercisable by the "appropriate authority". As defined in section 2(6)(a) of the Act, the appropriate authority for England and Wales and Scotland is the Secretary of State. In relation to Northern Ireland, as defined in section 2(6)(b)(ii), the appropriate authority can mean the Secretary of State and the Department of Health in Northern Ireland acting jointly.

(**b**) S.I. 2004/1031.

(b) in the definition of "adverse reaction" for "subject", in both places where it occurs, substitute "participant";

(c) omit the definition of "authorised health professional";

(d) after the definition of "assemble" insert—

""the Authority" is to be construed in accordance with regulation 5(3);";

(e) in the definition of "business" for "Schedule 2" substitute "regulation 9";

(f) for the definition of "chief investigator"(**a**) substitute—

""chief investigator" means—

(a) in relation to a clinical trial conducted at a single trial location, the investigator for that location, or

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

(g) in the definition of "clinical trial" for "subjects" substitute "participants";

(h) after the definition of "clinical trial" insert—

""Commission Delegated Regulation 2017/1569", other than in Parts 2 and 3 of Schedule 7, means, in the case of an investigational medicinal product manufactured or assembled in, or imported into, Northern Ireland, Commission Delegated Regulation (EU) 2017/1569 of 23 May 2017 supplementing Regulation (EU) No 536/2014 of the European Parliament and of the Council by specifying principles of and the guidelines for good manufacturing practice for investigational medicinal products for human use and arrangements for inspections, as that Regulation has effect in EU law(**b**);";

(i) in the definition of "Commission Directive 2003/94/EC"(**c**) omit paragraph (b);

(j) in paragraph (a) of the definition of "conducting a clinical trial" for "subject" substitute "participant";

(k) omit the definition of "the Directive"(**d**);

(l) in the definition of "ethics committee"—

(i) in paragraph (a)—

(aa) omit "or recognised";

(bb) insert "or" at the end;

(ii) in paragraph (b)—

(aa) for "the Ethics Committee" substitute "an Ethics Committee";

(bb) at the end, omit for ", or";

(iii) omit paragraph (c);

(m) after the definition of "ethics committee" insert—

(**a**) The definition of "chief investigator" was amended by S.I. 2006/1928.
(**b**) OJ No. L 238, 16.09.17, p. 12-21.
(**c**) The definition of "Commission Directive 2003/94/EC" was amended by S.I. 2019/744.
(**d**) The definition of "the Directive" was substituted by S.I. 2008/941.

""the EU Regulation" means Regulation 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, as that Regulation has effect in EU law(**a**);";

(n) omit the definition of "the Gene Therapy Advisory Committee"(**b**);

(o) omit the definition of "Health and Social Services Board";

(p) in the definition of "health care professional"—

(i) in paragraph (c), for "nurse" substitute "registered nurse as defined in regulation 8(1) of the 2012 Regulations";

(ii) in paragraph (f)(**c**), for "a register established and maintained under article 5 of" substitute "the Health and Care Professions Council register (as defined in regulation 8(1) of the 2012 Regulations) as a member of a relevant profession within the meaning of article 2 of, and paragraph 1 of Schedule 3 to, the";

(iii) in paragraph (h), at the end, omit "or";

(iv) in paragraph (i), at the end, insert "or";

(v) after paragraph (i) insert—

"(j) a registered midwife as defined in regulation 8(1) of the 2012 Regulations;";

(q) in the definition of "health centre" for "section 2 or 3 of the National Health Service Act 1977" substitute "section 2 or 3 of the National Health Service Act 2006(**d**), section 2 or 3 of the National Health Service (Wales) Act 2006(**e**)";

(r) in the definition of "health service body"—

(i) in paragraph (a)(**f**) for "Health and Social Services Board" substitute "the Department of Health in Northern Ireland";

(ii) for paragraph (g) substitute—

"(g) the Regional Business Services Organisation for the health and social care in Northern Ireland established under the Health and Social Care (Reform) Act (Northern Ireland) 2009,";

(s) in the definition of "insurance or indemnity" for paragraph (b)(iv) substitute—

"(iv) the Department of Health in Northern Ireland,";

(t) in the definition of "investigational medicinal product dossier"—

(i) for "authorisation" substitute "approval";

(ii) for "paragraph 11" substitute "paragraph 5(b)";

(u) for the definition of "investigator" substitute—

""investigator" means, in relation to a clinical trial, the health care professional who is responsible for the conduct of that trial at that trial location or, if more than one, the trial locations; and who is, if the trial is conducted by a team of health care professionals at that location or locations, the leader responsible for that team;";

(v) in the definition of "investigator's brochure" for "subjects" substitute "participants";

(w) in the definition of "legal representative" omit "Parts 2 to 4 of";

(**a**) OJ No. L 158, 27.05.14, p. 1-76.
(**b**) The definition of "the Gene Therapy Advisory Committee" was amended by S.I. 2008/941.
(**c**) Paragraph (f) of the definition of "health care professional" was amended by S.I. 2012/1479 and 2019/1094.
(**d**) 2006 c. 41; section 2 was substituted by the Health and Care Act 2022 (c. 31), Schedule 5, paragraph 10; section 3 was substituted by the Health and Care Act 2022 (c. 31), section 21.
(**e**) 2006 c. 42.
(**f**) Paragraph (a) of the definition of "health service body" was amended by S.I. 2013/235.

(x) after the definition "non-interventional trial" insert—

""non-investigational medicinal product" means a medicinal product used or to be used in a clinical trial, as described in the protocol, but not as an investigational medicinal product;

"notifiable trial" has the meaning given in regulation 11A;

"participant" 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;";

(y) omit the definition of "nurse";

(z) in the definition of "Phase I trial" for "subjects" substitute "participants";

(z1) in the definition of "the principles and guidelines of good manufacturing practice", after "Commission Directive 2003/94/EC" insert "in respect of Great Britain or Commission Delegated Regulation 2017/1569 in respect of Northern Ireland";

(z2) in paragraph (a) of the definition of "qualified person" for "Article 49 or 50 of Directive 2001/83" substitute "Schedule 7 to the 2012 Regulations";

(z3) after the definition of "qualified person" insert—

""radiopharmaceutical" has the same meaning as in regulation 8(1) of the 2012 Regulations;";

(z4) in the definition of "relevant ethics committee"—

(i) in paragraph (a)—

(aa) for "paragraph 13 of Schedule 2" substitute "regulation 6(3)";

(bb) for "sub-paragraph (5) of that paragraph" substitute "regulation 6(3)(b)";

(ii) in paragraph (b)—

(aa) for "an appeal panel" substitute "another ethics committee";

(bb) omit "paragraph 4(4) of";

(cc) for "that committee" substitute "the ethics committee which has given the favourable opinion";

(z5) omit the definition of "Strategic Health Authority";

(z6) omit the definition of "subject";

(z7) for the definition of "trial site" substitute—

""trial location" means a hospital, health centre, surgery or other establishment, or facility or premises at or from which a clinical trial, or any part of such a trial, is conducted;".

Amendment to regulation 3

4.—(1) Regulation 3 (sponsor of a clinical trial) is amended as follows.

(2) In paragraphs (4) and (5)—

(a) for "request for authorisation", in both places where it occurs, substitute "request for approval";

(b) for "regulation 17", in both places where it occurs, substitute "regulation 16".

(3) In paragraph (6)—

(a) for "authorised by the licensing authority" substitute "approved";

(b) for ", 19 or 20" substitute "or 18A";

(c) for "substantial amendment" substitute "modification of an important detail as defined in Part 3";

(d) for "authorisation" substitute "approval";

(e) for "regulations 24 to 26" substitute "regulation 22".

(4) In paragraph (7)—

(a) in sub-paragraph (a), omit ", except regulation 15";

(b) in sub-paragraph (b), omit "Parts 2 to 4 of";

(c) in sub-paragraph (c), omit ", in so far as it relates to decisions of the licensing authority under Part 3".

(5) In paragraph (10)—

(a) in sub-paragraph (a), for "regulations 15 and 28(1)" substitute "regulation 28(1)";

(b) in sub-paragraph (c), omit ", and Part 1 of Schedule 3".

Insertion of new regulation 3B

5. After regulation 3A (sponsor's responsibility for the investigator's brochure) insert—

"Investigator in a clinical trial

3B. The investigator, in relation to a clinical trial, shall be a health care professional who is appropriately trained to undertake that role in a clinical trial.".

PART 3

Amendment to Part 2 (Ethics Committees)

Amendment to regulation 5

6.—(1) Regulation 5 (United Kingdom Ethics Committees Authority) is amended as follows.

(2) In paragraphs (1), (2) and (3)—

(a) for "National Assembly for Wales", in each place where it occurs, substitute "Welsh Ministers";

(b) for "Department for Health, Social Services and Public Safety for Northern Ireland", in each place where it occurs, substitute "Department of Health in Northern Ireland".

(3) In paragraph (4), omit "(including conditions as to remuneration, benefits, allowances and reimbursement for expenses)".

(4) In paragraph (5), omit sub-paragraph (b) and the "or" preceding it.

Amendment to regulation 6

7.—(1) Regulation 6 (establishment of ethics committees) is amended as follows.

(2) In the heading, after "establishment" insert "and abolition".

(3) In paragraph (1)—

(a) for "ethics committees" substitute "an ethics committee";

(b) omit sub-paragraph (a).

(4) After paragraph (1) insert—

"(1A) The Authority must ensure that the arrangements for the membership and operation of that committee—

(a) enable that committee to perform the functions of an ethics committee; and

(b) comply with regulation 9.".

(5) For paragraph (2) substitute—

"(2) The Authority may—

(a) specify any conditions or limitations that apply to an ethics committee, including whether that committee may act for the entire United Kingdom or only for a particular area of the United Kingdom;

(b) where they consider it necessary or appropriate to do so—

(i) vary the description or class of clinical trial in relation to which that committee may act as an ethics committee, or

(ii) vary or revoke any conditions or limitations imposed under paragraph (2)(a); and

(c) abolish any such committee if the Authority is satisfied that—

(i) the arrangements for the membership and operation of that committee are no longer such that the committee is able to adequately perform its functions under these Regulations,

(ii) the committee is failing to perform its functions under these Regulations adequately or at all, or

(iii) it is otherwise necessary or appropriate to do so.".

(6) After paragraph (2) insert—

"(3) Where the Authority abolishes an ethics committee or an ethics committee ceases operation—

(a) the Authority may nominate another committee to be responsible for the work of that committee;

(b) the committee nominated in accordance with sub-paragraph (a) must—

(i) consider any applications made to the old committee in accordance with regulation 15, if the old committee had not given an opinion before the date of abolition or ceasing of operation, and

(ii) be the relevant ethics committee for any clinical trial in relation to which the old committee had given a favourable opinion in accordance with regulation 18 or 18B.".

Omission of regulations 7 and 8

8. Omit regulations 7 (recognition of ethics committees)(**a**) and 8 (revocation of recognition).

Substitution of regulation 9

9. For regulation 9 (constitution and operation of ethics committees) substitute—

(**a**) Regulation 7 was amended by S.I. 2006/1928.

"Operation of ethics committees

9.—(1) This regulation does not apply in relation to an Ethics Committee constituted by regulations made by the Scottish Ministers under section 51(6) of the Adults with Incapacity (Scotland) Act 2000.

(2) An ethics committee established under regulation 6 must—

(a) be constituted of 5 or more members, appointed by the Authority, who collectively have the qualifications and experience to review and evaluate the science, medical aspects, and ethics of the proposed trial; and

(b) include one member appointed by the Authority to be a Chairperson.

(3) An ethics committee may—

(a) establish 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 standard operating procedures adopted under paragraph (4).

(4) An ethics committee—

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

(b) may, subject to the approval of the Authority, vary or revoke such orders or procedures.

(5) The meetings and proceedings of an ethics committee and its sub-committees must be conducted in accordance with the standing orders made, and the standard operating procedures adopted, under paragraph (4).

(6) All applications for an ethics committee opinion must be considered by a full meeting of an ethics committee.

(7) In this regulation—

"a full meeting of an ethics committee" means a meeting at which—

(a) at least 5 members of the committee are in attendance, which may include attendance in person or remote attendance;

(b) the members present collectively satisfy the requirement in paragraph (2); and

(c) one of the members present is a lay member;

"lay member" means an individual who does not have a formal qualification related to, or professional experience in, the field of clinical research or healthcare.".

PART 4

Amendment to Part 3 (Authorisation for Clinical Trials and Ethics Committee Opinion)

Substitution of regulation 11

10. For regulation 11 (interpretation of Part 3) substitute—

"Interpretation of Part 3

11. In this Part—

"advanced therapy medicinal product" has the meaning given by regulation 2A of the 2012 Regulations(**a**);

"authorities" means the licensing authority and the ethics committee in collaboration with each other;

"modification of an important detail" means a modification to a clinical trial approval which—

(a) the authorities should be aware of for administrative or oversight purposes, but

(b) does not significantly impact the safety or rights of the participants;

"modification to a clinical trial approval" means a modification to—

(a) the terms of the request for approval of the clinical trial,

(b) the particulars or documents accompanying that request for approval, or

(c) where the request for approval of the clinical trial was made under regulation 16(5)—

(i) the terms of the request for authorisation to conduct that trial,

(ii) the application for an ethics committee opinion in relation to that trial, or

(iii) the particulars or documents accompanying that request for authorisation or application for ethics committee opinion;

"relevant committee" means—

(a) the Commission on Human Medicines, or

(b) such other body or committee as the licensing authority may consider appropriate in relation to the application under consideration;

"Route A substantial modification" means a modification to a clinical trial approval which is likely to have a substantial impact on the safety or rights of the participants or on the reliability or robustness of the data generated in the trial;

"Route B substantial modification" has the meaning given in regulation 11B;

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

(a) tissue engineered products,

(b) in the case of medicinal products for gene therapy or somatic cell therapy, the use of such therapies in the treatment of humans, or

(c) in the case of medicinal products containing genetically modified organisms, the administration of such products to humans;

"substantial modification" means—

(a) a Route A substantial modification, or

(b) a Route B substantial modification;

(**a**) S.I. 2012/1916; this definition was inserted by S.I. 2019/775.

"valid modification request" means a modification request which complies with the provisions of regulation 22;

"valid request for approval" means a request for approval which complies with the provisions of regulation 16.".

Insertion of new regulations 11A and 11B

11. After regulation 11 (interpretation of Part 3) insert—

"Definition of notifiable trial

11A.—(1) In these Regulations, "notifiable trial" means a trial—

(a) where there are no significant safety concerns with any of the investigational medicinal products, as far as the sponsor is aware having made reasonable enquiries;

(b) which meets either Condition A, Condition B or Condition C; and

(c) which does not involve either—

(i) participants who are—

(aa) under the age of 18 years,

(bb) pregnant, or

(cc) breastfeeding, or

(ii) an investigational medicinal product that is—

(aa) an advanced therapy medicinal product, or

(bb) used for the first time in humans.

(2) Condition A is that the investigational medicinal product or, if there is more than one, each of the investigational medicinal products, is authorised for use in the United Kingdom and either—

(a) the product is used in accordance with that authorisation; or

(b) the use of the product in the trial is supported by established clinical practice.

(3) Condition B is that a trial relating to the investigational medicinal product or, if there is more than one, each of the investigational medicinal products, has been approved in the United Kingdom within the preceding 2 years of the date of request for approval whereby—

(a) the product was investigated at—

(i) the same or higher dose,

(ii) the same or higher frequency, and

(iii) the same or longer duration;

(b) the same manufacturing process was utilised for the product; and

(c) the approved trial—

(i) utilised the same route of administration for the product, and

(ii) investigated the product for the same indication.

(4) Condition C is that the trial has undergone assessment, and been approved, by the appropriate authority responsible for the licensing of clinical trials in one or more of the following—

(a) the European Union;

(b) an EEA State;

(c) the United States of America.

Definition of Route B substantial modification

11B.—(1) In these Regulations, "Route B substantial modification" means a modification to the approval of a clinical trial ("the relevant clinical trial")—

(a) where there are no new significant safety concerns with any of the investigational medicinal products, as far as the sponsor is aware having made reasonable enquiries; and

(b) which meets either Condition A, Condition B or Condition C.

(2) Condition A is that—

(a) the relevant clinical trial does not involve an investigational medicinal product that is used for the first time in humans;

(b) the modification has been reviewed and approved by the appropriate authority responsible for the licensing of clinical trials in one or more of the following—

(i) the European Union;

(ii) an EEA State;

(iii) the United States of America; and

(c) the particulars and documents that have been reviewed in connection with the approval of the modification by the authority referred to in sub-paragraph (b)—

(i) are the same as those that accompany the modification request, and

(ii) do not include any particulars that are specific to the United Kingdom.

(3) Condition B is that the modification is limited to one or more of the following changes to the protocol for the relevant clinical trial—

(a) a change to the primary objective of the relevant clinical trial;

(b) an inclusion of new measurements for the primary endpoint;

(c) a change to the design of the relevant clinical trial, which has a significant impact on the statistical consideration;

(d) a change in the criteria by reference to which the relevant clinical trial ends;

(e) where the relevant clinical trial involves an investigational medicinal product that has been authorised for use in the United Kingdom, and which is used in accordance with the terms of that authorisation in the trial, a change to the number of planned interactions with the participants to assess their ongoing safety as a participant in the trial, which is not in response to a new safety concern;

(f) a change to the list of concomitant medication that a participant in the relevant clinical trial is or is not allowed to use;

(g) in relation to a clinical trial which is conducted in more than one country in accordance with a global protocol, a change to that protocol to include all requirements specific to the United Kingdom that were approved by the authorities in a separate protocol or addendum to the global protocol that is specific to the United Kingdom, where this change does not result in a change to the safety reporting requirements as set out in Part 5.

(4) Condition C is that the modification is limited to one or more of the following changes to the investigator's brochure or the summary of product characteristics for the relevant clinical trial—

(a) an inclusion of new toxicological or pharmacological data related to the investigational medicinal product, where there are no changes to the protocol of the relevant clinical trial as a result of safety concerns with the data;

(b) a change to the reference safety information which involves an increase in the frequency of adverse reactions, where there are no new expected adverse reactions;

(c) a change to the investigator's brochure which is not a change to—

(i) the assessment of the risks and benefits of the relevant clinical trial as approved by the authorities, or

(ii) the safety profile of any of the investigational medicinal products used in the relevant clinical trial;

(d) an update to the section of the summary of product characteristics which deals with undesirable effects of the investigational medicinal product.

(5) In this regulation—

"concomitant medication", in relation to a clinical trial, means any medicinal product that is not used for the purposes of the trial;

"primary endpoint" means the variable or measure capable of providing the most clinically relevant and convincing evidence directly related to the primary objective of the trial, for example, the period between the first receipt of treatment or a placebo by a participant and the occurrence of a pre-defined event;

"reference safety information" means information in the product information relating to expected serious adverse reactions associated with an investigational medicinal product, which is used to determine the adverse reactions that are to be treated as suspected unexpected serious adverse reactions in relation to that investigational medicinal product.".

Amendment to regulation 12

12.—(1) Regulation 12 (requirement for authorisation and ethics committee opinion) is amended as follows.

(2) In paragraph (2)—

(a) in sub-paragraph (a), for "subject" substitute "participant";

(b) in sub-paragraph (b), for "subjects" substitute "participants".

(3) For paragraph (3)(**a**) substitute—

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

(a) an ethics committee has given a favourable opinion in relation to the clinical trial; and

(b) the clinical trial has been authorised by the licensing authority,

in accordance with these Regulations.".

(4) Omit paragraph (4).

Amendment to regulation 13

13.—(1) Regulation 13 (supply of investigational medicinal products for the purpose of clinical trials) is amended as follows.

(**a**) Regulation 12(3) was amended by S.I. 2006/1928.

(2) In paragraph (1)(d), for "subject" substitute "participant".

(3) In paragraph (2)(b)(ii)(**a**)—

(a) in sub-paragraph (aa), for "Article 13 of the Directive" substitute "Article 62 of the EU Regulation";

(b) in sub-paragraph (bb), for "Article 13(3) and (4) of the Directive" substitute "Article 62 of the EU Regulation".

Substitution of regulations 14 to 26

14. For regulations 14 to 26 substitute—

"Request for authorisation to conduct a clinical trial

14.—(1) The sponsor must make a request for authorisation to conduct a clinical trial to the licensing authority in accordance with the procedure set out in regulation 16.

(2) Where the trial is a notifiable trial, the sponsor must indicate that it is a notifiable trial in accordance with regulation 16(2)(b).

Application for ethics committee opinion

15.—(1) The sponsor must make an application for an ethics committee opinion in relation to a clinical trial in accordance with the procedure set out in regulation 16.

(2) The application must be made to one ethics committee only, regardless of the number of trial locations at which the trial is to be conducted.

(3) Subject to paragraph (4), the application must be made to an ethics committee established or recognised—

(a) for the entire United Kingdom; and

(b) in relation to a description or class of clinical trial into which the proposed trial falls.

(4) If—

(a) a clinical trial is conducted at one or more trial locations in Scotland;

(b) the trial 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 must be made to an Ethics Committee constituted by regulations made by the Scottish Ministers under section 51(6) of the Adults with Incapacity (Scotland) Act 2000.

(5) For the purposes of paragraph (4), a chief investigator is professionally based at the hospital, health centre, surgery or other establishment or facility at or from which the chief investigator's professional practice is primarily conducted.

Request for approval and combined procedure

16.—(1) Subject to paragraph (5), the request for authorisation under regulation 14 and the application for an ethics committee opinion under regulation 15 must be made by way of a single application dossier (a "request for approval").

(**a**) Paragraph (2) was inserted by S.I. 2019/744.

(2) The request for approval must—

(a) be submitted to an online portal made available for this purpose;

(b) where the trial is a notifiable trial, include a statement confirming that the trial is a notifiable trial;

(c) be accompanied by—

(i) the particulars and documents specified in Part A1 of Schedule 3, and

(ii) subject to paragraph (3), any fee which may be payable in connection with that application under the Medicines (Products for Human Use) (Fees) Regulations 2016.

(3) Paragraph (2)(c)(ii) does not apply where arrangements have been made with the licensing authority or the ethics committee for payment of the fee referred to in that paragraph other than at the time of the request.

(4) The request for approval and accompanying material must be supplied in English.

(5) In exceptional circumstances (for example, in an urgent situation where it would be beneficial to progress one request or application while preparing the other), and if agreed in advance by the licensing authority or the ethics committee, a request for authorisation under regulation 14 and an application for an ethics committee opinion under regulation 15 may be made separately.

(6) Where an agreement has been reached under paragraph (5), the licensing authority or the ethics committee (as the case may be) must confirm—

(a) which of the particulars and documents specified in Part A1 of Schedule 3 must accompany—

(i) the request for authorisation, and

(ii) the application for an ethics committee opinion; and

(b) the arrangements for the payment of the fee specified in paragraph (2)(c)(ii).

(7) Where an agreement has been reached under paragraph (5), the submission of both the request for authorisation and the application of an ethics committee constitutes a "request for approval".

(8) The authorities must confirm whether the request for approval is valid within the period of 7 days beginning with the date of the submission of the request and notify the sponsor accordingly.

Assessment of request for approval

17.—(1) Where the licensing authority and an ethics committee receive a valid request for approval—

(a) the licensing authority must assess the request for authorisation in relation to the clinical trial to which the request for approval relates;

(b) the ethics committee must assess the application for an ethics committee opinion in relation to the clinical trial to which the request for approval relates.

(2) The licensing authority—

(a) must consider the safety of the clinical trial and the safeguarding of clinical trial participants; and

(b) may have regard to whether the sponsor has failed to comply with regulation 25(1) or 25(2)(a) in relation to another clinical trial, and not rectified that failure.

(3) The ethics committee must consider—

(a) whether the anticipated benefits to participants and other individuals or groups affected by the medical condition under investigation outweigh the anticipated risks and inconveniences, taking account of—

(i) the risks to the health of any of the participants posed by the medical condition for which the product is being investigated, and

(ii) the nature of the intervention compared to normal clinical care; and

(b) the measures used to—

(i) seek and obtain informed consent for participation in the trial, and

(ii) protect and promote the interests of participants and the general public (including by promoting transparency in research).

(4) Where the request for approval contains a statement under regulation 16(2)(b) confirming that the trial is a notifiable trial, the licensing authority may, if it considers appropriate and without undertaking further assessment, rely on that statement to provide an authorisation of the clinical trial to which the request for approval relates.

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

(a) the committee has been asked by the sponsor to consider the issue;

(b) it is, in the committee's opinion, relevant to the other matters considered by the committee in accordance with paragraph (3).

(6) The ethics committee may, before giving its opinion, obtain expert advice on any field which relates to the clinical trial.

(7) If the licensing authority or the ethics committee considers it appropriate to do so, they may consult either or both of the following—

(a) a relevant committee;

(b) a specialist group or committee.

(8) The authorities must not approve a clinical trial involving products for gene therapy if the use of those products in that trial would result in modifications to any participant's germ line genetic identity.

Approval procedure for clinical trials

18.—(1) Having carried out the assessments required by regulation 17—

(a) the licensing authority must provide its decision in relation to the request for authorisation to conduct the clinical trial in accordance with this regulation; and

(b) the ethics committee must give an opinion in relation to the clinical trial in accordance with this regulation.

(2) The authorities must notify the sponsor of the decision in paragraph (1)(a) and the opinion in paragraph (1)(b).

(3) A notice under paragraph (2) must—

(a) be in writing; and

(b) state that the authorities—

(i) approve the request for approval,

(ii) approve the request for approval, subject to conditions specified in the notice, or

(iii) do not approve the request for approval, setting out the grounds for this decision.

(4) Subject to paragraphs (7) and (8) and regulation 18C, the authorities must take all reasonable steps to ensure that the notice is given within the period of 30 days beginning with the date on which the authorities notified the sponsor that the request for approval was valid in accordance with regulation 16(8).

(5) If a notice is given in accordance with paragraph (3)(b)(ii)—

(a) the notice must specify whether the conditions relate to either or both of the following—

(i) the licensing authority's decision on the clinical trial authorisation;

(ii) the ethics committee opinion;

(b) the clinical trial is to be treated as approved only if the conditions specified in the notice are satisfied.

(6) If a notice is given in accordance with paragraph (3)(b)(iii), regulations 18A and 18B apply.

(7) The time period referred to in paragraph (4) is extended by 90 days where the licensing authority or the ethics committee consults either or both of the following—

(a) a relevant committee;

(b) a specialist group or committee.

(8) If the clinical trial involves a medicinal product for xenogenic cell therapy, the time periods set out in paragraphs (4) and (7) do not apply and the authorities may give written notice under this regulation at any time after the date on which the authorities notified the sponsor that the request for approval was valid in accordance with regulation 16(8).

(9) Where an ethics committee gives an opinion in accordance with this regulation, it must publish the conclusion of that opinion, whether favourable or unfavourable.

(10) Where a request for authorisation under regulation 14 and an application for an ethics committee opinion under regulation 15 are made separately in accordance with regulation 16(5)—

(a) the time periods mentioned in this regulation, regulation 18A and 18B applies separately to the request for authorisation and the application for an ethics committee opinion;

(b) the clinical trial is to be treated as approved upon receiving both the authorisation from the licensing authority and a favourable opinion from the ethics committee.

Request for further information regarding a request for approval

18A.—(1) A notice given in accordance with regulation 18(3)(b)(iii) must—

(a) request further information required to reconsider the approval of the request; and

(b) specify whether the request for further information relates to either or both of the following—

(i) the licensing authority's decision on the clinical trial authorisation;

(ii) the ethics committee opinion.

(2) If the sponsor is given a notice which contains a request for further information in accordance with paragraph (1), the sponsor may send an amended request for approval for further consideration within—

(a) the period of 60 days beginning with the day on which the notice is given; or

(b) any such extended period as the appropriate authority may in any particular case allow.

(3) An amended request for approval can be a response to the request for further information or an amendment to the request for approval.

(4) In this regulation, "appropriate authority" has the meaning given in regulation 18B(1).

Approval procedure for amended requests for approval

18B.—(1) An amended request for approval must be reviewed by the appropriate authority, which, for the purposes of this regulation, is either or both of the following—

(a) the licensing authority, if the request for further information relates to the licensing authority's decision on the clinical trial authorisation;

(b) the ethics committee, if the request for further information relates to the ethics committee opinion.

(2) The appropriate authority must notify the sponsor of its decision or its opinion, or both its decision and opinion.

(3) A notice under paragraph (2) must—

(a) be in writing; and

(b) state that the appropriate authority—

(i) approves the amended request,

(ii) approves the amended request, subject to conditions specified in the notice, or

(iii) does not approve the amended request, setting out the grounds for this decision.

(4) Subject to paragraphs (6) and (7) and regulation 18C, the appropriate authority must take all reasonable steps to ensure that the notice is given within the period of 10 days beginning with the date of receipt of an amended request for approval.

(5) If a notice is given in accordance with paragraph (3)(b)(ii)—

(a) the notice must specify whether the conditions relate to either or both of the following—

(i) the licensing authority's decision on the clinical trial authorisation;

(ii) the ethics committee opinion;

(b) the clinical trial is to be treated as approved only if the conditions specified in the notice are satisfied.

(6) The period of 10 days referred to in paragraph (4) is extended by a further—

(a) 30 days, where the licensing authority or the ethics committee consults either or both of the following—

(i) a relevant committee;

(ii) a specialist group or committee;

(b) 60 days, where—

(i) the investigational medicinal product is an advanced therapy medicinal product, and

(ii) the licensing authority or the ethics committee consults either or both of the groups or committees mentioned in sub-paragraph (a).

(7) If the clinical trial involves a medicinal product for xenogenic cell therapy, the time periods set out in paragraphs (4) and (6) do not apply and the appropriate authority may give written notice under this regulation at any time after receipt of an amended request for approval.

(8) The request for approval is to be treated as rejected and the authorities may not consider any further amendments to the request if—

(a) the authorities give written notice to the sponsor which contains a request for further information in accordance with regulation 18A(1) and the sponsor does not submit an amended request in accordance with regulation 18A(2); or

(b) the sponsor has submitted an amended request in accordance with regulation 18A(2), but the appropriate authority gives written notice to the sponsor in accordance with paragraph (3)(b)(iii).

Approval procedure time periods in special circumstances

18C.—(1) For the purposes of regulations 18(4) and 18B(4)—

(a) where the sponsor selects a date other than the next available ethics committee meeting, then the time periods referred to in those regulations will begin from the date that is 7 days before the chosen ethics committee meeting date; and

(b) where the clinical trial involves a medical device, then the time periods referred to in those regulations may begin from the date of formal acceptance under regulation 16(4) of the Medical Devices Regulations 2002(**a**).

(2) Where the valid request for approval or amended request for approval falls under both paragraphs (1)(a) and (1)(b), the time periods referred to in regulations 18(4) and 18B(4) will begin from the later of the dates mentioned in paragraphs (1)(a) and (1)(b).

Clinical trials conducted in countries other than the United Kingdom

19.—(1) If the licensing authority receives a request for authorisation which complies with regulations 14 and 16, relating to a clinical trial which is or is to be conducted in another country as well as the United Kingdom, the licensing authority may, if it thinks fit, require the production by the sponsor of either or both 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 in accordance with Schedule 1 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 approving the request for authorisation.

Modifications to clinical trial approval

20. A modification to a clinical trial approval may be made—

(**a**) S.I. 2002/618, amended by S.I. 2019/791; there are other amending instruments but none is relevant.

(a) by the licensing authority or the ethics committee, in accordance with regulation 21; or

(b) by the sponsor, in accordance with regulations 22, 22A and 22B.

Modifications by the licensing authority or the ethics committee

21.—(1) The appropriate authority may require the sponsor to make modifications to a clinical trial approval 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 appropriate authority proposes a modification in accordance with paragraph (1), that authority must, at least 7 days before the date on which it is proposed that the modification should take effect, serve a notice on the sponsor stating their proposal and the reasons for it.

(3) If, within the period of 7 days beginning with the date on which notice is served in accordance with paragraph (2), the sponsor makes representations in writing to the appropriate authority, that authority—

(a) must take those representations into account before deciding whether to require the sponsor to make the modification; and

(b) may delay the date the proposed modification is to take effect, in order to allow time for them to consider those representations.

(4) In this regulation, the "appropriate authority" means either or both of the following—

(a) the licensing authority;

(b) the ethics committee.

Modifications by the sponsor

22.—(1) A sponsor may make a modification to a clinical trial approval, other than a substantial modification, at any time and without the need for submitting a request under this regulation.

(2) A sponsor must—

(a) keep records of the modifications made in accordance with paragraph (1); and

(b) send those records to the licensing authority or the ethics committee, where the authority or committee (as the case may be) gives written notice requiring the sponsor to provide those records.

(3) If a sponsor makes a modification of an important detail, the sponsor must notify the authorities of the modification through an online portal made available for this purpose.

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

(a) the terms of the request for approval of the clinical trial; or

(b) the particulars or documents that accompanied that request for approval,

the sponsor must submit a modification request to the authorities in accordance with paragraphs (6) and (7).

(5) Where the request for approval of the clinical trial was made under regulation 16(5), then a valid modification request must be submitted pursuant to paragraph (4) if the sponsor

proposes to make a substantial modification to the clinical trial approval which consists of, or includes, a substantial modification to—

(a) the terms of the request for authorisation of the clinical trial;

(b) the application for an ethics committee opinion in relation to the trial; or

(c) the particulars or documents that accompanied—

(i) the request for authorisation, or

(ii) the application for an ethics committee opinion.

(6) A modification request must—

(a) be submitted to an online portal made available for this purpose;

(b) clearly identify the proposed substantial modification and whether it relates to the authorisation by the licensing authority or the ethics committee opinion;

(c) where the proposed substantial modification is a Route B substantial modification, include a statement confirming that it is a Route B substantial modification;

(d) be accompanied by—

(i) the particulars and documents specified in Part 3 of Schedule 3, and

(ii) any fee which may be payable in connection with that application under the Medicines (Products for Human Use) (Fees) Regulations 2016.

(7) The modification request and accompanying material in paragraph (6) must be supplied in English.

(8) The authorities must confirm whether the modification request is valid within the period of 7 days beginning with the date of the submission of the request and notify the sponsor accordingly.

Approval procedure for substantial modifications

22A.—(1) Where the licensing authority and an ethics committee receive a valid modification request in relation to a substantial modification to a clinical trial approval—

(a) the licensing authority must—

(i) review the request in relation to the authorisation to conduct the clinical trial, and

(ii) provide its decision in accordance with this regulation;

(b) the ethics committee must—

(i) review the request in relation to the ethics committee opinion for the clinical trial, and

(ii) provide an opinion in accordance with this regulation.

(2) Where the modification request contains a statement under regulation 22(6)(c) confirming that the modification is a Route B substantial modification, the licensing authority may, if it considers appropriate and without undertaking further assessment, rely on that statement to provide its decision on the modification request.

(3) The authorities must notify the sponsor of the decision in paragraph (1)(a)(ii) or the opinion in paragraph (1)(b)(ii), or both the decision and the opinion.

(4) A notice under paragraph (3) must—

(a) be in writing; and

(b) state that the authorities—

(i) approve the proposed modification,

(ii) approve the proposed modification, subject to conditions specified in the notice, or

(iii) do not approve the proposed modification, setting out the grounds for this decision.

(5) The authorities must take all reasonable steps to ensure that the notice is given within the period of 35 days beginning with the date on which the authorities notified the sponsor that the modification request was valid in accordance with regulation 22(8).

(6) If a notice is given in accordance with paragraph (4)(b)(ii)—

(a) the notice must specify whether the conditions relate to either or both of the following—

(i) the licensing authority's decision on the clinical trial authorisation;

(ii) the ethics committee opinion;

(b) the modification is to be treated as approved only if the conditions specified in the notice are satisfied.

(7) If a notice is given in accordance with paragraph (4)(b)(iii), regulations 22B and 22C apply.

Request for further information regarding proposed substantial modifications

22B.—(1) A notice given in accordance with regulation 22A(4)(b)(iii) may request further information required to reconsider the approval of the request.

(2) If the notice contains a request for further information in accordance with paragraph (1), then the notice must specify whether the request for further information relates to either or both of the following—

(a) the licensing authority's decision;

(b) the ethics committee opinion.

(3) If the sponsor is given a notice in accordance with regulation 22A(4)(b)(iii) which contains a request for further information in accordance with paragraph (1), the sponsor may send an amended modification request for further consideration within—

(a) the period of 60 days beginning with the day on which the notice is given; or

(b) such extended period as the appropriate authority may in any particular case allow.

(4) An amended modification request can be a response to the request for further information or an amendment to the modification request.

(5) In this regulation, "appropriate authority" has the meaning given in regulation 22C(1).

Approval procedure for amended requests regarding substantial modifications

22C.—(1) An amended modification request must be reviewed by the appropriate authority, which, for the purposes of this regulation, is either or both of the following—

(a) the licensing authority, if the request for further information relates to the licensing authority's decision;

(b) the ethics committee, if the request for further information relates to the ethics committee opinion.

(2) The appropriate authority must notify the sponsor of its decision or its opinion, or both its decision and opinion.

(3) A notice under paragraph (2) must—

(a) be in writing; and

(b) state that the appropriate authority—

(i) approves the amended request,

(ii) approves the amended request, subject to conditions specified in the notice, or

(iii) does not approve the amended request, setting out the grounds for this decision.

(4) The appropriate authority must take all reasonable steps to ensure that the notice is given within the period of 10 days beginning with the date of receipt of an amended modification request.

(5) If a notice is given in accordance with paragraph (3)(b)(ii)—

(a) the notice must specify whether the conditions relate to either or both of the following—

(i) the licensing authority's decision;

(ii) the ethics committee opinion;

(b) the modification is to be treated as approved only if the conditions specified in the notice are satisfied.

(6) The modification request is to be treated as rejected and the authorities may not consider any further amendments to that request if—

(a) the authorities give written notice to the sponsor in accordance with regulation 22A(4)(b)(iii) and—

(i) the notice does not contain a request for further information in accordance with regulation 22B(1), or

(ii) the sponsor does not submit an amended request in accordance with regulation 22B(2); or

(b) the sponsor has submitted an amended request in accordance with regulation 22B(3), but the appropriate authority gives written notice to the sponsor in accordance with paragraph (3)(b)(iii).

Reference to the appropriate committee or the Medicines Commission

23.—(1) This regulation applies where—

(a) a sponsor has been notified under regulation 18(2) or 18B(2) that—

(i) the trial is not approved and the grounds for not approving the trial relate to the licensing authority's decision on the clinical trial authorisation, or

(ii) the trial is approved subject to specified conditions and those conditions relate to the licensing authority's decision;

(b) the licensing authority has modified a clinical trial approval under regulation 21; or

(c) the sponsor has been notified under regulation 22A(3) or 22C(2) that—

(i) a proposed substantial modification is not approved and the grounds for not approving the modification relate to the licensing authority's decision, or

(ii) the proposed substantial modification is approved subject to conditions and those conditions relate to the licensing authority's decision.

(2) Where this regulation applies, the sponsor may, within the period of 28 days beginning with the day on which notice is given or such extended period as the licensing authority may in any particular case allow, give notice in writing to the licensing authority of the sponsor's wish to make written or oral representations to the appropriate committee.

(3) Schedule 5 has effect to regulate the procedure for reference to the appropriate committee following receipt of a notice in accordance with paragraph (1).

Review and appeal relating to ethics committee opinion

24.—(1) This regulation applies where—

(a) a sponsor has been notified under regulations 18(2) or 18B(2) that—

(i) the trial is not approved and the grounds for not approving the trial relate to the ethics committee opinion, or

(ii) the trial is approved subject to specified conditions and those conditions relate to the ethics committee opinion;

(b) the ethics committee has modified a clinical trial approval under regulation 21; or

(c) the sponsor has been notified under regulation 22A(3) or 22C(2) that—

(i) a proposed substantial modification is not approved and the grounds for not approving the modification relate to the ethics committee opinion, or

(ii) the proposed substantial modification is approved subject to conditions and those conditions relate to the ethics committee opinion.

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

(a) an Ethics Committee constituted by regulations made by the Scottish Ministers under section 51(6) of the Adults with Incapacity (Scotland) Act 2000; or

(b) an ethics committee pursuant to paragraph 2 of Schedule 4.

(3) Where this regulation applies, the sponsor may, within the period of 28 days beginning with the day on which notice is given or such extended period as the Authority may in any particular case allow, give notice in writing to the Authority—

(a) stating the sponsor's wish to appeal against the opinion; and

(b) setting out their representations with respect to that opinion.

(4) Schedule 4 has effect to regulate the procedure where the Authority receives a notice in accordance with paragraph (3).

Transparency requirements

25.—(1) Subject to paragraphs (5), (7) and (10), the sponsor must register a clinical trial in a public registry by the earlier of the following—

(a) the date on which the first individual is recruited to be a participant in that trial;

(b) 90 days after the date of approval of the clinical trial.

(2) Subject to paragraphs (5), (7) and (10), within the period of 12 months beginning with the day after the conclusion of the clinical trial in accordance with regulation 27, the sponsor must—

(a) publish a summary of the results of the clinical trial in the same public registry or registries (if more than one) as the trial was registered in accordance with paragraph (1); and

(b) offer to all relevant persons a summary of the results written in a manner that is understandable to laypersons.

(3) The sponsor may apply for a deferral or waiver of the requirement to register a clinical trial in accordance with paragraph (1), stating why the deferral or waiver is needed—

(a) at the time of the request for approval under regulation 16; or

(b) at any time before the date specified in paragraph (1).

(4) The sponsor may apply for a deferral or waiver of either or both of the requirements in paragraph (2), stating why the deferral or waiver is needed—

(a) at the time of the request for approval under regulation 16; or

(b) at any time before the date specified in paragraph (2).

(5) Where the sponsor applies for a deferral or a waiver in accordance with paragraphs (3) or (4), the Authority may—

(a) where they consider appropriate, defer the requirement for up to a period of 30 months beginning with the day after the conclusion of the trial, for example, in order to protect commercially confidential information; or

(b) in exceptional circumstances, waive the requirement, for example, for reasons of national defence and security.

(6) The sponsor may apply for a further deferral, stating why the deferral is needed, at any time before the expiry of the previous deferral.

(7) Where the sponsor applies for a further deferral in accordance with paragraph (6), the Authority may, where they consider appropriate, defer the requirement for up to a period of 30 months beginning with the day after the end of the previous deferral period, for example, in order to protect commercially confidential information.

(8) The Authority must give written notice of their decision to the sponsor—

(a) at the time the ethics committee provides a favourable opinion in accordance with regulation 18 or 18B, where the sponsor makes the application to defer or waive under paragraph (3)(a) or (4)(a); or

(b) subject to paragraph (9), within the period of 10 days beginning with the date of receipt of the application to defer or waive the requirement, where this application is made under paragraphs (3)(b), (4)(b) or (6).

(9) Where the sponsor makes an application under paragraph (3)(b) before the ethics committee provides a favourable opinion in accordance with regulation 18 or 18B, then the Authority may give written notice of their decision on the application for a deferral or waiver to the sponsor at the time the ethics committee provides a favourable opinion.

(10) Where the clinical trial is a Phase I trial, the Authority may provide an automatic deferral of—

(a) the requirement to register the trial in accordance with paragraph (1) for up to a period of 30 months beginning with the day after the conclusion of the trial, provided that the sponsor registers the required minimum information in a public registry before the date specified in paragraph (1);

(b) the requirements in paragraph (2) for up to a period of 30 months beginning with the day after the conclusion of the trial.

(11) The combined period of deferrals granted under paragraphs (5), (7) and (10) must not be more than the period of 10 years beginning with the day after the conclusion of the trial.

(12) In this regulation—

"public registry" means a a primary or partner registry of, or a data provider to, the WHO International Clinical Trials Registry Platform, provided that the registry, or the data provider, facilitates public access to information about the trial in the United Kingdom;

"relevant person" includes—

(a) a participant as defined in regulation 2(1);

(b) where the participant is a minor or an adult unable to give informed consent to take part in the trial by virtue of physical or mental incapacity, the person who has given informed consent in accordance with Schedule 1;

(c) where the participant would now be unable to consent due to an incapacity the onset of which occurred after the start of the trial, a person who is engaged in caring for the participant or is interested in the participant's welfare, for example, their legal representative (if there is one) or their next of kin;

(d) where the participant is unable to receive the summary of results due to death, a person who was engaged in caring for the participant or was interested in the participant's welfare, for example, their next of kin;

"required minimum information" includes the particulars identifying the trial and the details of the sponsor and investigator.

Lapse of clinical trial approval

26.—(1) Subject to the extension of the period in paragraphs (3) and (5), the clinical trial approval lapses at the end of the period of 24 months beginning with the date of approval of the trial if there are no participants recruited to take part in the trial.

(2) The sponsor may apply for an extension of the time period referred to in paragraph (1), stating why an extension is needed—

(a) at the time of the request for approval under regulation 16; or

(b) at any time before the expiry of the two-year period specified in paragraph (1).

(3) Where the sponsor applies for an extension in accordance with paragraph (2), the authorities may, where they consider appropriate, agree to extend the period for up to 36 months beginning with the day after the expiry of the period specified in paragraph (1), for example, where the trial involves the study of a rare disease or the trial is in anticipation of a disease causing a pandemic.

(4) The sponsor may apply for a further extension, stating why the extension is needed, at any time before the expiry of the previous extension.

(5) Where the sponsor applies for a further extension in accordance with paragraph (4), the authorities may, where they consider appropriate, agree to extend the period for up to 24 months beginning with the day after the end of the previous extension period, for example, where the trial involves the study of a rare disease or the trial is in anticipation of a disease causing a pandemic.

(6) The authorities must give written notice of their decision to the sponsor—

(a) at the time they approve the request for approval or amended request for approval in accordance with regulation 18 or 18B, where the sponsor makes the application to extend under paragraph (2)(a); or

(b) within the period of 30 days beginning with the date of receipt of the application to extend, where this application is made under paragraphs (2)(b) or (4).

(7) If the period has lapsed in accordance with paragraph (1)—

(a) the sponsor must notify the authorities in writing that the trial has ended; or

(b) the trial will be terminated in accordance with regulation 31.".

Amendment to regulation 27A

15. In regulation 27A (information sharing)(**a**), after "licensing authority" insert ", the Authority".

Substitution of regulation 27B

16. For regulation 27B (publication of information) substitute—

"Publication of information

27B.—(1) Subject to paragraph (3), the Authority may make accessible to the public information contained in the items listed in paragraph (2) insofar as it relates to a clinical trial carried out, or being carried out, under these Regulations.

(2) The items listed in this paragraph are—

(a) the request for approval made under regulation 16;

(b) any amended request for approval made under regulation 18A;

(c) any substantial modification to the clinical trial approval made under regulation 21, 22, 22A or 22B;

(d) the favourable opinion of the ethics committee given in accordance with regulation 18(1)(b);

(e) the notification of the end of the clinical trial made under regulation 27.

(3) Prior to making information available to the public under paragraph (1), the Authority must, after consulting such persons as they consider appropriate, publish a list of the information which may be made accessible to the public under paragraph (1).".

PART 5

Amendment to Part 4 (Good Clinical Practice and the Conduct of Clinical Trials)

Amendment to regulation 28

17.—(1) Regulation 28 (good clinical practice and protection of clinical trial subjects) is amended as follows.

(2) In the heading, for "subjects" substitute "participants".

(3) After paragraph (1) insert—

"(1A) The conditions and principles of good clinical practice include those in the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guideline for Good Clinical Practice, as amended from time to time(**b**).

(1B) For the avoidance of doubt—

(a) the functions of the sponsor include functions in relation to—

(**a**) Regulation 27A was inserted by S.I. 2006/1928.

(**b**) The Guideline can be found at https://ich.org/page/efficacy-guidelines. A printed version of the document can be made available on request by the Department of Health and Social Care, 39 Victoria Street, London SW1H 0EU.

(i) the development and maintenance of trial specific computerised systems, and

(ii) the selection and oversight of a laboratory in relation to the analysis or evaluation of human samples collected as part of the clinical trial; and

(b) conducting a trial includes the analysis or evaluation of human samples collected as part of the clinical trial.".

(4) In paragraph (3), for "subjects" substitute "participants".

(5) In paragraph (4), for "subject" substitute "participant".

(6) In paragraph (5)—

(a) for "site", in both places where it occurs, substitute "location";

(b) for "sites", in both places where it occurs, substitute "locations".

Amendment to regulation 29

18.—(1) Regulation 29 (conduct of trial in accordance with clinical trial authorisation etc.) is amended as follows.

(2) In paragraphs (a) and (b)—

(a) for "amended" substitute "modified";

(b) for "regulations 22 to 25" substitute "regulations 20 to 22C".

(3) In paragraph (c)(**a**)—

(a) omit "by the licensing authority";

(b) for "regulation 18(2) or (6), 19(8), 20(5), 24(5)" substitute "regulation 18(3), 18B(3), 22A(4), 22C(3)".

Amendment to regulation 29A

19.—(1) Regulation 29A (notification of serious breaches)(**b**) is amended as follows.

(2) In paragraph (1)(b)—

(a) for "amended" substitute "modified";

(b) for "regulations 22 to 25" substitute "regulations 20 to 22C".

(3) In paragraph (2)(a), for "subjects" substitute "participants".

Amendment to regulation 30

20.—(1) Regulation 30 (urgent safety measures) is amended as follows.

(2) In paragraph (1), for "subjects" substitute "participants".

(3) In paragraph (2)(b)(**c**), for "3 days" substitute "7 days".

Amendment to regulation 31

21.—(1) Regulation 31 (suspension or termination of clinical trial) is amended as follows.

(2) In paragraph (1)—

(a) after "clinical trial" insert "or part of a clinical trial";

(**a**) Regulation 29(c) was amended by S.I. 2006/1928.
(**b**) Regulation 29A was inserted by S.I. 2006/1928.
(**c**) Regulation 30(2) was substituted by S.I. 2009/1164.

(b) in sub-paragraph (a)(ii)(**a**)—

(i) omit "by the licensing authority";

(ii) for "regulation 18(2) or (6), 19(8), 20(5), 24(5)" substitute "regulation 18(3), 18B(3), 22A(4), 22C(3)";

(c) in the words after sub-paragraph (a)(ii), for "site); or" substitute "location);";

(d) in sub-paragraph (b), for "site," substitute "location; or";

(e) after sub-paragraph (b), insert—

"(c) the trial has lapsed in accordance with regulation 26 and the sponsor has not notified the licensing authority that the trial has ended,".

(3) In paragraph (2), for "trial site", in each place where it occurs, substitute "trial location".

(4) In paragraph (3)—

(a) in sub-paragraph (a), for "sites" substitute "locations";

(b) in sub-paragraph (b), after "the trial" insert "in whole or in part, and, if it applies to part of the trial, to which part it applies";

(c) in sub-paragraph (c)(ii), for "site" substitute "location".

(5) In paragraph (5)—

(a) for "site", in both places where it occurs, substitute "location";

(b) in sub-paragraph (a), after "terminating the trial" insert "(in whole or in part)".

(6) In paragraph (6), for "subjects" substitute "participants".

Amendment to regulation 31A

22.—(1) Regulation 31A (trial master file and archiving) is amended as follows.

(2) In paragraph (7)—

(a) at the beginning, insert "Subject to paragraph (7A),";

(b) after "master file" insert "(including documents contained in electronic form)";

(c) for "5 years" substitute "the period of 25 years beginning with the day".

(3) After paragraph (7) insert—

"(7A) If, at the date of the expiry of the 25 years referred to in paragraph (7), the data generated by the trial is being used to support an application for a UK marketing authorization, the sponsor shall ensure the documents referred to in paragraph (7) are retained for at least the period of 2 years beginning with the day after the grant of that UK marketing authorization.".

(4) In paragraph (8)—

(a) for "subjects" substitute "participants";

(b) for "5 years after conclusion of the trial" substitute "the period of 25 years beginning with the day after conclusion of the trial, or such period as is required by any other enactment, if longer".

(**a**) Regulation 31(1)(a)(ii) was amended by S.I. 2006/1928.

PART 6

Amendment to Part 5 (Pharmacovigilance)

Insertion of new regulation A32

23. In Part 5, before regulation 32 (notification of adverse events) insert—

"Record keeping

A32.—(1) A sponsor shall keep detailed records of all serious adverse events and serious adverse reactions, including suspected unexpected serious adverse reactions, which occur during the course of a clinical trial—

(a) in the United Kingdom;

(b) conducted outside of the United Kingdom where—

(i) the sponsor of both the trial in the United Kingdom and the trial outside of the United Kingdom is the same or, where the sponsor is a company, in the same group, and

(ii) the investigational medicinal product being tested or used in the trial conducted outside of the United Kingdom is the same as the investigational medicinal product being tested or used in the clinical trial mentioned in sub-paragraph (a).

(2) A sponsor shall evaluate the events and reactions mentioned in paragraph (1), with a view to—

(a) minimising and preventing any risk presented by the use of the investigational medicinal product to which those events and reactions relate; and

(b) taking appropriate measures as soon as reasonably practicable to investigate the risks presented and implement actions for minimising and preventing those risks.

(3) For purposes of paragraph (1)(b)(i), "group" has the same meaning as in Part 15 of the Companies Act 2006 (see section 474(1) of that Act).".

Amendment to regulation 32

24. In regulation 32 (notification of adverse events), for "subject", in each place where it occurs, substitute "participant".

Amendment to regulation 33

25.—(1) Regulation 33 (notification of suspected unexpected serious adverse reactions) is amended as follows.

(2) For paragraph (1)(**a**) substitute—

"(1) A sponsor shall ensure that all relevant information about a suspected unexpected serious adverse reaction which occurs during the course of a clinical trial in the United Kingdom and is fatal or life-threatening is reported as soon as possible to the licensing authority, and in any event no later than 7 days after the sponsor was first aware of the reaction.".

(**a**) Regulation 33(1) was amended by S.I. 2019/744.

(3) In paragraph (2)—

(a) for "paragraph (1)(b)" substitute "paragraph (1)";

(b) for "persons or bodies listed in that paragraph" substitute "licensing authority".

(4) For paragraph (3)(**a**) substitute—

"(3) A sponsor shall ensure that a suspected unexpected serious adverse reaction which occurs during the course of a clinical trial in the United Kingdom, other than those referred to in paragraph (1), is reported as soon as possible to the licensing authority, and in any event no later than 15 days after the sponsor is first aware of the reaction.".

(5) Before paragraph (5) insert—

"(4A) Paragraphs (1) to (3) do not apply to suspected unexpected serious adverse reactions specified in the protocol as not requiring immediate reporting.

(4B) The sponsor shall report suspected unexpected serious adverse reactions to which paragraph (4A) applies to the licensing authority in accordance with the reporting requirements, including the time periods for such reporting, that are specified in the protocol.".

(6) Omit paragraph (5).

Amendment to regulation 35

26.—(1) Regulation 35 (annual list of suspected serious adverse reactions and safety report) is amended as follows.

(2) In the heading, omit "list of suspected serious adverse reactions and".

(3) For paragraph (1) substitute—

"(1) Within the period of 60 days beginning with the day after the day on which the reporting year ends, a sponsor shall, in relation to each investigational medicinal product tested in clinical trials referred to in regulation A32(1), provide the licensing authority with a report on the safety of the participants of those trials.".

(4) After paragraph (1) insert—

"(1A) A report under paragraph (1) shall include—

(a) the records of, and evaluation relating to, any serious adverse reactions and serious adverse events which have occurred during the reporting year, including suspected unexpected serious adverse reactions, kept or conducted under regulation A32;

(b) the record of the taking of any measures referred to in regulation A32(2)(b);

(c) a description of how any safety concerns in the clinical trial have been assessed and managed; and

(d) a description of the overall safety profile of each investigational medicinal product being tested or used in the trials referred to in regulation A32(1), as well as a summary description of the processes adopted by the sponsor to monitor the overall safety profile of those products.

(1B) The records of serious adverse reactions and serious adverse events referred to in paragraph (1A)(a) may take the form of a list.

(1C) The licensing authority may request that the sponsor provide a list of serious adverse reactions and serious adverse events, including suspected unexpected serious adverse

(**a**) Regulation 33(3) was amended by S.I. 2019/744.

reactions, which have occurred at any time during the reporting year, in relation to a clinical trial referred to in regulation A32(1), where it considers it necessary to do so to investigate specific safety issues—

(a) which emerge from the report under paragraph (1); or

(b) which have otherwise come its attention, and raise concerns about the safety of the trial or the participants.

(1D) The sponsor shall provide the list requested under paragraph (1C) within the period of 30 days beginning with the day of receiving the request, or within such shorter period as the licensing authority may specify in the request.".

(5) In paragraph (2), at the beginning, for "paragraph (1)" substitute "this regulation".

PART 7

Amendment to Part 6 (Manufacture and Importation of Investigational Medicinal Products)

Amendment to regulation 36

27. In regulation 36 (requirement for authorisation to manufacture or import investigational medicinal products), in paragraph (1), for "regulation 37" substitute "regulations 37 and 37A".

Insertion of new regulation 37A

28. After regulation 37 (exemption for hospitals and health centres) insert—

"Exemption for radiopharmaceuticals used for diagnostic purposes

37A.—(1) The restriction imposed by regulation 36(1) does not apply to the manufacture or assembly of a radiopharmaceutical used for diagnostic purposes where the conditions in paragraph (2) are satisfied.

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

(a) the manufacture or assembly is carried out by the holder of a manufacturer's licence, as defined in regulation 8(1) of the 2012 Regulations, which does not relate to the manufacture of investigational medicinal products; and

(b) the radiopharmaceutical is exclusively for use in a hospital or health centre which is—

(i) a trial location for the clinical trial in which the product is to be used, or

(ii) taking part in the clinical trial.".

Amendment to regulation 40

29. In regulation 40 (grant or refusal of manufacturing authorisation), in paragraph (1)(a)(ii)(**a**), after "Commission Directive 2003/94/EC" insert "in respect of Great Britain, or of Commission Delegated Regulation 2017/1569 in respect of Northern Ireland".

Amendment to regulation 43

30.—(1) Regulation 43 (qualified persons) is amended as follows.

(**a**) Regulation 40(1)(a)(ii) was substituted by S.I. 2006/1928.

(2) In paragraph (2A)(b)(**a**), for "Article 13 of the Directive" substitute "Article 62 of the EU Regulation".

(3) In paragraph (2C)(b), after "Commission Directive 2003/94/EC" insert "in respect of Great Britain or Commission Delegated Regulation 2017/1569 in respect of Northern Ireland".

(4) In paragraph (5)(**b**), for "the said Article 49 or 50" substitute "Schedule 7 to the 2012 Regulations".

(5) In paragraph (6)(a)(i), for "the said Articles 49 or 50 of Directive 2001/83/EC" substitute "Schedule 7 to the 2012 Regulations".

PART 8

Insertion of new Part 6A (Non-Investigational Medicinal and Non-Medicinal Products)

Insertion of new Part 6A

31. After Part 6, insert—

"PART 6A

NON-INVESTIGATIONAL MEDICINAL AND NON-MEDICINAL PRODUCTS

Non-investigational medicinal and non-medicinal products

45A.—(1) A non-investigational medicinal product shall be manufactured or assembled in accordance with the principles and guidelines for good manufacturing practice which apply under these Regulations or the 2012 Regulations.

(2) A product which is not a medicinal product but which is used or to be used in a clinical trial, as described in the protocol, must—

(a) comply with safety standards applicable to that product; and

(b) be listed in the investigational medicinal product dossier with information about its properties, labelling, manufacture and safety controls, appropriate to the product.".

PART 9

Substitution of Part 7 (Labelling of Investigational Medicinal Products)

Substitution of Part 7

32. For Part 7 (labelling of investigational medicinal products) substitute—

(**a**) Paragraph (2A) was inserted by S.I. 2019/744.
(**b**) Paragraph (5) was substituted by S.I. 2019/744.

“PART 7

LABELLING

Labelling of investigational medicinal products

46.—(1) Subject to paragraph (4), where the investigational medicinal product is not an authorised medicinal product, it must be labelled with the following information—

(a) the words “for clinical trial use only”;

(b) a warning that the product must be stored out of the reach and sight of children (unless the product is to be exclusively administered in a hospital or health centre taking part in the clinical trial);

(c) information to identify the sponsor and contact persons involved in the clinical trial;

(d) information to allow identification of the clinical trial, for example the clinical trial reference code;

(e) information linking the product to the participant, for example, the participant identification number;

(f) information to allow identification of the medicinal product, including—

(i) the common name of the active substance,

(ii) the strength and pharmaceutical form,

(iii) the contents by weight, volume or number of doses, and

(iv) the batch or code number;

(g) information related to the use of the medicinal product, including—

(i) instructions for use (which may be by reference to a patient information leaflet),

(ii) method or route of administration,

(iii) expiry date, and

(iv) any special storage precautions; and

(h) in the case of trials in which blinding occurs, the name of any comparator or placebo product used alongside the investigational medicinal product.

(2) Subject to paragraph (4), where the investigational medicinal product is an authorised medicinal product, it must be labelled either—

(a) in accordance with paragraph (1); or

(b) in accordance with Part 13 of the 2012 Regulations.

(3) Paragraph (4) applies to an investigational medicinal product which is—

(a) an authorised medicinal product to be exclusively administered in a hospital or health centre taking part in the clinical trial; or

(b) a radiopharmaceutical used for diagnostic purposes.

(4) Where paragraph (3) applies, the investigational medicinal product must be labelled with at least the following information—

(a) the words "for clinical trial use only”, or equivalent wording;

(b) information linking the product to the participant, for example, the participant identification number;

(c) information to allow identification of the medicinal product, including—

(i) the common name of the active substance,

(ii) the strength and pharmaceutical form,

(iii) the contents by weight, by volume or by number of doses, and

(iv) the batch or code number;

(d) information related to the use of the medicinal product (which may be by reference to a patient information leaflet);

(e) the expiry date; and

(f) any other information relating to the clinical trial or the product that the authorities, as defined in regulation 11 (interpretation of Part 3), may require by guidelines published under paragraph (8).

(5) The sponsor may request to disapply or vary any of the requirements of this regulation at the time of the application under regulation 16.

(6) If a request under paragraph (5) is agreed—

(a) the licensing authority must inform the sponsor by a notice in writing at the time of approval under regulation 18 or 18B; and

(b) the sponsor must record that decision and any conditions in the investigational medicinal product dossier.

(7) Where—

(a) the trial is a notifiable trial; and

(b) the request concerns an authorised medicinal product which is to be exclusively administered in a hospital or health centre taking part in the trial,

the request is to be treated as agreed if no notice is given in accordance with paragraph (6)(a).

(8) The licensing authority may publish guidance on labelling of investigational medicinal products, which may include guidance on how the labelling requirements are to be met in relation to products that are—

(a) radiopharmaceuticals used for diagnostic purposes;

(b) used exclusively in a hospital or health centre;

(c) provided in differently sized or differently assembled packs, for example blister packs and small packages.

(9) For the purposes of this regulation, a medicinal product is authorised if there is a UK marketing authorisation or Article 126a authorisation, each as defined in regulation 8(1) of the 2012 Regulations, in force for the product.

(10) This regulation is subject to regulation 46B (labelling of certain POC investigational medicinal products).

Labelling of non-investigational medicinal products

46A.—(1) Subject to paragraph (2), a non-investigational medicinal product must be labelled in accordance with the requirements set out in regulation 46, and any reference in that regulation to "investigational medicinal product" is to be construed as a reference to "non-investigational medicinal product" accordingly.

(2) Regulation 46(4) does not apply to a non-investigational medicinal product which falls within sub-paragraph (a) of regulation 46(3).

Labelling of certain POC investigational medicinal products

46B. Regulation 46 does not apply to a POC investigational medicinal product that is to be administered in its entirety immediately after manufacture.".

PART 10

Amendment to Part 8 (Enforcement and Related Provisions)

Amendment to regulation 48

33. In regulation 48 (infringement notices), for paragraph (4)(**a**) substitute—

"(4) This regulation applies to regulations 3A, 12(1) and (2), 13(1), 22(2) to (5), 25(1) and (2)(a), 27, 28(1) to (3), 29, 29A, 30(2), 31A to 35, 36(1), 36A, 36B, 42, 43(1) and (6), 45A, 46 and 46A.".

Amendment to regulation 49

34.—(1) Regulation 49 (offences) is amended as follows.

(2) In paragraph (1)(**b**)—

(a) after sub-paragraph (b) insert—

"(ba) regulation 22(2) to (5);

(bb) regulation 25(1) and (2)(a);

(bc) regulation 26(7)(a);";

(b) after sub-paragraph (ff) insert—

"(fg) regulation A32;";

(c) in sub-paragraph (l), at the end, omit "and";

(d) in sub-paragraph (m), for "(6)," substitute "(6); and";

(e) after sub-paragraph (m), insert—

"(n) regulation 45A,".

(3) In paragraphs (6) and (7), in each place where it occurs, for "subject" substitute "participant".

(4) After paragraph (7) insert—

"(8) Any sponsor who sells or supplies, or procures the sale or supply of, a non-investigational medicinal product—

(a) to a participant for the purposes of a clinical trial; or

(b) to a person for the purpose of administering the product to such a participant,

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

(9) Any person who sells or supplies, or procures the sale or supply of, a non-investigational medicinal product—

(**a**) Regulation 48(4) was amended by S.I. 2006/1928.
(**b**) Regulation 49(1) was amended by S.I. 2006/1928.

(a) to a participant for the purposes of a clinical trial; or

(b) to a person for the purpose of administering the product to such a participant,

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

Amendment to regulation 50

35. In regulation 50 (false or misleading information), in paragraph (1)—

(a) in sub-paragraph (b), at the end, omit "or";

(b) after sub-paragraph (c) insert—

"(d) notifying a modification of an important detail; or

(e) making a modification request,".

PART 11

Amendment to Part 9 (Miscellaneous Provisions)

Amendment to regulation 58

36. In regulation 58 (detailed guidance), in paragraph (c), for "substantial amendment to the clinical trial authorisation" substitute "substantial modification, as defined in regulation 11 (interpretation of Part 3),".

PART 12

Amendment to the Schedules

Amendment to Schedule 1

37.—(1) Schedule 1 (conditions and principles of good clinical practice and for the protection of clinical trial subjects) is amended as follows.

(2) In the heading, for "subjects" substitute "participants".

(3) In Part 1 (application and interpretation)—

(a) for "any subject", in each place where it occurs, substitute "any participant";

(b) for "that subject", in each place where it occurs, substitute "that participant";

(c) for "a subject", in each place where it occurs, substitute "a participant";

(d) in paragraph 1(7)(**a**)—

(i) for "the subject" substitute "the participant";

(ii) omit "or by an appeal panel appointed under Schedule 4";

(e) in paragraph 2, in the definition of "Declaration of Helsinki" omit ", as amended by the General Assembly of the Association in October 1975, October 1983, September 1989 and October 1996";

(f) in paragraph 3—

(i) in sub-paragraph (1)—

(**a**) Paragraph 1(7) of Schedule 1 was inserted by S.I. 2006/2984.

(aa) at the beginning, insert "Subject to sub-paragraph (3),";

(bb) in paragraph (b)(ii), for "given orally" substitute "communicated (whether by talking, using sign language or any other means);

(ii) after sub-paragraph (2), insert—

"(3) Where sub-paragraph (4) applies, the protocol for the clinical trial for which consent is given may make provision for simplified arrangements for obtaining and evidencing consent, which shall include—

(a) the reason for obtaining consent using simplified arrangements;

(b) the information to be provided to the participant, and the means of providing that information; and

(c) the means by which consent shall be evidenced.

(4) This sub-paragraph applies where—

(a) the investigational medicinal product or, if there is more than one, each of the investigational medicinal products, is authorised for use in the United Kingdom and is used in accordance with that authorisation;

(b) the investigational medicinal product or, if there is more than one, each of the investigational medicinal products, is given to the participant in the course of that participant's routine health care; and

(c) the participant receives no additional medication and undergoes no additional intervention or diagnostic procedure, solely for the purposes of the clinical trial.

(5) For the purposes of sub-paragraph (4)—

"intervention" includes complementary or alternative therapies, the taking of tissue samples, and requirements in relation to imaging and radiotherapy; and

"medication" includes nutritional products and alternative remedies.".

(4) For Part 2 (conditions and principles which apply to all clinical trials) substitute(**a**)—

"PART 2

CONDITIONS AND PRINCIPLES WHICH APPLY TO ALL CLINICAL TRIALS

1. Clinical trials must be conducted in accordance with the principles of good clinical practice set out in the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guideline for Good Clinical Practice, as amended from time to time(**b**).

2. Except where it would be a contravention of these Regulations, clinical trials must be conducted in accordance with the principles of the Declaration of Helsinki.

3. The investigator and sponsor must have regard to all relevant guidance with respect to commencing and conducting a clinical trial.

4. Provision must be made for insurance or indemnity to cover all liabilities of the investigator and sponsor which may arise in relation to the clinical trial.".

(**a**) Part 2 of Schedule 1 was substituted by S.I. 2006/1928.

(**b**) The Guideline can be found at https://ich.org/page/efficacy-guidelines. A printed version of the document can be made available on request by the Department of Health and Social Care, 39 Victoria Street, London SW1H 0EU.

(5) In Part 3 (conditions which apply in relation to an adult able to consent or who has given consent prior to the onset of incapacity), for "the subject", in each place where it occurs, substitute "the participant".

(6) In Part 5 (conditions and principles which apply in relation to an incapacitated adult)—

(a) for "the subject", in each place where it occurs, substitute "the participant";

(b) in paragraph 1, for "the subject's" substitute "the participant's";

(c) in paragraph 7, for "a subject" substitute "a participant".

Omission of Schedule 2

38. Omit Schedule 2 (additional provisions relating to ethics committees).

Amendment to Schedule 3

39.—(1) Schedule 3 (particulars and documents that must accompany an application for an ethics committee opinion, a request for authorisation, a notice of amendment and a notification of the conclusion of a trial) is amended as follows.

(2) In the heading, for "an application for an ethics committee opinion, a request for authorisation, a notice of amendment" substitute "a request for approval, a modification request".

(3) At the beginning of the Schedule insert—

"PART A1

REQUEST FOR APPROVAL

1. A completed application.

2. A statement or cover letter drawing attention to any features which are particular to the clinical trial, if required.

3. The protocol for the proposed trial describing the objective, design, methodology, statistical considerations, purpose and organisation of the clinical trial.

4. The investigator's brochure or equivalent document.

5. The following documents or, in each case, an explanation of why that document is not being provided—

(a) documentation relating to compliance with the principles and guidelines of good manufacturing practice, where applicable;

(b) a dossier providing the following information or cross-referring to the document in paragraph 4 if it contains such information—

(i) details of the quality of any investigational medicinal product or non-investigational medicinal product,

(ii) details of the manufacture and control of the investigational medicinal product, and

(iii) data from non-clinical studies and from clinical use of the product;

(c) a copy of the scientific advice of the licensing authority, or of any third country, with regard to the clinical trial;

(d) a description of the content of the labelling;

(e) all information given to the participants, or their legal representatives, before their decision to participate or abstain from participation in the clinical trial;

(f) proof of insurance, a guarantee, or any other similar arrangement, where applicable;

(g) responses to areas for discussion raised by the Commission on Human Medicines, where applicable.".

(4) Omit Parts 1 (application for ethics committee opinion) and 2 (request for authorisation).

(5) In Part 3 (notice of amendment)—

(a) in the heading to Part 3, for "notice of amendment" substitute "modification request";

(b) omit paragraph 1;

(c) in paragraph 2(b)(**a**), for "on the European database referred to in Article 11 of the Directive" substitute "by the authorities";

(d) in paragraph 3, for "amendment" substitute "modification";

(e) in paragraph 4, for "amendment" substitute "modification, and if more than one modification, a statement for each modification";

(f) in paragraph 5(b), for "authorisation or the application for an ethics committee opinion" substitute "approval";

(g) in paragraph 6—

(i) in sub-paragraph (a), for "amendment" substitute "modification or modifications";

(ii) in sub-paragraph (b), for "assessment referred to in paragraph 11(2) of Part 2" substitute "summary assessment of the potential risks and benefits of using the product in the proposed trial".

(6) In Part 4 (notification of conclusion of a clinical trial)—

(a) omit paragraph 1;

(b) in paragraph 2(b)(**b**), for "on the European database referred to in Article 11 of the Directive" substitute "by the authorities";

(c) in paragraph 4—

(i) in sub-paragraph (2)—

(aa) for "site" substitute "location";

(bb) for "sites" substitute "locations";

(ii) for sub-paragraph (3), substitute—

"(3) If the trial was conducted at any trial locations outside the United Kingdom, a statement as to whether the trial has ended at any of those locations and—

(a) if ended, the date on which the trial ended; or

(b) if not ended, the anticipated end date of the trial.".

Amendment to Schedule 4

40.—(1) Schedule 4 (appeal against unfavourable ethics committee opinion) is amended as follows.

(2) In paragraph 1—

(**a**) Paragraph 2 was amended by S.I. 2006/1928.
(**b**) Paragraph 2 was amended by S.I. 2006/1928.

(a) in sub-paragraph (1)(**a**)—

(i) for "regulation 16(3), 4(b) or (7)" substitute "regulation 24(3)";

(ii) for "chief investigator" substitute "sponsor";

(iii) omit paragraph (b) and the "or" preceding it;

(b) in sub-paragraph (2) omit—

(i) "Subject to sub-paragraph (4),";

(ii) "or appoint a panel";

(c) in sub-paragraph (3)—

(i) omit "or appoint a panel";

(ii) for "chief investigator" substitute "sponsor";

(d) omit sub-paragraph (4).

(3) In paragraph 2—

(a) in sub-paragraph (a)—

(i) for "ethics committee which gave the unfavourable opinion" substitute "Authority";

(ii) for "chief investigator" substitute "sponsor";

(iii) at the end, omit "and";

(b) in sub-paragraph (b), for "regulation 15," substitute "regulation 17; and";

(c) after sub-paragraph (b), insert—

"(c) that committee shall within 30 days beginning with the day on which the application is sent to the committee under paragraph (a), or such extended period as the Authority may in any particular case allow, either confirm the opinion or give a favourable opinion.".

(4) Omit paragraphs 3 to 6.

Amendment to Schedule 5

41.—(1) Schedule 5 (procedural provisions relating to the refusal or amendment of, or imposition of conditions relating to, clinical trial authorisations and the suspension or termination of clinical trials) is amended as follows.

(2) In paragraph 1(**b**), for "regulation 26(1)" substitute "regulation 23(2)".

(3) In paragraph 2—

(a) in sub-paragraph (1)—

(i) in the opening words, for "an amendment to the clinical trial authorisation" substitute "a substantial modification";

(ii) in paragraph (a), for "amendment" substitute "modification";

(iii) in paragraph (b), for "amendment to the clinical trial authorisation" substitute "modification";

(b) in sub-paragraph (2), for "notice of amendment to a clinical trial authorisation" substitute "valid modification request".

(**a**) Paragraph 1(1) was amended by S.I. 2006/1928.
(**b**) Paragraph 1 was substituted by S.I. 2005/2754.

Amendment to Schedule 7

42.—(1) Schedule 7 (standard provisions for manufacturing authorisations) is amended as follows.

(2) In Part 1 (interpretation)—

(a) before the definition of "Commission Directive 2003/94/EC" insert—

> ""Commission Delegated Regulation 2017/1569", in relation to the holder of an authorisation in Northern Ireland, means Commission Delegated Regulation (EU) 2017/1569 of 23 May 2017 supplementing Regulation (EU) No 536/2014 of the European Parliament and of the Council by specifying principles of and the guidelines for good manufacturing practice for investigational medicinal products for human use and arrangements for inspections, as that Regulation has effect in EU law(**a**);";

(b) in the definition of "Commission Directive 2003/94/EC"(**b**) omit paragraph (b).

(3) In Part 2 (provisions which may be incorporated in an authorisation relating to the manufacture or assembly of investigational medicinal products)—

(a) in paragraph 3, after "Commission Directive 2003/94/EC" insert "in respect of Great Britain, or Article 10(1) of Commission Delegated Regulation 2017/1569 in respect of Northern Ireland,";

(b) in paragraph 4, after "Commission Directive 2003/94/EC" insert "in respect of Great Britain, or Article 10(2) of Commission Delegated Regulation 2017/1569 in respect of Northern Ireland,";

(c) in paragraph 7(a), after "Commission Directive 2003/94/EC" insert "in respect of Great Britain or Article 8 of Commission Delegated Regulation 2017/1569 in respect of Northern Ireland";

(d) in paragraph 8, after "Commission Directive 2003/94/EC" insert "in respect of Great Britain or Article 11 of Commission Delegated Regulation 2017/1569 in respect of Northern Ireland".

(4) In Part 3 (provisions which may be incorporated in an authorisation relating to the importation of investigational medicinal products)—

(a) in paragraph 2, after "Commission Directive 2003/94/EC" insert "in respect of Great Britain, or Article 10(2) of Commission Delegated Regulation 2017/1569 in respect of Northern Ireland,";

(b) in paragraph 5(a), after "Commission Directive 2003/94/EC" insert "in respect of Great Britain or Article 8 of Commission Delegated Regulation 2017/1569 in respect of Northern Ireland".

PART 13

Consequential provisions

Amendment of the Medicines (Products for Human Use) (Fees) Regulations 2016

43.—(1) The Medicines (Products for Human Use) (Fees) Regulations 2016(**c**) are amended as follows.

(2) In regulation 20—

(**a**) OJ No. L 238, 16.09.17, p. 12-21.
(**b**) The definition of "Commission Directive 2003/94/EC" was inserted by S.I. 2019/744.
(**c**) S.I. 2016/190.

(a) in the heading, for "amendments" substitute "modifications";

(b) in paragraph (1)—

(i) for "valid notice of amendment under regulation 24 (amendments" substitute "modification request under regulation 22 (modifications";

(ii) for "paragraphs 10 or 11 of Part 2 of Schedule 3 (request for authorisation)" substitute "paragraphs 2 or 5(a) of Part A1 of Schedule 3 (request for approval)".

(3) In Schedule 2, in Part 4, in paragraph 49, for "notice of amendment relating to an amendment" substitute "modification request relating to a modification".

PART 14

Transitional provisions

Amendment to regulation 56

44. In regulation 56 (transitional provisions), for "Schedules 12 and 13" substitute "Schedules 12, 13 and 14".

Insertion of Schedule 14

45. After Schedule 13 (transitional provisions relating to EU Exit) insert—

"SCHEDULE 14

Regulation 56

Transitional provisions relating to the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025

Interpretation

1.—(1) In this Schedule—

"end of trial date" is the date of the conclusion of the trial that is specified in the protocol of a clinical trial and which, in the case of a clinical trial conducted in other countries as well as the United Kingdom, is the end of the date of the trial in all the participating countries;

"the new rules" means these Regulations as in force on and after the relevant day;

"new rules clinical trial" means a clinical trial which is not an old rules clinical trial;

"old committee" means an ethics committee recognised under the old rules that has been abolished or has ceased to operate as an ethics committee for the purposes of these Regulations;

"the old rules" means these Regulations as in force immediately before the relevant day;

"old rules clinical trial" is to be construed in accordance with paragraph 2(1)(a);

"the relevant day" means the day on which this Schedule comes into force.

(2) Where, by virtue of this Schedule, the old rules continue to apply, regulation 2 of the old rules applies to the interpretation of the old rules, except in so far as it is necessary for regulation 2 of the new rules to apply to their interpretation in order to give effect to

a provision of this Schedule (for example, because a new committee is performing functions of an old committee).

(3) For purposes of this Schedule, "sponsor", in the context of the old rules, has the meaning given in regulation 3 of the old rules.

(4) Regulation 53 of the new rules applies to both the new rules and the old rules.

Application of the old rules to the authorisation etc of existing clinical trials

2.—(1) If a request for authorisation to conduct a clinical trial has been received by the licensing authority before the relevant day, or an application for an ethics committee opinion in relation to a clinical trial has been received before the relevant day, Part 3 of the old rules including its related Schedules, rather than Part 3 of the new rules including its related Schedules, applies in respect of—

(a) that trial (an "old rules clinical trial"), including—

(i) the authorisation of that trial and any amended requests for authorisation,

(ii) the giving of an ethics committee opinion in relation to that trial, or a review or appeal relating to such an opinion, and

(iii) information sharing and the publication of information; and

(b) the supply of any investigational medicinal product for a purpose related to that trial,

subject to the following sub-paragraphs.

(2) An ethics committee established under regulation 6(1) of the new rules ("a new committee") may, with the agreement of the Authority, take over and perform any function under the old rules of an ethics committee recognised under the old rules.

(3) Where a new committee performs functions of an ethics committee under the old rules pursuant to this Schedule, the new committee may, with the agreement of the Authority, regulate its proceedings and business in relation to old rules clinical trials in a manner that is consistent, subject to any necessary modifications, with how it regulates its proceedings and business in relation to new rules clinical trials, provided that there is no detriment to—

(a) the sponsor of an old rules clinical trial; or

(b) achieving the outcome of performing the functions of an old committee under the old rules.

(4) Any recognition of an ethics committee under regulation 7 of the old rules may, with the agreement of the Authority, continue in effect notwithstanding the repeal of regulation 7, but—

(a) solely for the purposes of that committee performing the functions under the old rules of an ethics committee, and Part 2 of the old rules and its related Schedules continue to apply for that purpose; and

(b) subject to any conditions or limitations imposed by the Authority.

(5) In a case where the licensing authority or ethics committee receives a valid notice of amendment to a clinical trials authorisation from a sponsor before the relevant day, Part 3 of the old rules including its related Schedules, rather than Part 3 of the new rules including its related Schedules, applies in respect of that notice of amendment, including—

(a) the giving of a written notice by the licensing authority, and the review of any amended notice of amendment or any appeal relating to such written notice; and

(b) the giving of an opinion by an ethics committee, and the review of any amended notice of amendment,

but no notice of amendment received on or after the relevant day pursuant to the old rules is to be treated as valid.

(6) In a case where the licensing authority serves a notice on a sponsor pursuant to regulation 23 of the old rules before the relevant day, the old rules continue to apply for the purposes of the consideration of representations relating to, and any making of an amendment as a consequence of, that notice.

(7) As regards the modifications to an old rules clinical trial authorisation on and after the relevant day, except in a case to which sub-paragraph (5) or (6) applies, that modification (including a modification that would have been an amendment by the sponsor under regulation 24 of the old rules) is to be made in accordance with and subject to the requirements of the new rules.

(8) Regulation 25 of the new rules applies to old rules clinical trials as it does to new rules clinical trials (including automatic deferrals in regulation 25(10)), except that—

(a) it does not apply to an old rules clinical trial that has an end of trial date that is before the relevant day; and

(b) in the case of an old rules trial that has been approved but its end of trial date is on or after the relevant day—

(i) where, before the relevant day the first individual has not yet been recruited to be a participant in that trial, regulation 25(1) applies as if the reference to approval of the trial were a reference to the relevant day,

(ii) where, before the relevant day the first individual has been recruited to be a participant in that trial, regulation 25(1) applies as if the reference to approval of the trial were a reference to the relevant day and sub-paragraph (a) were omitted, and

(iii) regulation 25(2)(b) does not apply.

Application of Good Clinical Practice to old rules clinical trials

3.—(1) Part 4 of the new rules applies in respect of old rules clinical trials as it does in respect of new rules clinical trials, subject to the following sub-paragraph.

(2) Regulation 31A(7) of the old rules, rather than regulation 31A(7) of the new rules, applies in respect of old rules clinical trials.

Pharmacovigilance in respect of old rules clinical trials

4.—(1) Part 5 of the new rules applies in respect of old rules clinical trials as it does in respect of new rules clinical trials, subject to the following sub-paragraphs.

(2) The sponsor of an old rules clinical trial may elect that Part 5 of the old rules is to apply, temporarily, in respect of the clinical trial, rather than Part 5 of the new rules, provided that the licensing authority has received notification of that election—

(a) unless paragraph (b) applies, within the period of 60 days beginning with the day after the relevant day;

(b) where, in order to comply with the old rules, a reporting or notification obligation under the old rules needs to be discharged before that 60 day period expires, when or before that reporting or notification obligation is discharged (which must

be on or before the latest day on which that reporting notification needs to be discharged in order to comply with the old rules).

(3) Where a sponsor of an old rules clinical trial has made a valid election pursuant to sub-paragraph (2), once the sponsor has discharged their obligations under regulation 35(1) of the old rules, or the period during which the sponsor is required to do so has expired, whichever is the sooner, the election ceases to have effect.

Manufacture and importation of investigational medicinal products used in old rules clinical trials

5.—(1) Part 6 of the new rules, including its related Schedules, applies in respect of the manufacture and importation of investigational medicinal products used in old rules clinical trials as it does in respect of the manufacture and importation of investigational medicinal products used in new rules clinical trials, subject to the following sub-paragraph.

(2) Regulation 37A does not apply to radiopharmaceuticals used for diagnostic purposes.

Labelling of investigational medicinal products used in old rules clinical trials

6. Part 7 of the old rules applies in respect of investigational medicinal products used in old rules clinical trials, if those products are manufactured before the relevant day, and in these circumstances investigational medicinal products—

(a) manufactured before the relevant day; and

(b) labelled in accordance with regulation 46 of the old rules,

may continue to be used in a clinical trial for which they are for use, subject to complying with Part 7 of the old rules.

Enforcement etc

7.—(1) Where the old rules continue to apply by virtue of this Schedule, with or without modifications, Part 8 of the old rules applies to the enforcement of those old rules, subject to the following sub-paragraph.

(2) Where, by virtue of this Schedule, a provision (whether of the old rules or the new rules) applies with modifications, for the purposes of securing the effective enforcement of that provision as so modified, an enforcement authority may include those modifications in an infringement notice.".

Signed by authority of the Secretary of State for Health and Social Care

Merron
Parliamentary Under Secretary of State
28th April 2025 Department of Health and Social Care

Sealed with the Official Seal of the Department of Health in Northern Ireland



Cathy Harrison
24th April 2025 A senior officer of the Department of Health in Northern Ireland

EXPLANATORY NOTE

(This note is not part of the Regulations)

These Regulations amend the Medicines for Human Use (Clinical Trials) Regulations 2004 ("the 2004 Regulations") which implement Directive 2001/20/EC 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 in humans.

Following withdrawal of the UK from the European Union, these Regulations are made in exercise of the powers conferred by sections 2(1), 5(1)(a) to (e), 6(1)(b) and 43 of the Medicines and Medical Devices Act 2021, in respect of clinical trials in the United Kingdom.

These Regulations make provision for the following matters:

(a) Part 3 amends the provisions on the operation and constitution of the ethics committee, which are contained in Part 2 of the 2004 Regulations.

(b) Part 4, which amends Part 3 of the 2004 Regulations, revises the approval procedure for clinical trials, combining the separate applications for regulatory authorisation and ethics committee opinion into one application route, leading to a co-ordinated review and a single UK decision. For trials considered lower risk, this will be notified and can be given automatic regulatory authorisation. The combined procedure is extended to substantial amendments to the trial approval, and references to amendments are replaced with references to modifications. This Part also introduces transparency requirements, which are to require registration of the trial in a public register, to publish a summary of the trial results, and to share those results with the participants.

(c) Part 5 amends the provisions on the principles and conditions of good clinical practice by reference to the ICH guideline and makes clear, in applying those principles and conditions that the functions of the sponsor include those in relation to the development and maintenance of trial specific computerised systems.

(d) Part 6 makes a number of changes to Part 5 of the 2004 Regulations, which concerns the pharmacovigilance requirements that apply to clinical trials under Part 5, in particular to allow aggregate reporting, and to impose specific requirements with respect to record keeping and the content of the annual report on the safety of trials.

(e) Part 7 amends Part 6 of the 2004 Regulations on manufacturing and importation, and provides for an exemption from the need, in certain circumstances, for a manufacturing authorisation in respect of radiopharmaceuticals used for diagnostic purposes.

(f) Part 8, which inserts a new Part 6A to the 2004 Regulations, makes a new provision concerning medicinal products which are used in the trial, but which are not being tested.

(g) Part 9, which amends Part 7 of the 2004 Regulations, makes similar provision to the EU Clinical Trials Regulation in respect of labelling of investigational and non-investigational medicinal products.

(h) Part 10 makes consequential changes to Part 8 of the 2004 Regulations relating to enforcement of the Regulations and extends the power of the licensing authority to issue infringement notices to facilitate compliance with the Regulations.

(i) Part 11 amends all the Schedules that are related to the changes made to Parts 2 to 4 of the 2004 Regulations.

(j) Part 12 inserts a new Schedule 14, which makes transitional provisions in relation to existing authorisations and applications.

References throughout the Regulations to a clinical trial subject are replaced with references to a participant; and similarly, references to a trial site, are replaced with references to a trial location.

A full impact assessment has not been produced for this instrument as no, or no significant, impact on the private, voluntary or public sector is foreseen. A de minimis assessment is available from the Department of Health and Social Care, 39 Victoria Street, London, SW1H 0EU and is published with the explanatory memorandum alongside this instrument at www.legislation.gov.uk.

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