STATUTORY INSTRUMENTS

2019 No. 791

The Medical Devices (Amendment etc.) (EU Exit) Regulations 2019

PART 4

New Schedules to the 2002 Regulations

12. After Schedule 2 to the 2002 Regulations insert—

"SCHEDULE 2A Regulation 1A

Modification of Annexes to Directives 90/385, 93/42, 98/79

PART 1

Modification of Annexes to Directive 90/385

1. The Annexes to Directive 90/385 are modified so that they read as if amended by paragraphs 2 to 8.

2. In Annex 1 for Section 10 substitute—

"**10.** Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product as defined in regulation 2 of the Human Medicines Regulations 2012, and which is liable to act upon the body with an action ancillary to that of the device, the quality, safety and usefulness of the substance must be verified by analogy with the methods specified in Annex I to Directive 2001/83/EC as modified by Schedule 8B to the Human Medicines Regulations 2012(**1**).

Where changes are made to an ancillary substance incorporated in a device, in particular related to its manufacturing process, the notified body shall be informed of the changes.".

3. In Annex 2—

(a) in Section 2, omit "established within the Community";

(b) in Section 3.3, for the first sentence substitute—

"The quality system shall be audited by the notified body to determine whether it meets the requirements referred to in Section 3.2.";

(c) of Section 3.4, in the second paragraph, for the first sentence substitute—

"The proposed modifications shall be evaluated by the notified body so as to verify whether the quality system so modified would still meet the requirements referred to in Section 3.2.";

(**1**) Schedule 8B is inserted by the Human Medicines (Amendment etc.) (EU Exit) Regulations 2019.

(d) omit Section 4.3;

(e) in Section 6.1, after "national authorities" insert "and the Secretary of State";

(f) for Section 6.2, substitute—

"**6.2.** On request, a UK notified body shall make available to other notified bodies and to the Secretary of State all relevant information relating to the withdrawal of its approval for a quality system.";

(g) in Section 7, for the words "issued by" to the end, substitute—

"a laboratory designated for the purpose by an EU Member State in accordance with Article 114(2) of Directive 2001/83/EC or a laboratory provided or arranged in accordance with section 57(1)(d) of the Health and Social Care Act 2012(**2**).".

4. In Annex 3—

(a) in Section 2, omit "established in the Community";

(b) omit Sections 4 and 5;

(c) for Section 7.1 substitute—

"**7.1.** On request, a UK notified body shall make available to other notified bodies (including other UK notified bodies) and to the Secretary of State all relevant information on EC type-examination certificates and addenda to those certificates.";

(d) for Section 7.2 substitute—

"**7.2.** A UK notified body must cooperate with other notified bodies (including other UK notified bodies) with regard to making available copies of the EC type examination certificates or addenda to those certificates but, as regards copies of annexes to the certificates, must only make those available to other notified bodies with the consent of the manufacturer.".

5. In Annex 4—

(a) in Sections 1 and 2, omit "established within the Community" in each place where those words appear;

(b) in Section 5, for the first sentence substitute—

"A product must have had, in respect of it, the appropriate examinations and tests carried out by a notified body to check the conformity of the product to the requirements of this Directive by examination and testing of products on a statistical basis as specified in Section 6.";

(c) in Section 6.4, for the first two paragraphs substitute—

"Where the notified body has drawn up a written certificate of conformity in relation to a batch, all products in that batch to which that body has affixed, or caused to be affixed, an identification number may be placed on the market.";

(d) in Section 7, for the words from "issued by" to the end, substitute "a laboratory designated for the purpose by an EU Member State in accordance with Article 114(2) of Directive 2001/83/EC or a laboratory provided or arranged in accordance with section 57(1)(d) of the Health and Social Care Act 2012.".

6. In Annex 5—

(a) in Section 2, in the second paragraph, omit "established within the Community";

(b) in Section 3.3, for the first sentence substitute—

(**2**) 2012 c. 7.

"The quality system shall be audited by the notified body to determine whether it meets the requirements referred to in Section 3.2.";

(c) in Section 3.4, for the first sentence of the second paragraph—

"The proposed modifications shall be evaluated by the notified body so as to verify whether the quality system modified would meet the requirements referred to in Section 3.2;"

7. In Annex 6, in Section 1, omit "established within the Community".

8. In Annex 8—

(a) in the title for "when designating" substitute "by";

(b) in Section 6, omit the words from "unless liability" to the end of that Section.

PART 2

Modification of Annexes to Directive 93/42

9. The Annexes to Directive 93/42 are modified so that they read as if amended by paragraphs 10 to 19.

10. In Annex I—

(a) for Section 7.4 substitute—

"**7.4.** Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product as defined in regulation 2 of the Human Medicines Regulations, and which is liable to act upon the body with action ancillary to that of the device, the quality, safety and usefulness of the substance must be verified by analogy with the methods specified in Annex I to Directive 2001/83/EC as modified by the Human Medicines Regulations;

Where changes are made to an ancillary substance incorporated in a device, in particular related to its manufacturing process, the notified body shall be informed of the changes.".

(b) in Section 8.2, omit the second paragraph;

(c) in Section 13.3 in point (f), omit the second sentence.

11. In Annex II—

(a) in Section 1 omit "Community";

(b) in Section 3.3, for the first sentence substitute—

"The quality system must be audited by the notified body to determine whether it meets the requirements referred to in Section 3.2.";

(c) in Section 3.4, for the second sentence substitute—

"The proposed changes must be assessed by the notified body so as to verify whether the quality system after these changes would still meet the requirements referred to in Section 3.2.";

(d) omit Section 4.3;

(e) in Section 6.1, after "national authorities" insert "and the Secretary of State";

(f) in Section 8, for the words "issued by" to the end of that Section, substitute "a laboratory designated for the purpose by an EU Member State in accordance with Article 114(2)

of Directive 2001/83/EC or a laboratory provided or arranged in accordance with section 57(1)(d) of the Health and Social Care Act 2012.".

12. In Annex III—

(a) in Section 2, in the second indent, for the last line substitute, "The applicant shall provide samples as necessary at the request of the notified body,";

(b) omit Sections 4 to 5;

(c) for Section 7.2 substitute—

"**7.2.** A UK notified body must cooperate with other notified bodies (including other UK notified bodies) with regard to making available copies of the EC type examination certificates or addenda to those certificates but, as regards copies of annexes to the certificates, must only make those available to other notified bodies with the consent of the manufacturer.".

13. In Annex IV—

(a) omit Sections 4 to 5.2;

(b) omit Sections 6.2 and 6.3;

(c) in Section 6.4, for the first two paragraphs, substitute—

"Where the notified body has drawn up a written certificate of conformity in relation to a batch, all products in that batch to which that body has affixed, or caused to be affixed, an identification number may be placed on the market.";

(d) in Section 7, after "national authorities" insert "and the Secretary of State";

(e) in Section 9, from the words "issued by" to the end of that Section, substitute "a laboratory designated for the purpose by an EU Member State in accordance with Article 114(2) of Directive 2001/83/EC or a laboratory provided or arranged in accordance with section 57(1)(d) of the Health and Social Care Act 2012.".

14. In Annex V—

(a) in Section 1, omit "Community";

(b) in Section 3.3 for the first sentence substitute—

"The quality system must be audited by the notified body to determine whether it meets the requirements referred to in Section 3.2.";

(c) in Section 3.4, for the last two paragraphs, substitute—

"The proposed changes must be evaluated by the notified body so as to verify whether the quality system after these changes would still meet the requirements referred to in Section 3.2.";

(d) in Section 5.1, after "national authorities", insert "and the Secretary of State";

(e) omit Section 6.4.

(f) in Section 7, for the words from "issued by" to the end of that Section, substitute—

"a laboratory designated for the purpose by an EU Member State in accordance with Article 114(2) of Directive 2001/83/EC or a laboratory provided or arranged in accordance with section 57(1)(d) of the Health and Social Care Act 2012.".

15. In Annex VI—

(a) in Section 3.3, for the first sentence substitute—

"The quality system must be audited by the notified body to determine whether it meets the requirements referred to in Section 3.2.";

(b) in Section 3.4, for the second paragraph substitute—

"The proposed changes must be assessed by the notified body so as to verify whether the quality system after these changes would still meet the requirements referred to in Section 3.2."

(c) in Section 5.1, after "national authorities", insert "and the Secretary of State".

16. In Annex VII—

(a) in Section 2, after "national authorities", insert "and the Secretary of State";

(b) in Section 4, after "competent authorities", insert "and the Secretary of State";

(c) in Section 5, omit "and the intervention by the notified body.".

17. In Annex VIII, in Section 3 after "national authorities", insert "and the Secretary of State".

18. In Annex X, in Section 2.3.5, after "competent authorities of the Member States", insert "and the Secretary of State".

19. In Annex XI—

(a) in the title, for "for the designation of" substitute "by";

(b) in Section 2, for "national authorities" substitute "the Secretary of State";

(c) in Section 6, omit the words from "unless liability" to the end of that Section.

PART 3

Modification of Annexes to Directive 98/79

20. The Annexes to Directive 98/79 are modified so that they read as if amended by paragraphs 21 to 27.

21. In Annex I—

(a) in Section 8.1, omit the sixth paragraph;

(b) in Section 8.4, in point (a), after "distribution in the Community" insert "or the United Kingdom".

22. In Annex III—

(a) in Section 5, after "competent authorities", insert "and the Secretary of State";

(b) omit Section 6.2;

23. In Annex IV—

(a) in Section 3.3 for the first sentence substitute—

"The quality system must be audited by the notified body to determine whether it meets the requirements referred to in Section 3.2.";

(b) in Section 3.4, in the second paragraph, for the first sentence , substitute—

"The proposed changes must be assessed by the notified body so as to verify whether the quality system after these changes would meet the requirements referred to in Section 3.2.";

(c) omit Section 4.3.

24. In Annex V—

(a) in Section 2, in the second paragraph, at the end of the second indent, omit ".The notified body may request other samples as necessary";

(b) omit Sections 4 and 5;

(c) for Section 7 substitute—

"A UK notified body must cooperate with other notified bodies (including other UK notified bodies) with regard to making available copies of the EC type examination certificates or addenda to those certificates but, as regards copies of annexes to the certificates, must only make those available to other notified bodies with the consent of the manufacturer.".

25. In Annex VI—

(a) omit Sections 4 and 5;

(b) omit Sections 6.2 and 6.3;

(c) for the first two paragraphs of Section 6.4, substitute—

"Where the notified body has drawn up a written certificate of conformity in relation to a batch, all products in that batch to which that body has affixed, or caused to be affixed, an identification number may be placed on the market.".

26. In Annex VII—

(a) in Section 3.3 for the first sentence substitute—

"The quality system must be audited by the notified body to determine whether it meets the requirements referred to in Section 3.2.";

(b) for the second paragraph of Section 3.4, substitute—

"The proposed changes must be assessed by the notified body so as to verify whether the quality system after these changes would meet the requirements referred to in Section 3.2.".

27. In Annex IX—

(a) in the heading, omit the words "the designation of";

(b) in Section 2, for "national authorities" substitute "the Secretary of State";

(c) in Section 6, omit the words from "unless liability" to the end of that Section.

SCHEDULE 3

Regulation 1A

General safety and performance requirements for general medical devices

PART 1

General requirements

1. Devices must—

(a) achieve the performance intended by their manufacturer;

(b) be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose;

(c) be safe and effective and not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed

against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art.

2. The requirement in this Schedule to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio.

3.—(1) Manufacturers must establish, implement, document and maintain a risk management system.

(2) Risk management is to be understood as a continuous iterative process throughout the entire lifecycle of a device, which requires regular systematic updating and, in carrying out risk management, manufacturers must—

(a) establish and document a risk management plan for each device;

(b) identify and analyse the known and foreseeable hazards associated with each device;

(c) estimate and evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse;

(d) eliminate or control the risks referred to in sub-paragraph (c) in accordance with the requirements of paragraph 4;

(e) evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, benefit-risk ratio and risk acceptability;

(f) based on the evaluation of the impact of the information referred to in paragraph (e), if necessary amend control measures in line with the requirements of paragraph 4.

4.—(1) Risk control measures adopted by manufacturers for the design and manufacture of the devices must conform to safety principles, taking account of the generally acknowledged state of the art.

(2) To reduce risks, manufacturers must manage risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable.

(3) In selecting the most appropriate solutions, manufacturers must, in the following order of priority—

(a) eliminate or reduce risks as far as possible through safe design and manufacture;

(b) where appropriate, take adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated; and

(c) provide information for safety (warnings, precautions, contra-indications) and, where appropriate, training to users;

(d) inform users of any residual risks.

5. In eliminating or reducing risks related to use error, the manufacturer must—

(a) reduce as far as possible the risks related to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety);

(b) give consideration to the technical knowledge, experience, education, training and use environment, where applicable, and the medical and physical conditions of intended users (design for lay, professional, disabled or other users).

6. The characteristics and performance of a device must not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the

device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.

7. Devices must be designed, manufactured and packaged in such a way that their characteristics and performance during their intended use are not adversely affected during transport and storage, for example, through fluctuations of temperature and humidity, taking account of the instructions and information provided by the manufacturer.

8. All known and foreseeable risks, and any undesirable side-effects, must be minimised and be acceptable when weighed against the evaluated benefits to the patient or user arising from the achieved performance of the device during normal conditions of use.

9. For the devices referred to in Schedule 16, the general safety requirements set out in paragraphs 1 and 8 must be understood to mean that the device, when used under the conditions and for the purposes intended, does not present a risk at all or presents a risk that is no more than the maximum acceptable risk related to the product's use which is consistent with a high level of protection for the safety and health of persons.

PART 2

Requirements regarding design and manufacture

Chemical, physical and biological properties

10.—(1) Devices must be designed and manufactured in such a way as to ensure that the characteristics and performance requirements referred to in paragraphs 1 to 9 are fulfilled.

(2) Particular attention must be paid to—

(a) the choice of materials and substances used, particularly as regards toxicity and, where relevant, flammability;

(b) the compatibility between the materials and substances used and biological tissues, cells and body fluids, taking account of the intended purpose of the device and, where relevant, absorption, distribution, metabolism and excretion;

(c) the compatibility between the different parts of a device which consists of more than one implantable part;

(d) the impact of processes on material properties;

(e) where appropriate, the results of biophysical or modelling research the validity of which has been demonstrated beforehand;

(f) the mechanical properties of the materials used, reflecting, where appropriate, matters such as strength, ductility, fracture resistance, wear resistance and fatigue resistance;

(g) surface properties;

(h) the confirmation that the device meets any defined chemical or physical specifications.

(3) Devices must be designed, manufactured and packaged in such a way as to minimise the risk posed by contaminants and residues to—

(a) patients, taking account of the intended purpose of the device;

(b) persons involved in the transport, storage and use of the device,

and particular attention must be paid to tissues exposed to those contaminants and residues and to the duration and frequency of exposure.

(4) Devices must be designed and manufactured in such a way that they can be used safely with the materials and substances, including gases, with which they enter into contact during their intended use.

(5) If the devices are intended to administer medicinal products they must—

(a) be designed and manufactured in such a way as to be compatible with the medicinal products concerned in accordance with the provisions and restrictions governing those medicinal products;

(b) ensure that the performance of both the medicinal products and of the devices is maintained in accordance with their respective indications and intended use.

Substances

Design and manufacture of devices

(6) Devices must be designed and manufactured in such a way as to reduce, as far as possible, the risks posed by substances or particles, including wear debris, degradation products and processing residues that may be released from the device.

(7) Devices, parts of those devices or materials used in those devices listed in sub-paragraph (8) may only contain the following substances in a concentration that is above 0.1% weight where that is justified in accordance with sub-paragraph (9)—

(a) substances which are carcinogenic, mutagenic or toxic to reproduction ('CMR'), of category 1A or 1B, and on the UK mandatory classification and labelling list established and maintained in accordance with Article 38A(**3**) of Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006; or

(b) substances having endocrine-disrupting properties for which there is scientific evidence of probable serious effects to human health and which are identified in accordance with—

(i) the procedure set out in Article 59 of Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC; or

(ii) Commission Delegated Regulation (EU) 2017/2100 of 4 September 2017 setting out the scientific criteria for the determination of endocrine-disrupting properties pursuant to Regulation (EU) 528/2012 of the European Parliament and Council.

(8) The devices (or parts or materials) to which sub-paragraph (7) relates are devices which—

(a) are invasive and come into direct contact with the human body;

(b) administer or re-administer medicines, body liquids or other substances, including gases, to the body; or

(c) transport or store medicines, body fluids or substances, including gases, to be administered or re-administered to the body.

(9) The justification for the presence of the substances listed in sub-paragraph (7) must be based upon—

(**3**) Article 38A is inserted into Regulation (EC) No 1272/2008 by the Chemicals (Health and Safety) and Genetically modified Organisms (Contained Use) (Amendment etc.) (EU Exit) Regulations 2019.

(a) an analysis and estimation of potential patient or user exposure to the substance;

(b) an analysis of possible alternative substances, materials or designs, including, where available, information about independent research, peer-reviewed studies, scientific opinions from relevant scientific committees and an analysis of the availability of such alternatives;

(c) arguments as to why possible substance or material substitutes, if available, or design changes, if feasible, are inappropriate in relation to maintaining the functionality, performance and the benefit-risk ratios of the product; including, where relevant having regard to the intended use of the device, taking account of the vulnerability to such substances or materials of particular patient groups including children and pregnant or breastfeeding women;

(d) where applicable and available, the latest scientific guidelines relating to the risks and benefits (including the availability of alterative substances, materials, designs or treatments) of phthalates and other CMR and endocrine-disrupting substances.

Labelling

(10) Where the devices (parts or materials) referred to in sub-paragraph (7) contain the substances in paragraph (a) and (b) of sub-paragraph (7) in a concentration above 0.1% weight by weight (w/w), the presence of those substances must—

(a) be labelled on the device itself or on the packaging for each unit or, where appropriate, on the sales packaging, with the list of such substances;

(b) if the intended use of such devices includes treatment of particular patient groups (including children or pregnant or breastfeeding women) who are particularly vulnerable to those substances, be contained in information on residual risks for those patient groups and, if applicable, in appropriate precautionary measures in the instructions for use.

(11) Devices must be designed and manufactured in such a way as to reduce, as far as possible, the risks posed by the unintentional ingress of substances into the device, taking into account the device and the nature of the environment in which it is intended to be used.

(12) Unless they come into contact with intact skin only, devices must be designed and manufactured in such a way as to reduce, as far as possible, the risks linked to the size and the properties of particles which are or can be released into the patient's or user's body, and special attention must be given to nanomaterials.

Infection and microbial contamination

11.—(1) Devices and their manufacturing processes must be designed in such a way as to eliminate or to reduce as far as possible the risk of infection to patients, users and, where applicable, other persons and the design must—

(a) reduce as far as possible and appropriate the risks from unintended cuts and pricks, such as needle stick injuries;

(b) allow easy and safe handling;

(c) reduce as far as possible any microbial leakage from the device or microbial exposure during use;

(d) prevent microbial contamination of the device or its content such as specimens or fluids.

(2) Where necessary devices must be designed to facilitate their safe cleaning, disinfection or re-sterilisation.

(3) Devices labelled as having a specific microbial state must be designed, manufactured and packaged to ensure that they remain in that state when placed on the market and remain so under the transport and storage conditions specified by the manufacturer.

(4) Devices delivered in a sterile state must—

(a) be designed, manufactured and packaged in accordance with appropriate procedures, to ensure that they are sterile when placed on the market and that, unless the packaging which is intended to maintain their sterile condition is damaged, they remain sterile, under the transport and storage conditions specified by the manufacturer, until that packaging is opened at the point of use;

(b) ensure that the integrity of the packaging is clearly evident to the final user.

(5) Devices labelled as sterile must be processed, manufactured, packaged and, sterilised by means of appropriate, validated methods.

(6) Devices intended to be sterilised must be manufactured and packaged in appropriate and controlled conditions and facilities.

(7) Packaging systems for non-sterile devices must—

(a) maintain the integrity and cleanliness of the product;

(b) where the devices are to be sterilised prior to use, minimise the risk of microbial contamination;

(c) be suitable taking account of the method of sterilisation indicated by the manufacturer.

(8) The labelling of the device must distinguish between identical or similar devices placed on the market in both a sterile and a non-sterile condition in addition to the symbol used to indicate that devices are sterile.

Devices incorporating a substance considered to be a medicinal product and device that are composed of substances that are absorbed by or locally dispersed in the human body

12.—(1) In the case of devices referred to in regulation 68(8), the quality, safety and usefulness of the substance which, if used separately, would be considered to be a medicinal product within the meaning of regulation 2 of the Human Medicines Regulations 2002, must be verified by analogy with the methods specified in Annex I to Directive 2001/83/EC read subject to modifications made by the Human Medicines Regulations 2012, as required by the applicable conformity assessment procedure under Part VIII.

(2) Devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body, and that are absorbed by or locally dispersed in the human body must comply, where applicable and in a manner limited to the aspects not covered by Part VIII, with the relevant requirements laid down in Annex I to Directive 2001/83/EC read subject to the modifications made by the Human Medicines Regulations 2012 for the evaluation of absorption, distribution, metabolism, excretion, local tolerance, toxicity, interaction with other devices, medicinal products or other substances and potential for adverse reactions, as required by the applicable conformity assessment procedure under Part VIII.

Devices incorporating materials of biological origin

13.—(1) For devices manufactured utilising derivatives of tissues or cells of human origin which are non-viable or are rendered non-viable which are covered by Part VIII in accordance with regulation 68(6)(g), the following apply—

(a) donation, procurement and testing of the tissues and cells must be done in accordance with Human Tissue (Quality and Safety for Human Application) Regulations 2007;

(b) processing, preservation and any other handling of those tissues and cells or their derivatives must be carried out so as to provide safety for patients, users and, where applicable, other persons and, in particular, safety with regard to viruses and other transmissible agents must be addressed by appropriate methods of sourcing and by implementation of validated methods of elimination or inactivation in the course of the manufacturing process;

(c) the traceability system for those devices must be complementary and compatible with the traceability and data protection requirements laid down in Human Tissue (Quality and Safety for Human Application) Regulations 2007 and in the Blood Safety and Quality Regulations 2005.

(2) For devices manufactured utilising tissues or cells of animal origin, or their derivatives, which are non-viable or rendered non-viable the following apply—

(a) where feasible taking into account the animal species, tissues and cells of animal origin, or their derivatives, the tissues or cells must originate from animals that have been subjected to veterinary controls that are adapted to the intended use of the tissues and information on the geographical origin of those animals must be retained by manufacturers;

(b) sourcing, processing, preservation, testing and handling of tissues, cells and substances of animal origin, or their derivatives, must be carried out so as to provide safety for patients, users and, where applicable, other persons;

(c) safety with regard to viruses and other transmissible agents must be addressed by implementation of validated methods of elimination or viral inactivation in the course of the manufacturing process, except when the use of such methods would lead to unacceptable degradation compromising the clinical benefit of the device;

(d) in the case of devices manufactured utilising tissues or cells of animal origin, or their derivatives, as referred to in the Regulation (EU) No 722/2012 the particular requirements laid down in that Regulation shall apply.

(3) For devices manufactured utilising non-viable biological substances other than those referred to in sub-paragraphs (1) and (2), the processing, preservation, testing and handling of those substances must be carried out so as to provide safety for patients, users and, where applicable, other persons, including in the waste disposal chain and, safety with regard to viruses and other transmissible agents, must be addressed by appropriate methods of sourcing and by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.

Construction of devices and interaction with the environment

14.—(1) If the device is intended for use in combination with other devices or equipment—

(a) the whole combination, including the connection system must be safe and must not impair the specified performance of the devices;

(b) any restrictions on use applying to such combinations must be indicated on the label or in the instructions for use;

(c) connections which the user has to handle, such as fluid, gas transfer, electrical or mechanical coupling, must be designed and constructed in such a way as to minimise all possible risks, such as misconnection.

(2) Devices must be designed and manufactured in such a way as to remove or reduce as far as possible—

(a) the risk of injury, in connection with their physical features, including the volume or pressure ratio, dimensional and where appropriate ergonomic features;

(b) risks connected with reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, temperature, variations in pressure and acceleration or radio signal interferences;

(c) the risks associated with the use of the device when it comes into contact with materials, liquids, and substances, including gases, to which it is exposed during normal conditions of use;

(d) the risks associated with the possible negative interaction between software and the information technology environment within which it operates and interacts;

(e) the risks of accidental ingress of substances into the device;

(f) the risks of reciprocal interference with other devices normally used in the investigations or for the treatment given;

(g) risks arising where maintenance or calibration are not possible (as with implants), from ageing of materials used or loss of accuracy of any measuring or control mechanism.

(3) Devices must be designed and manufactured in such a way as to minimise the risks of fire or explosion during normal use and in single fault condition and particular attention must be paid to devices the intended use of which includes exposure to or use in association with flammable or explosive substances or substances which could cause combustion.

(4) Devices must be designed and manufactured in such a way that adjustment, calibration and maintenance can be done safely and effectively.

(5) Devices that are intended to be operate together with other devices or products must be designed and manufactured in such a way that the interoperability and compatibility are reliable and safe.

(6) Any measurement, monitoring or display scale must be designed and manufactured in line with ergonomic principles, taking account of the intended purpose, users and the environmental conditions in which the devices are intended to be used.

(7) In relation to the safe disposal of devices and related waste substances—

(a) devices must be designed and manufactured in such a way as to facilitate their safe disposal and the safe disposal of related waste substances by the user, patient or other person;

(b) manufacturers must identify and test procedures and measures as a result of which their devices can be safely disposed after use and such procedures must be described in the instructions for use.

Devices with a diagnostic or measuring function

15.—(1) Diagnostic devices and devices with a measuring function must be designed and manufactured in such a way as to provide sufficient accuracy, precision and stability for their intended purpose, based on appropriate scientific and technical methods and the limits of accuracy shall be indicated by the manufacturer.

(2) The measurements made by devices with a measuring function shall be expressed in legal units conforming to the provisions of Units of Measurement Regulations 1986(**4**).

Protection against radiation

16.—(1) Devices must be designed, manufactured and packaged in such a way that exposure of patients, users and other persons to radiation is reduced as far as possible, and in a manner that is compatible with the intended purpose, whilst not restricting the application of appropriate specified levels for therapeutic and diagnostic purposes.

(2) The operating instructions for devices emitting hazardous or potentially hazardous radiation must contain—

(a) detailed information as to—

(**4**) S.I. 1986/1082 amended by S.I. 2001/55.

(i) the nature of the emitted radiation, the means of protecting the patient and the user, and;

(ii) on ways of avoiding misuse and of reducing the risks inherent to installation as far as possible and appropriate;

(b) information regarding the acceptance and performance testing, the acceptance criteria, and the maintenance procedure.

(3) Devices which are designed to emit hazardous, or potentially hazardous, levels of ionizing or non-ionizing radiation necessary for a specific medical purpose, the benefit of which is considered to outweigh the risks inherent to the emission, must—

(a) make it possible for the user to control the emissions;

(b) must be designed and manufactured to ensure reproducibility of relevant variable parameters within an acceptable tolerance;

(c) be fitted, where possible, with visual displays or audible warnings of those emissions;

(d) be designed and manufactured in such a way that exposure of patients, users and other persons to the emission of unintended, stray or scattered radiation is reduced as far as possible;

(e) where possible and appropriate, ensure that methods are selected which reduce the exposure to radiation of patients, users and other persons who may be affected.

(4) Devices intended to emit ionizing radiation must—

(a) be designed and manufactured taking into account the requirements of any retained EU law which transposed Directive 2013/59/Euratom laying down basic safety standards for protection against the dangers arising from exposure to ionising radiation;

(b) be designed and manufactured in such a way as to ensure that, where possible, taking into account the intended use, the quantity, geometry and quality of the radiation emitted can be varied and controlled, and, if possible, monitored during treatment;

(c) where the device is intended for diagnostic radiology, be designed and manufactured in such a way as to achieve an image or output quality that is appropriate to the intended medical purpose whilst minimising radiation exposure of the patient and user;

(d) where the device is intended for therapeutic radiology, be designed and manufactured in such a way as to enable reliable monitoring and control of the delivered dose, the beam type, energy and, where appropriate, the quality of radiation.

Electronic programmable systems — devices that incorporate electronic programmable systems and software that are devices in themselves

17.—(1) Devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, must—

(a) be designed to ensure repeatability, reliability and performance in line with their intended use;

(b) in the event of a single fault condition, be designed with appropriate means to eliminate or reduce as far as possible consequent risks or impairment of performance.

(2) For devices that incorporate software or for software that are devices in themselves, the software must be developed and manufactured in accordance with the state of the art taking into account the principles of development life cycle, risk management, including information security, verification and validation.

(3) Software referred to in this paragraph that is intended to be used in combination with mobile computing platforms must be designed and manufactured taking into account the specific

features of the mobile platform (for example size and contrast ratio of the screen) and the external factors related to their use (varying environment as regards level of light or noise).

(4) Manufacturers must set out minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorised access, necessary to run the software as intended.

Active devices and devices connected to them

18.—(1) For non-implantable active devices, in the event of a single fault condition, appropriate means must be adopted to eliminate or reduce as far as possible consequent risks.

(2) Devices, where the safety of the patient depends on an internal power supply, must be equipped with—

(a) a means of determining the state of the power supply;

(b) an appropriate warning or indication for when the capacity of the power supply becomes critical, if necessary, such warning or indication must be given prior to the power supply becoming critical.

(3) Devices where the safety of the patient depends on an external power supply must include an alarm system to signal any power failure.

(4) Devices intended to monitor one or more clinical parameters of a patient must be equipped with appropriate alarm systems to alert the user of situations which could lead to death or severe deterioration of the patient's state of health.

(5) Devices must be designed and manufactured in such a way as to reduce as far as possible the risks of creating electromagnetic interference which could impair the operation of the device in question or other devices or equipment in the intended environment.

(6) Devices must be designed and manufactured in such a way as to provide a level of intrinsic immunity to electromagnetic interference that is adequate to enable them to operate as intended.

(7) Devices must be designed and manufactured in such a way as to avoid, as far as possible, the risk of accidental electric shocks to the patient, user or any other person, both during normal use of the device and in the event of a single fault condition in the device, provided the device is installed and maintained as indicated by the manufacturer.

(8) Devices must be designed and manufactured in such a way as to protect, as far as possible, against unauthorised access that could hamper the device from functioning as intended.

Particular requirements for active implantable devices

19.—(1) Active implantable devices must be designed and manufactured in such a way as to remove or minimize as far as possible—

(a) risks connected with the use of energy sources with particular reference, where electricity is used, to insulation, leakage currents and overheating of the devices;

(b) risks connected with medical treatment, in particular those resulting from the use of defibrillators or high- frequency surgical equipment;

(c) risks which may arise where maintenance and calibration are impossible, including—

(i) excessive increase of leakage currents;

(ii) ageing of the materials used;

(iii) excess heat generated by the device;

(iv) decreased accuracy of any measuring or control mechanism.

(2) Active implantable devices must be designed and manufactured in such a way as to ensure—

(a) if applicable, the compatibility of the devices with the substances they are intended to administer;

(b) the reliability of the source of energy.

(3) Active implantable devices and, if appropriate, their component parts must be identifiable to allow any necessary measure to be taken following the discovery of a potential risk in connection with the devices or their component parts.

(4) Active implantable devices must bear a code—

(a) by which they and their manufacturer can be unequivocally identified (particularly with regard to the type of device and its year of manufacture); and

(b) which it is possible to read, if necessary, without the need for a surgical operation.

Protection against mechanical and thermal risks

20.—(1) Devices must be designed and manufactured in such a way as to protect patients and users against mechanical risks connected with, for example, resistance to movement, instability and moving parts.

(2) Devices must be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from vibration generated by the devices, taking account of technical progress and of the means available for limiting vibrations, particularly at source, unless the vibrations are part of the specified performance.

(3) Devices must be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from the noise emitted, taking account of technical progress and of the means available to reduce noise, particularly at source, unless the noise emitted is part of the specified performance.

(4) Terminals and connectors to the electricity, gas or hydraulic and pneumatic energy supplies which the user or other person has to handle, must be designed and constructed in such a way as to minimise all possible risks.

(5) Errors likely to be made when fitting or refitting certain parts which could be a source of risk —

(a) must be made impossible by the design and construction of such parts or by information given on the parts themselves or their housings; and

(b) must contain the same information on moving parts or their housings where the direction of movement needs to be known in order to avoid a risk.

(6) Accessible parts of devices (excluding the parts or areas intended to supply heat or reach given temperatures) and their surroundings must not attain potentially dangerous temperatures under normal conditions of use.

Protection against the risks posed to the patient or user by devices supplying energy or substances

21.—(1) Devices for supplying the patient with energy or substances must be designed and constructed in such a way that the amount to be delivered can be set and maintained accurately enough to ensure the safety of the patient and of the user.

(2) Devices must—

(a) be fitted with the means of preventing or indicating any inadequacies in the amount of energy delivered or substances delivered which could pose a danger;

(b) incorporate suitable means to prevent, as far as possible, the accidental release of dangerous levels of energy or substances from an energy and/or substance source.

(3) The function of the controls and indicators—

(a) must be clearly specified on devices;

(b) where a device bears instructions required for its operation or indicates operating or adjustment parameters by means of a visual system, such information must be understandable to the user and, as appropriate, the patient.

Protection against the risks posed by medical devices intended by the manufacturer for use by lay persons

22.—(1) Devices for use by lay persons must—

(a) be designed and manufactured in such a way that they perform appropriately for their intended purpose taking into account the skills and the means available to lay persons and the influence resulting from variation that can be reasonably anticipated in the lay person's technique and environment; and

(b) be provided by the manufacturer with information and instructions which are easy for the lay person to understand and apply.

(2) Devices for use by lay persons must be designed and manufactured in such a way as to—

(a) ensure that the device can be used safely and accurately by the intended user at all stages of the procedure, if necessary after appropriate training or information;

(b) reduce, as far as possible and appropriate, the risk from unintended cuts and pricks such as needle stick injuries; and

(c) reduce as far as possible the risk of error by the intended user in the handling of the device and, if applicable, in the interpretation of the results.

(3) Devices for use by lay persons must, where appropriate, include a procedure by which the lay person—

(a) can verify that, at the time of use, the device will perform as intended by the manufacturer;

(b) is warned if the device has failed to provide a valid result.

PART 3

Requirements regarding instructions for use

Label and instructions for use

23.—(1) Each device must be accompanied by the information (which may appear on the device itself, on the packaging or in the instructions for use) needed to identify the device and its manufacturer, and by any safety and performance information relevant to the user, or any other person, as appropriate.

(2) The information in paragraph (1) must, if the manufacturer has a website, be made available and kept up to date on the website.

(3) The label and instructions for use must take into account the following—

(a) that the medium, format, content, legibility, and location of the label and instructions for use must be appropriate to the particular device, its intended purpose and the technical knowledge, experience, education or training of the intended users and, in particular, instructions for use must be written in terms readily understood by the intended user and, where appropriate, supplemented with drawings and diagrams;

(b) the information required on the label must be provided on the device itself or, if this is not practicable or appropriate, some or all of the information may appear on the packaging for each unit, or on the packaging of multiple devices;

(c) labels must be provided in a human-readable format and may be supplemented by machine-readable information, such as radio-frequency identification ('RFID') or bar codes;

(d) in general, instructions for use must be provided together with devices but, by way of exception, instructions for use are not required for Class I and Class IIa devices if such devices can be used safely without any such instructions and unless otherwise provided for elsewhere in this paragraph;

(e) where multiple devices are supplied to a single user or location, a single copy of the instructions for use may be provided if so agreed by the purchaser who in any case may request further copies to be provided free of charge;

(f) instructions for use may be provided to the user in non-paper format (for example electronic) to the extent, and only under the conditions, set out in Regulation (EU) No 207/2012;

(g) residual risks which are required to be communicated to the user or other person must be included as limitations, contra-indications, precautions or warnings in the information supplied by the manufacturer;

(h) where appropriate, the information supplied by the manufacturer —

(i) must take the form of internationally recognised symbols;

(ii) must conform, in terms of any symbol or identification colour used, to the relevant standards; and

(iii) in areas for which no relevant standards exist, the symbols and colours must be described in the documentation supplied with the device.

Information on the label

(4) The label must bear the following particulars—

(a) the name or trade name of the device;

(b) the details strictly necessary for a user to identify the device, the contents of the packaging and, where it is not obvious for the user, the intended purpose of the device;

(c) the name, registered trade name or registered trade mark of the manufacturer and the address of its registered place of business;

(d) if the manufacturer has its registered place of business outside the United Kingdom, the name and address of the person placing the device on the market;

(e) where applicable, an indication that the device contains or incorporates—

(i) a medicinal substance, including a human blood or plasma derivative, or tissues or cells, or their derivatives, of human origin; or

(ii) tissues or cells of animal origin, or their derivatives, as referred to in Regulation (EU) No 722/2012;

(f) where applicable, information labelled in accordance with paragraph 10(10);

(g) the lot number or the serial number of the device preceded by the words LOT NUMBER or SERIAL NUMBER or an equivalent symbol, as appropriate;

(h) the UDI carrier referred to in regulation 91(4) and Part C of Schedule 8;

(i) an unambiguous indication of the time limit for using or implanting the device safely, expressed at least in terms of year and month, where this is relevant;

(j) where there is no indication of the date until when it may be used safely, the date of manufacture and this date of manufacture may be included as part of the lot number or serial number, provided the date is clearly identifiable;

(k) an indication of any special storage or handling condition that applies;

(l) if the device is supplied sterile, an indication of its sterile state and the sterilisation method;

(m) warnings or precautions to be taken that need to be brought to the immediate attention of the user of the device, and to any other person (this information may be kept to a minimum in which case, more detailed information must appear in the instructions for use, taking into account the intended users);

(n) if the device is intended for single use, an indication of that fact;

(o) if the device is a single-use device that has been reprocessed, an indication of that fact, the number of reprocessing cycles already performed, and any limitation as regards the number of reprocessing cycles;

(p) if the device is custom-made, the words 'custom-made device';

(q) an indication that the device is a medical device and, if the device is intended for clinical investigation only, the words 'exclusively for clinical investigation';

(r) in the case of devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body via a body orifice or applied to the skin and that are absorbed by or locally dispersed in the human body, the overall qualitative composition of the device and quantitative information on the main constituent or constituents responsible for achieving the principal intended action;

(s) for active implantable devices, the serial number, and for other implantable devices, the serial number or the lot number.

(5) Where packaging maintains the sterile condition of the device ("sterile packaging") the following particulars must appear on that sterile packaging—

(a) an indication permitting the sterile packaging to be recognised as such;

(b) a declaration that the device is in a sterile condition;

(c) the method of sterilisation;

(d) the name and address of the manufacturer;

(e) a description of the device;

(f) if the device is intended for clinical investigations, the words 'exclusively for clinical investigations';

(g) if the device is custom-made, the words 'custom-made device';

(h) the month and year of manufacture;

(i) an unambiguous indication of the time limit for using or implanting the device safely expressed at least in terms of year and month;

(j) an instruction to check the instructions for use for what to do if the sterile packaging is damaged or unintentionally opened before use.

Information in instructions for use

(6) The instructions for use must contain all the following particulars—

(a) the particulars referred to in paragraphs (a), (c), (e), (f), (k), (l), (n) and (r) of paragraph 23(4);

(b) the device's intended purpose with a clear specification of indications, contra-indications, the patient target group or groups, and of the intended users, as appropriate;

(c) where applicable, a specification of the clinical benefits to be expected;

(d) where applicable, links to the summary of safety and clinical performance referred to in regulation 96;

(e) the performance characteristics of the device;

(f) where applicable, information allowing the healthcare professional to verify if the device is suitable and select the corresponding software and accessories;

(g) any residual risks, contra-indications and any undesirable side-effects, including information to be conveyed to the patient in this regard;

(h) specifications the user requires to use the device appropriately, for example if the device has a measuring function, the degree of accuracy claimed for it;

(i) details of any preparatory treatment or handling of the device before it is ready for use or during its use, such as sterilisation, final assembly, calibration, including the levels of disinfection required to ensure patient safety and all available methods for achieving those levels of disinfection;

(j) any requirements for special facilities, or special training, or particular qualifications of the device user or other persons;

(k) the information needed to verify whether the device is properly installed and is ready to perform safely and as intended by the manufacturer, together with, where relevant—

(i) details of the nature, and frequency, of preventive and regular maintenance, and of any preparatory cleaning or disinfection;

(ii) identification of any consumable components and how to replace them;

(iii) information on any necessary calibration to ensure that the device operates properly and safely during its intended lifetime;

(iv) methods for eliminating the risks encountered by persons involved in installing, calibrating or servicing devices;

(l) if the device is supplied sterile, instructions in the event of the sterile packaging being damaged or unintentionally opened before use;

(m) if the device is supplied non-sterile with the intention that it is sterilised before use, the appropriate instructions for sterilisation;

(n) if the device is reusable, information must be provided—

(i) on the appropriate processes for allowing reuse, including cleaning, disinfection, packaging and, where appropriate, the validated method of re-sterilisation; and

(ii) to identify when the device should no longer be reused, for example signs of material degradation or the maximum number of allowable reuses;

(o) an indication, if appropriate, that a device can be reused only if it is reconditioned under the responsibility of the manufacturer to comply with the general safety and performance requirements;

(p) if the device bears an indication that it is for single use—

(i) information on known characteristics and technical factors known to the manufacturer that could pose a risk if the device were to be re-used;

(ii) the information must be based on a specific section of the manufacturer's risk management documentation, where such characteristics and technical factors must be addressed in detail;

(iii) if, in accordance with sub-paragraph (3)(d), no instructions for use are required, this information must be made available to the user upon request;

(q) for devices intended for use together with other devices or general purpose equipment—

(i) information to identify such devices or equipment, in order to obtain a safe combination;

(ii) information on any known restrictions to combinations of devices and equipment;

(r) if the device emits radiation for medical purposes—

(i) detailed information as to the nature, type and where appropriate, the intensity and distribution of the emitted radiation;

(ii) the means of protecting the patient, user, or other person from unintended radiation during use of the device;

(s) information that allows the user or patient to be informed of, or as the case may be, briefed about any warnings, precautions, contra-indications, measures to be taken and limitations of use regarding the device and this information must cover, where appropriate—

(i) warnings, precautions or measures to be taken in the event of malfunction of the device or changes in its performance that may affect safety;

(ii) warnings, precautions or measures to be taken as regards the exposure to reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, or temperature;

(iii) warnings, precautions or measures to be taken as regards the risks of interference posed by the reasonably foreseeable presence of the device during specific diagnostic investigations, evaluations, or therapeutic treatment or other procedures such as electromagnetic interference emitted by the device affecting other equipment;

(iv) if the device is intended to administer medicinal products, tissues or cells of human or animal origin, or their derivatives, or biological substances, any limitations or incompatibility in the choice of substances to be delivered;

(v) warnings, precautions or limitations related to the medicinal substance or biological material that is incorporated into the device as an integral part of the device; and

(vi) precautions related to materials incorporated into the device that contain or consist of CMR substances or endocrine-disrupting substances, or that could result in sensitisation or an allergic reaction by the patient or user;

(t) in the case of devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body and that are absorbed by or locally dispersed in the human body, warnings and precautions, where appropriate, related to—

(i) the general profile of interaction of the device and its products of metabolism with other devices, medicinal products and other substances;

(ii) contra-indications, undesirable side-effects and risks relating to overdose;

(u) in the case of implantable devices, the overall qualitative and quantitative information on the materials and substances to which patients can be exposed;

(v) warnings or precautions to be taken in order to facilitate the safe disposal of the device, its accessories and the consumables used with it, which must, where appropriate cover—

(i) infection or microbial hazards such as explants, needles or surgical equipment contaminated with potentially infectious substances of human origin, and

(ii) physical hazards such as from sharps;

(iii) if, in accordance with the sub-paragraph (3)(d), no instructions for use are required, this information must be made available to the user upon request;

(w) for devices intended for use by lay persons, the circumstances in which the user should consult a healthcare professional;

(x) for the devices covered by Part VIII of these Regulations pursuant to regulation 68(2)(b), information regarding the absence of a clinical benefit and the risks related to use of the device;

(y) the date of issue of the instructions for use or, if they have been revised, the date of issue and the identifier of the latest revision of the instructions for use;

(z) a notice to the user or patient that any serious incident that has occurred in relation to the device should be reported to the manufacturer and to the Secretary of State;

(aa) information to be supplied to the patient with an implanted device in accordance with regulation 83;

(bb) for devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, minimum requirements concerning hardware, Information Technology networks characteristics and Information Technology security measures, including protection against unauthorised access, necessary to run the software as intended.

SCHEDULE 4

Regulation 1A

Technical Documentation

1. The technical documentation and, if applicable, the summary of that documentation drawn up by the manufacturer must be presented in clear, organised, readily searchable and unambiguous manner and must include the elements listed in this Schedule.

Device description and specification including variants and accessories

Device description and specification

2.—(1) The description and specification of a device must contain the following—

(a) the product or trade name and a general description of the device including its intended purpose and intended users;

(b) the Basic UDI-DI as referred to in Part C of Schedule 8 assigned by the manufacturer to the device in question, as soon as identification of this device becomes based on a UDI system, or otherwise a clear identification by means of product code, catalogue number or other unambiguous reference allowing traceability;

(c) the intended patient population and medical conditions to be diagnosed, treated or monitored and other considerations such as patient selection criteria, indications, contra-indications, warnings;

(d) principles of operation of the device and its mode of action, scientifically demonstrated if necessary;

(e) the rationale for the qualification of the product as a device;

(f) the risk class of the device and the justification for the classification rules applied in accordance with Schedule 9;

(g) an explanation of any novel features;

(h) a description of the accessories for the device, other devices and other products that are not devices, which are intended to be used in combination with it;

(i) a description or complete list of the various configurations or variants of the device that are intended to be made available on the market;

(j) a general description—

(i) of the key functional elements, for example its parts or components (including software if appropriate), its formulation, its composition, its functionality and, where relevant, its qualitative and quantitative composition; and

(ii) which, where appropriate, must include labelled pictorial representations (for example diagrams, photographs, and drawings), clearly indicating key parts or components, including sufficient explanation to understand the drawings and diagrams;

(k) a description of the raw materials incorporated into key functional elements and those making either direct contact with the human body or indirect contact with the body, for example during extracorporeal circulation of body fluids;

(l) technical specifications, such as features, dimensions and performance attributes, of the device and any variants or configurations and accessories that would typically appear in the product specification made available to the user, for example in brochures, catalogues and similar publications.

Reference to previous and similar generations of the device

(2) Where applicable the technical documentation must contain—

(a) an overview of the previous generation or generations of the device produced by the manufacturer, where such devices exist;

(b) an overview of identified similar devices available on the international markets, where such devices exist.

Information to be supplied by the manufacturer

3. The manufacturer must supply a complete set of—

(a) the label or labels on the device and on its packaging, such as single unit packaging, sales packaging, transport packaging in case of specific management conditions in English; and

(b) the instructions for use in English.

Design and manufacturing information

4. The following design and manufacturing information must be supplied—

(a) information (including full data) to allow the design stages applied to the device to be understood;

(b) complete information (including full data) and specifications, including the manufacturing processes and their validation, their adjuvants, the continuous monitoring and the final product testing.

General safety and performance requirements

5.—(1) The documentation must contain information for the demonstration of conformity with the general safety and performance requirements set out in Schedule 3 that are applicable to the device taking into account its intended purpose, and must include a justification, validation and verification of the solutions adopted to meet those requirements.

(2) The demonstration of conformity in sub-paragraph (1) must include—

(a) the general safety and performance requirements that apply to the device and an explanation as to why others do not apply;

(b) the method or methods used to demonstrate conformity with each applicable general safety and performance requirement;

(c) the standards or other solutions applied;

(d) the precise identity of the controlled documents offering evidence of conformity with each standard, or other method applied to demonstrate conformity with the general safety and performance requirements; and

(e) the information referred to paragraph (d) must incorporate a cross-reference to the location of such evidence within the full technical documentation and, if applicable, the summary technical documentation.

Benefit-risk analysis and risk management

6. The technical documentation must contain information on—

(a) the benefit-risk analysis referred to in paragraphs 1 and 8 of Schedule 3;

(b) the solutions adopted and the results of the risk management referred to in paragraph 3 of Schedule 3.

Product verification and validation

7.—(1) The documentation must contain the results and critical analyses of all verifications and validation tests or studies undertaken to demonstrate conformity of the device with the requirements of Part VIII and in particular the applicable general safety and performance requirements.

Pre-clinical and clinical data.

(2) The documentation must contain the following pre-clinical and clinical data—

(a) results of tests, such as engineering, laboratory, simulated use and animal tests, and evaluation of published literature applicable to the device, taking into account its intended purpose, or to similar devices, regarding the pre-clinical safety of the device and its conformity with the specifications;

(b) detailed information regarding test design, complete test or study protocols, methods of data analysis, in addition to data summaries and test conclusions regarding in particular—

(i) the biocompatibility of the device including the identification of all materials in direct or indirect contact with the patient or user;

(ii) physical, chemical and microbiological characterisation;

(iii) electrical safety and electromagnetic compatibility;

(iv) software verification and validation which must—

(aa) describe the software design and development process and provide evidence of the validation of the software, as used in the finished device;

(bb) typically include the summary results of all verification, validation and testing performed both in-house and in a simulated or actual user environment prior to final release; and

(cc) address all of the different hardware configurations and, where applicable, operating systems identified in the information supplied by the manufacturer;

(v) stability, including shelf life; and

(vi) performance and safety.

(3) Where applicable, conformity with the Good Laboratory Practice Regulations 1999(**5**) must be demonstrated.

(4) Where no new testing has been undertaken, the documentation must incorporate a rationale for that decision (for example, a rationale would be that biocompatibility testing on identical materials was conducted when those materials were incorporated in a previous version of the device that has been legally placed on the market or put into service).

(5) The documentation must also include—

(a) the clinical evaluation report and its updates and the clinical evaluation plan referred to in regulation 102(14) and Part A of Schedule 14;

(b) the PMCF plan and PMCF evaluation report referred to in Part B of Schedule 14 or a justification why a PMCF is not applicable.

Additional information required in specific cases

(6) The additional information specified is required as part of the technical documentation in the following cases—

(a) where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product within the meaning of regulation 2(1) of the Human Medicines Regulations 2012 including a medicinal product derived from human blood or human plasma, as referred to in regulation 68(8)—

(i) a statement indicating this fact; and

(ii) documentation sufficient to identify the source of that substance and contain the data of the tests conducted to assess its safety, quality and usefulness, taking account of the intended purpose of the device;

(b) where a device is manufactured utilising tissues or cells of human or animal origin, or their derivatives, and is covered by Part VIII in accordance with sub-paragraphs (g) and (h) of regulation 68(6), and where a device incorporates, as an integral part, tissues or cells of human origin or their derivatives that have an action ancillary to that of the device and is covered by Part VIII in accordance with regulation 68(14)—

(i) a statement indicating this fact; and

(ii) documentation sufficient to identify all materials of human or animal origin used and provide detailed information concerning the conformity with sub-paragraphs (1) and (2) of paragraph 13 of Schedule 3;

(c) in the case of devices that are composed of substances or combinations of substances that are intended to be introduced into the human body and that are absorbed by or locally dispersed in the human body, detailed information, including test design, complete test or study protocols, methods of data analysis, and data summaries and test conclusions, regarding studies in relation to—

(i) absorption, distribution, metabolism and excretion;

(ii) possible interactions of those substances, or of their products of metabolism in the human body, with other devices, medicinal products or other substances, considering the target population, and its associated medical conditions;

(iii) local tolerance;

(iv) toxicity, including single-dose toxicity, repeat-dose toxicity, genotoxicity, carcinogenicity and reproductive and developmental toxicity, as applicable depending on the level and nature of exposure to the device and in the absence of such studies, a justification shall be provided;

(**5**) S.I. 1999/3106; relevant amendment S.I. 2004/994.

(d) in the case of devices containing CMR or endocrine-disrupting substances referred to in paragraph 10(7) of Schedule 3, the justification referred to in paragraph 10(9) of that Schedule;

(e) in the case of devices placed on the market in a sterile or defined microbiological condition, a description of the environmental conditions for the relevant manufacturing steps;

(f) in the case of devices placed on the market in a sterile condition—

(i) a description of the methods used; and

(ii) validation reports, with respect to packaging, sterilisation and maintenance of sterility which must address bioburden testing, pyrogen testing and, if applicable, testing for sterilant residues;

(g) in the case of devices placed on the market with a measuring function, a description of the methods used in order to ensure the accuracy as given in the specifications;

(h) if the device is to be connected to other devices in order to operate as intended, a description of this combination or configuration including proof that it conforms to the general safety and performance requirements when connected to any such devices having regard to the characteristics specified by the manufacturer.

SCHEDULE 5

Regulation 1A

Technical documentation on post-market surveillance

1.—(1) The technical documentation on post-market surveillance drawn up by the manufacturer in accordance with regulations 121 to 123 must be presented in a clear, organised, readily searchable and unambiguous manner and must include in particular the elements described in sub-paragraphs (2) to (4) this Schedule.

(2) In the post-market surveillance plan drawn up in accordance with regulation 122, the manufacturer must prove that the requirements of regulation 121 have been met.

(3) The post-market surveillance plan must—

(a) address the collection and utilization of available information, in particular—

(i) information concerning serious incidents, including information from PSURs, and field safety corrective actions;

(ii) records referring to non-serious incidents and data on any undesirable side-effects;

(iii) information from trend reporting;

(iv) information, including feedbacks and complaints, provided by users, distributors and importers;

(v) publicly available information about similar medical devices;

(b) cover at least—

(i) a proactive and systematic process to collect any information referred to in sub-paragraph 1(2). The process must allow a correct characterisation of the performance of the devices and must also allow a comparison to be made between the device and similar products available on the market;

(ii) effective and appropriate methods and processes to assess the collected data;

(iii) suitable indicators and threshold values that must be used in the continuous reassessment of the benefit-risk analysis and of the risk management as referred to in paragraph 3 of Schedule 3;

(iv) effective and appropriate methods and tools to investigate complaints and analyse market-related experience collected in the field;

(v) methods and protocols to manage the events subject to the trend report as provided for in regulation 126, including the methods and protocols to be used to establish any statistically significant increase in the frequency or severity of incidents as well as the observation period;

(vi) methods and protocols to communicate effectively to the Secretary of State, economic operators and users;

(vii) reference to procedures to fulfil the manufacturers obligations laid down in regulations 121, 122 and 124;

(viii) systematic procedures to identify and initiate appropriate measures including corrective actions;

(ix) effective tools to trace and identify devices for which corrective actions might be necessary;

(x) a PMCF plan as referred to in Part B of Schedule 14, or a justification as to why a PMCF is not applicable.

(4) The PSUR referred to in regulation 124 and the post-market surveillance report referred to in regulation 123.

SCHEDULE 6

Regulation 1A

Declaration of conformity

The declaration of conformity must contain the following information—

(a) the name, registered trade name or registered trade mark of the manufacturer, and, if applicable, its authorised representative, and the address of their registered place of business or, if they have no such address, an address where they can be contacted and their location be established;

(b) a statement that the declaration of conformity is issued under the sole responsibility of the manufacturer;

(c) the Basic UDI-DI as referred to in Part C of Schedule 8;

(d) the product and trade name;

(e) the product code, catalogue number or other unambiguous reference allowing identification and traceability of the device (which can be provided by means of the UDI-DI referred to in paragraph (c)) covered by the declaration of conformity, such as a photograph;

(f) the product's intended purpose;

(g) the risk class of the device in accordance with the rules set out in Schedule 9;

(h) a statement that the device, covered by the declaration, is in conformity with Part VIII or Regulation (EU) 2017/745 and, if applicable, with any other relevant product safety legislation that provides for the issuing of a declaration of conformity;

(i) references to any designated standards used and in relation to which conformity is declared;

(j) where applicable, the name and identification number of the notified body, a description of the conformity assessment procedure performed and identification of the certificate or certificates issued;

(k) where applicable, any additional information;

(l) place and date of issue of the declaration, name and function of the person who signed it as well as an indication for, and on behalf of whom, that person signed;

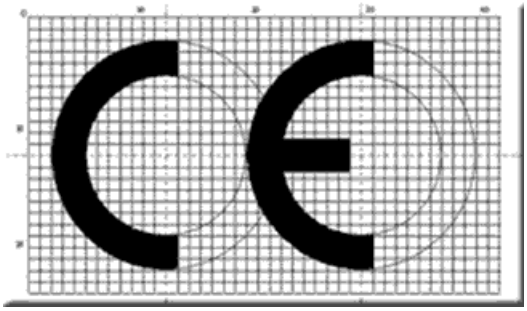
(m) a signature.

SCHEDULE 7

Regulation 1A

CE marking of conformity

1. The CE marking must consist of the initial 'CE' taking the following form—



2. If the CE marking is reduced or enlarged, the proportions given in the above graduated drawing must be respected.

3. The various components of the CE marking must have substantially the same vertical dimension, which may not be less than 5 mm but this minimum dimension may be waived for small-scale devices.

SCHEDULE 8

Regulation 1A

Information to be submitted upon registration of devices and economic operators in accordance with regulations 93 and 95, core data elements to be provided to the UDI database together with the UDI-DI in accordance with regulations 93 and 95 and the UDI system

Part A

Information to be submitted upon the registration of devices and economic operators in accordance with regulations 93 and 95

1. The information relating to the economic operator is as follows—

(a) type of economic operator (manufacturer, importer, authorised representative, UK responsible person or distributor);

(b) the name of the economic operator and the United Kingdom address and contact details for the economic operator;

(c) where submission of information is carried out by another person on behalf of any of the economic operators the name, address and contact details of that person;

(d) name, address and contact details of the person or persons responsible for regulatory compliance referred to in regulation 80.

2. The information relating to the device is as follows—

(a) basic UDI-DI;

(b) type, number and expiry date of the certificate issued by the notified body and the name or identification number of that notified body and the link to the information that appears on the certificate;

(c) if the device has been placed on the market of a state other than the United Kingdom before being placed on the United Kingdom market, the name of that state;

(d) in the case of Class IIa, Class IIb or Class III devices, the name of the state, other than the United Kingdom, where the device is or is to be made available;

(e) the risk class of the device;

(f) whether the device is a reprocessed single-use device;

(g) the presence of a substance which, if used separately, may be considered to be a medicinal product and name of that substance;

(h) the presence of a substance which, if used separately, may be considered to be a medicinal product derived from human blood or human plasma and name of this substance;

(i) whether tissues or cells or human origin, or their derivatives are present;

(j) whether tissues or cells of animal origin, or their derivatives, as referred to in Regulation (EU) No 722/2012 are present;

(k) where applicable, the single identification number of the clinical investigation or investigations conducted in relation to the device or a link to the clinical investigation registration in the electronic system on clinical investigations;

(l) in the case of devices listed in Schedule 16, specification as to whether the intended purpose of the device is other than a medical purpose;

(m) in the case of devices designed and manufactured by another legal or natural person as referred in regulation 76(23), the name, address and contact details of that legal or natural person;

(n) in the case of Class III or implantable devices, the summary of safety and clinical performance;

(o) status of the device (on the market, no longer placed on the market, recalled, field safety corrective action initiated).

Part B

Core data elements to be provided to the UDI database together with the UDI-DI in accordance with regulations 92 and 93

3. The person placing the product on the market must provide to the UDI database the UDI-DI and all of the following information relating to the manufacturer and the device—

(a) the quantity per package configuration;

(b) the Basic UDI-DI as referred to in regulation 93 and any additional UDI-DIs;

(c) the manner in which production of the device is controlled (expiry date or manufacturing date, lot number, serial number);

(d) if applicable, the unit of use UDI-DI (where a UDI is not labelled on the device at the level of its unit of use, a 'unit of use' DI shall be assigned so as to associate the use of a device with a patient);

(e) the name and address of the manufacturer (as indicated on the label);

(f) if applicable, name and address of the authorised representative (as indicated on the label);

(g) the medical device nomenclature code as provided for in regulation 90;

(h) risk class of the device;

(i) if applicable, name or trade name;

(j) if applicable, device model, reference or catalogue number;

(k) if applicable, clinical size (including volume, length, gauge, diameter);

(l) any additional product description;

(m) if applicable, storage and handling conditions (as indicated on the label or in the instructions for use);

(n) if applicable, additional trade names of the device;

(o) whether the device is labelled as a single use device;

(p) if applicable, the maximum number of reuses;

(q) whether the device is labelled sterile;

(r) whether there is a need for the device to be sterilised before use;

(s) whether the device contains latex;

(t) where applicable, information labelled in accordance with paragraph 10(10) of Schedule 3;

(u) URL for additional information, such as electronic instructions for use (optional);

(v) if applicable, critical warnings or contra-indications;

(w) the status of the device (on the market, no longer placed on the market, recalled, field safety corrective action initiated).

Part C

The UDI system

Definitions

4. In this Schedule—

"automatic identification and data capture" or "(AIDC)" means a technology used to automatically capture data, for example, bar codes, smart cards, biometrics and RFID;

"Basic UDI-DI" is the primary identifier of a device model assigned at the level of the device unit and the main key for records in the UDI database which is referenced in the relevant certificates and declarations of conformity;

"configurable device" means a device that consists of several individual components (which can be devices in themselves) which can be assembled by the manufacturer in multiple

configurations and includes: computed tomography (CT) systems, ultrasound systems, anaesthesia systems, physiological monitoring systems, radiology information systems (RIS);

"configuration" means a combination of items of equipment, as specified by the manufacturer, that operate together as a device to achieve an intended purpose and which may be modified, adjusted or customized to meet specific needs; examples of configurations include—

(a) gantries, tubes, tables, consoles and other items of equipment that can be configured or combined to deliver an intended function in computed tomography;

(b) ventilators, breathing circuits, vaporizers combined to deliver an intended function in anaesthesia;

"human readable interpretation ('HRI')" means a legible interpretation of the data characters encoded in the UDI carrier;

"packaging levels" means the various levels of device packaging that contain a defined quantity of devices, such as a carton or case;

"Radio Frequency Identification" or "RFID" means a technology that uses communication through the use of radio waves to exchange data between a reader and an electronic tag attached to an object, for the purpose of identification;

"shipping container" means a container in relation to which traceability is controlled by a process specific to logistics systems;

"UDI carrier" means the method of conveying (by for example ID or linear bar code, 2D Matrix bar code or RFID) the UDI by using AIDC and, if applicable, its HRI;

"UDI-DI" means a unique numeric or alphanumeric code specific to a model of device and that is also used as the 'access key' to information stored in a UDI database;

"unique device identifier" or "UDI", which is comprised of the UDI-DI and UDI-PI, means a series of numeric or alphanumeric characters created through a globally accepted device identification and coding standard and which allows for the unambiguous identification of a specific device on the market;

"UDI-PI" means a numeric or alphanumeric code that identifies the unit of device production, and types of UDI-PI include serial number, lot number, software identification, manufacturing date or expiry date;

"units of use DI" means a device identifier used to associate the use of the device with the patient in instances in which a UDI is not labelled on the individual device at the level of its unit of use, for example where several units of the same device are packaged together.

General requirements

5.—(1) The affixing of the UDI is an additional requirement and does not replace any other marking or labelling requirements laid down in Schedule 3 to these regulations.

(2) The manufacturer must assign and maintain UDIs for its devices.

(3) Only the manufacturer may place the UDI on the device or its packaging.

(4) Only coding standards provided by issuing entities, as set out in regulation 91(2), may be used.

The UDI

6.—(1) A UDI must be assigned to the device itself or its packaging and higher levels of packaging must have their own UDI.

(2) Shipping containers are exempt from the requirement in sub-paragraph (1), for example, a UDI is not required on a logistics unit so that where a healthcare provider orders multiple devices using the UDI or model number of individual devices and the manufacturer places those devices in a container for shipping or to protect the individually packaged devices, the container (logistics unit) is not be subject to UDI requirements.

(3) The UDI must contain two parts: a UDI-DI and a UDI-PI.

(4) The UDI-DI must be unique at each level of device packaging.

(5) Where on the label there is—

(a) a lot number, serial number, software identification or expiry date, it must be part of the UDI-PI; or

(b) only a manufacturing date, this must be used as the UDI-PI,

but, where there is both a lot number, serial number, software identification or expiry date and a manufacturing date, the manufacturing date does not need to be included within the UDI- PI.

(6) Each component that is considered to be a device and is commercially available on its own must be assigned a separate UDI unless the components are part of a configurable device that is marked with its own UDI.

(7) Systems and procedure packs as referred to in regulation 87 must be assigned and bear their own UDI.

(8) The manufacturer must assign the UDI to a device following the relevant coding standard.

(9) A new UDI-DI is required whenever there is a change that could lead to misidentification of a device or ambiguity in its traceability and in particular, any change of one of the following UDI database data elements requires a new UDI-DI—

(a) name or trade name;

(b) device version or model;

(c) labelled as single use;

(d) packaged sterile;

(e) need for sterilization before use;

(f) quantity of devices provided in a package;

(g) critical warnings or contra-indications for example, containing latex or Di (2-ethylhexyl) phthalate.

(10) Manufacturers that repackage or relabel devices, with their own label must retain a record of the original device manufacturer's UDI.

UDI carrier

7.—(1) The UDI carrier (AIDC and HRI representation of the UDI) must be placed on the label or on the device itself and on all higher levels of device packaging other than shipping containers.

(2) Where there are significant space constraints on the unit of use packaging, the UDI carrier may be placed on the next higher packaging level.

(3) Subject to paragraph (4), for single-use devices of Classes I and IIa, packaged and labelled individually, the UDI carrier is not required to appear on the packaging but it must appear on a higher level of packaging, for example a carton containing several individually packaged devices.

(4) When the healthcare provider is not expected to have access, in cases such as in home healthcare settings, to the higher level of device packaging, the UDI must be placed on the packaging of the individual device.

(5) For devices exclusively intended for retail sale the UDI-PIs in AIDC is not be required to appear on the point of sale packaging.

(6) When AIDC carriers other than the UDI carrier are part of the product labelling, the UDI carrier shall be readily identifiable.

(7) If linear bar codes are used the UDI-DI and UDI-PI may be concatenated or non-concatenated in two or more bar codes but all parts and elements of the linear bar code must be distinguishable and identifiable.

(8) Subject to paragraph (9), where there are significant constraints limiting the use of both AIDC and HRI on the label, only the AIDC format is required to appear on the label.

(9) For devices intended to be used outside healthcare facilities, such as devices for home care, the HRI must appear on the label even if this results in there being no space for the AIDC.

(10) The HRI format must follow the rules of the UDI code-issuing entity.

(11) If the manufacturer is using RFID technology, a linear or 2D bar code in line with the standard provided by the issuing entities shall also be provided on the label.

(12) Subject to sub-paragraph (13), devices that are reusable—

(a) must bear a UDI carrier on the device itself; and

(b) for reusable devices that require cleaning, disinfection, sterilisation or refurbishing between patient uses, the UDI carrier must be permanent and readable after each process performed to make the device ready for the subsequent use throughout the intended lifetime of the device.

(13) The requirements in sub-paragraph (12) do not apply to devices in the following circumstances—

(a) any type of direct marking would interfere with the safety or performance of the device;

(b) the device cannot be directly marked because it is not technologically feasible.

(14) The UDI carrier must be readable during normal use and throughout the intended lifetime of the device.

(15) If the UDI carrier is readily readable or, in the case of AIDC, scannable, through the device's packaging, the placing of the UDI carrier on the packaging is not required.

(16) In the case of single finished devices made up of multiple parts that must be assembled before their first use, it is sufficient to place the UDI carrier on only one part of each device.

(17) The UDI carrier must be placed in a manner such that the AIDC can be accessed during normal operation or storage.

(18) Bar code carriers that include both a UDI-DI and a UDI-PI may also include essential data for the device to operate or other data.

General principles of the UDI database

8.—(1) The UDI database must support the use of all core UDI database data elements referred to in Part B of this Schedule.

(2) Manufacturers must be responsible for the initial submission and updates of the identifying information and other device data elements in the UDI database.

(3) Appropriate methods or procedures for validation of the data provided must be implemented.

(4) Manufacturers must periodically verify the correctness of all of the data relevant to devices they have placed on the market, except for devices that are no longer available on the market.

(5) The presence of the device UDI-DI in the UDI database shall not be assumed to mean that the device is in conformity with Part VIII.

(6) The database must allow for the linking of all the packaging levels of the device.

(7) The data for new UDI-DIs must be available at the time the device is placed on the market.

(8) Manufacturers must update the relevant UDI database record within 30 days of a change being made to an element, which does not require a new UDI-DI.

(9) Internationally-accepted standards for data submission and updates must, wherever possible, be used by the UDI database.

(10) The user interface must be available in English.

(11) Data relating to devices that are no longer available on the market must be retained in the UDI database.

Rules for specific device types

Implantable devices

9.—(1) Implantable devices must, at their lowest level of packaging, be identified, or marked using AIDC, with a UDI (UDI-DI plus UDI-PI);

(2) The UDI-PI shall have at least the following characteristics—

(a) the serial number for active implantable devices,

(b) the serial number or lot number for other implantable devices.

(3) The UDI of the implantable device shall be identifiable prior to implantation.

Reusable devices requiring cleaning, disinfection, sterilisation or refurbishing between uses

(4) The UDI for reusable devices must be placed on the device and be readable after each procedure to make the device ready for the next use.

(5) The UDI-PI characteristics such as the lot or serial number shall be defined by the manufacturer.

Systems and procedure packs as referred to in regulation 89

10.—(1) The person referred to in regulation 89 is responsible for identifying the system or procedure pack with a UDI including both UDI-DI and UDI-PI.

(2) Device contents of system or procedure packs must bear a UDI carrier on their packaging or on the device itself except where—

(a) individual single-use disposable devices, the uses of which are generally known to the persons by whom they are intended to be used, which are contained within a system or procedure pack, and which are not intended for individual use outside the context of the system or procedure pack, are not required to bear their own UDI carrier;

(b) devices that are exempted from bearing a UDI carrier on the relevant level of packaging shall not be required to bear a UDI carrier when included within a system or procedure pack.

(3) The UDI carrier should be placed on system and procedure packs as follows—

(a) the system or procedure pack UDI carrier must, as a general rule, be affixed to the outside of the packaging;

(b) the UDI carrier must be readable, or, in the case of AIDC, scannable, whether placed on the outside of the packaging of the system or procedure pack or inside transparent packaging.

Configurable devices

11.—(1) A UDI must be assigned to the configurable device in its entirety and shall be called the configurable device UDI.

(2) The configurable device UDI-DI must be assigned to groups of configurations, not per configuration within the group. A group of configurations is defined as the collection of possible configurations for a given device as described in the technical documentation.

(3) A configurable device UDI-PI must be assigned to each individual configurable device.

(4) The carrier of the configurable device UDI must be placed on the assembly that is most unlikely to be exchanged during the lifetime of the system and must be identified as the configurable device UDI.

(5) Each component that is considered a device and is commercially available on its own must be assigned a separate UDI.

Device software

12.—(1) The UDI assignment criteria for device software are—

(a) the UDI must be assigned at the system level of the software but only software which is commercially available on its own and software which constitutes a device in itself is subject to that requirement;

(b) the software identification must be considered to be the manufacturing control mechanism and must be displayed in the UDI-PI.

(2) A new UDI-DI is required whenever there is a modification that changes—

(a) the original performance;

(b) the safety or the intended use of the software; or

(c) interpretation of the data;

and such modifications include new or modified algorithms, database structures, operating platform, architecture or new user interfaces or new channels for interoperability.

(3) Minor software revisions—

(a) require a new UDI-PI and not a new UDI-DI;

(b) are generally associated with bug fixes, usability enhancements that are not for safety purposes, security patches or operating efficiency; and

(c) must be identified by a manufacturer-specific form of identification.

(4) the UDI placement criteria for software are—

(a) where the software is delivered on a physical medium, for example CD or DVD, each packaging level must bear the human readable and AIDC representation of the complete UDI;

(b) the UDI that is applied to the physical medium containing the software and its packaging must be identical to the UDI assigned to the system level software;

(c) the UDI must be provided on a readily accessible screen for the user in an easily-readable plain-text format, such as an ‘about’ file, or included on the start-up screen;

(d) software lacking a user interface such as middleware for image conversion, must be capable of transmitting the UDI through an application programming interface (API);

(e) only the human readable portion of the UDI is required in electronic displays of the software but the marking of UDI using AIDC is not to be required in the electronic displays, such as on the ‘about’ menu or splash screen (a window consisting of an image or logo typically used to notify the user that a programme is in the process of loading) etc.;

(f) the human readable format of the UDI for the software must include the Application Identifiers (AI) for the standard used by the issuing entities, so as to assist the user in identifying the UDI and determining which standard is being used to create the UDI.

SCHEDULE 9 Regulation 1A

Classification rules

Chapter 1

Definitions specific to classification rules

1. In this Schedule—

(a) in relation to the duration of use—

"long term" means normally intended for continuous use for more than 30 days;

"short term" means normally intended for continuous use for between 60 minutes and 30 days;

"transient" means normally intended for continuous use for less than 60 minutes;

(b) in relation to invasive and active devices—

"active device intended for diagnosis and monitoring" means any active device used, whether alone or in combination with other devices, to supply information for detecting, diagnosing, monitoring or treating physiological conditions, states of health, illnesses or congenital deformities;

"active therapeutic device" means any active device used, whether alone or in combination with other devices, to support, modify, replace or restore biological functions or structures with a view to treatment or alleviation of an illness, injury or disability;

"body orifice" means any natural opening in the body, as well as the external surface of the eyeball, or any permanent artificial opening, such as a stoma;

"central circulatory system" means the following blood vessels—

arteriae pulmonales, aorta ascendens, arcus aortae, aorta descendens to the bifurcatio aortae, arteriae coronariae, arteria carotis communis, arteria carotis externa, arteria carotis interna, arteriae cerebrales, truncus brachiocephalicus, venae cordis, venae pulmonales, vena cava superior and vena cava inferior;

"central nervous system" means the brain, meninges and spinal cord;

"injured skin or mucous membrane" means an area of skin or a mucous membrane presenting a pathological change or change following disease or a wound;

"reusable surgical instrument" means an instrument intended for surgical use in cutting, drilling, sawing, scratching, scraping, clamping, retracting, clipping or similar procedures, without a connection to an active device and which is intended by the manufacturer to be reused after appropriate procedures such as cleaning, disinfection and sterilisation have been carried out;

"surgically invasive device" means—

(a) an invasive device which penetrates inside the body through the surface of the body, including through mucous membranes of body orifices with the aid or in the context of a surgical operation; and

(b) a device which penetrates other than through a body orifice;

Chapter 2

Implementing rules

2.—(1) Application of the classification rules must be governed by the intended purpose of the devices.

(2) If the device in question is intended to be used in combination with another device—

(a) the classification rules must apply separately to each of the devices;

(b) accessories for a medical device and for a product listed in Schedule 16 must be classified in their own right separately from the device with which they are used.

(3) Software, which drives a device or influences the use of a device, must fall within the same class as the device but, if the software is independent of any other device, it must be classified in its own right.

(4) If the device is not intended to be used solely or principally in a specific part of the body, it must be considered and classified on the basis of the most critical specified use.

(5) If several rules or, if, within the same rule, several sub-rules, apply to the same device based on the device's intended purpose, the strictest rule and sub-rule resulting in the higher classification must apply.

(6) In calculating the duration of use referred to in paragraph 1(a), continuous use means—

(a) the entire duration of use of the same device without regard to temporary interruption of use during a procedure or temporary removal for purposes such as cleaning or disinfection of the device (and, whether the interruption of use or the removal is temporary must be established in relation to the duration of the use prior to and after the period when the use is interrupted or the device removed);

(b) the accumulated use of a device that is intended by the manufacturer to be replaced immediately with another of the same type.

(7) A device is considered to allow direct diagnosis when it provides the diagnosis of the disease or condition in question by itself or when it provides decisive information for the diagnosis.

Chapter 3

Classification rules

Non-invasive devices

Rule 1

3.—(1) All non-invasive devices are classified as Class I, unless one of the other rules set out in this Schedule applies.

Rule 2

(2) All non-invasive devices intended for channelling or storing blood, body liquids, cells or tissues, liquids or gases for the purpose of eventual infusion, administration or introduction into the body are classified as Class IIa—

(a) if they may be connected to a Class IIa, Class IIb or Class III active device; or

(b) if they are intended for use for channelling or storing blood or other body liquids or for storing organs, parts of organs or body cells and tissues, except for blood bags which are classified as Class IIb;

such devices are classified as Class I, in all other cases.
Rule 3

(3) All non-invasive devices intended for modifying the biological or chemical composition of human tissues or cells, blood, other body liquids or other liquids intended for implantation or administration into the body are classified as Class IIb, unless the treatment for which the device is used consists of filtration, centrifugation or exchanges of gas, heat, in which case they are classified as Class IIa.

(4) All non-invasive devices consisting of a substance or a mixture of substances intended to be used in vitro in direct contact with human cells, tissues or organs taken from the human body or used in vitro with human embryos before their implantation or administration into the body are classified as Class III.
Rule 4

(5) All non-invasive devices which come into contact with injured skin or mucous membrane are classified as—

(a) Class I if they are intended to be used as a mechanical barrier, for compression or for absorption of exudates;

(b) Class IIb if they are intended to be used principally for injuries to skin which have breached the dermis or mucous membrane and can only heal by secondary intent;

(c) Class IIa if they are principally intended to manage the micro-environment of injured skin or mucous membrane;

(d) Class IIa in all other cases.

This rule also applies to the invasive devices that come into contact with injured mucous membrane.

Invasive devices

Rule 5

4.—(1) All invasive devices with respect to body orifices, other than surgically invasive devices, which are not intended for connection to an active device or which are intended for connection to a Class I active device are classified as—

(a) Class I if they are intended for transient use;

(b) Class IIa if they are intended for short-term use, except if they are used in the oral cavity as far as the pharynx, in an ear canal up to the ear drum or in the nasal cavity, in which case they are classified as class I;

(c) Class IIb if they are intended for long-term use, except if they are used in the oral cavity as far as the pharynx, in an ear canal up to the ear drum or in the nasal cavity and are not liable to be absorbed by the mucous membrane, in which case they are classified as class IIa.

All invasive devices with respect to body orifices, other than surgically invasive devices, intended for connection to a Class IIa, Class IIb or Class III active device, are classified as Class IIa.

Rule 6

(2) All surgically invasive devices intended for transient use are classified as class IIa unless they—

(a) are intended specifically to control, diagnose, monitor or correct a defect of the heart or of the central circulatory system through direct contact with those parts of the body, in which case they are classified as Class III;

(b) are reusable surgical instruments, in which case they are classified as class I;

(c) are intended specifically for use in direct contact with the heart or central circulatory system or the central nervous system, in which case they are classified as Class III;

(d) are intended to supply energy in the form of ionising radiation in which case they are classified as Class IIb;

(e) have a biological effect or are wholly or mainly absorbed in which case they are classified as Class IIb; or

(f) are intended to administer medicinal products by means of a delivery system, if such administration of a medicinal product is done in a manner that is potentially hazardous taking account of the mode of application, in which case they are classified as Class IIb.

Rule 7

(3) All surgically invasive devices intended for short-term use are classified as Class IIa unless they—

(a) are intended specifically to control, diagnose, monitor or correct a defect of the heart or of the central circulatory system through direct contact with those parts of the body, in which case they are classified as class III;

(b) are intended specifically for use in direct contact with the heart or central circulatory system or the central nervous system, in which case they are classified as Class III;

(c) are intended to supply energy in the form of ionizing radiation in which case they are classified as Class IIb;

(d) have a biological effect or are wholly or mainly absorbed in which case they are classified as Class III;

(e) are intended to undergo chemical change in the body in which case they are classified as Class IIb, except if the devices are placed in the teeth; or

(f) are intended to administer medicines, in which case they are classified as Class IIb.

Rule 8

(4) All implantable devices and long-term surgically invasive devices are classified as Class IIb unless they—

(a) are intended to be placed in the teeth, in which case they are classified as Class IIa;

(b) are intended to be used in direct contact with the heart, the central circulatory system or the central nervous system, in which case they are classified as Class III;

(c) are intended to undergo chemical change in the body in which case they are classified as Class III, except if the devices are placed in the teeth;

(d) are intended to administer medicinal products, in which case they are classified as Class III;

(e) are active implantable devices or their accessories, in which case they are classified as Class III;

(f) are breast implants or surgical meshes, in which cases they are classified as Class III;

(g) are total or partial joint replacements, in which case they are classified as Class III, with the exception of ancillary components such as screws, wedges, plates and instruments; or

(h) are spinal disc replacement implants or are implantable devices that come into contact with the spinal column, in which case they are classified as Class III with the exception of components such as screws, wedges, plates and instruments.

Active devices

Rule 9

5.—(1) All active therapeutic devices intended to administer or exchange energy are classified as Class IIa unless their characteristics are such that they may administer energy to or exchange energy with the human body in a potentially hazardous way, taking account of the nature, the density and site of application of the energy, in which case they are classified as Class IIb.

(2) All active devices intended to control or monitor the performance of active therapeutic Class IIb devices, or intended directly to influence the performance of such devices are classified as Class IIb.

(3) All active devices intended to emit ionizing radiation for therapeutic purposes, including devices which control or monitor such devices, or which directly influence their performance, are classified as Class IIb.

(4) All active devices that are intended for controlling, monitoring or directly influencing the performance of active implantable devices are classified as Class III.

Rule 10

(5) Active devices intended for diagnosis and monitoring are classified as Class IIa—

(a) if they are intended to supply energy which will be absorbed by the human body, except for devices intended to illuminate the patient's body, in the visible spectrum, in which case they are classified as class I;

(b) if they are intended to image in vivo distribution of radiopharmaceuticals;

(c) if they are intended to image in vivo distribution of radiopharmaceuticals; or

(d) if they are intended to allow direct diagnosis or monitoring of vital physiological processes, unless they are specifically intended for monitoring of vital physiological parameters and the nature of variations of those parameters is such that it could result in immediate danger to the patient, for instance variations in cardiac performance, respiration, activity of the central nervous system, or they are intended for diagnosis in clinical situations where the patient is in immediate danger, in which cases they are classified as Class IIb.

(6) Active devices intended to emit ionizing radiation and intended for diagnostic or therapeutic radiology, including interventional radiology devices and devices which control or monitor such devices, or which directly influence their performance, are classified as Class IIb.

Rule 11

(7) Software intended to provide information which is used to take decisions with diagnosis or therapeutic purposes is classified as Class IIa, except if such decisions have an impact that may cause—

(a) death or an irreversible deterioration of a person's state of health, in which case it is in class III; or

(b) a serious deterioration of a person's state of health or a surgical intervention, in which case it is classified as Class IIb.

(8) Software intended to monitor physiological processes is classified as Class IIa, except if it is intended for monitoring of vital physiological parameters, where the nature of variations of those parameters is such that it could result in immediate danger to the patient, in which case it is classified as Class IIb.

(9) All other software is classified as Class I.

Rule 12

(10) All active devices intended to administer or remove medicinal products, body liquids or other substances to or from the body are classified as Class IIa, unless this is done in a manner that is potentially hazardous, taking account of the nature of the substances involved, of the part of the body concerned and of the mode of application in which case they are classified as Class IIb.

Rule 13

(11) All other active devices are classified as Class I.

Special rules

Rule 14

6.—(1) All devices incorporating, as an integral part, a substance which, if used separately, can be considered to be a medicinal product, as defined in regulation 2(1) of the Human Medicines Regulations 2012, including a medicinal product derived from human blood or human plasma, and that has an action ancillary to that of the devices, are classified as Class III.

Rule 15

(2) All devices used for contraception or prevention of the transmission of sexually transmitted diseases are classified as Class IIb, unless they are implantable or long term invasive devices, in which case they are classified as class III.

Rule 16

(3) All devices intended specifically to be used for disinfecting, cleaning, rinsing or, where appropriate, hydrating contact lenses are classified as Class IIb.

(4) All devices intended specifically to be used for disinfecting or sterilising medical devices are classified as Class IIa, unless they are disinfecting solutions or washer-disinfectors intended specifically to be used for disinfecting invasive devices, as the end point of processing, in which case they are classified as Class IIb.

(5) Rule 16 does not apply to devices that are intended to clean devices other than contact lenses by means of physical action only.

Rule 17

(6) Devices specifically intended for recording of diagnostic images generated by X-ray radiation are classified as Class IIa.

Rule 18

(7) All devices manufactured utilising tissues or cells of human or animal origin, or their derivatives, which are non-viable or rendered non-viable, are classified as class III, unless such devices are manufactured utilising tissues or cells of animal origin, or their derivatives, which are non-viable or rendered non-viable and are devices intended to come into contact with intact skin only.

Rule 19

(8) All devices incorporating or consisting of nanomaterial are classified as—

(a) Class III if they present a high or medium potential for internal exposure;

(b) Class IIb if they present a low potential for internal exposure;

(c) Class IIa if they present a negligible potential for internal exposure.

Rule 20

(9) All invasive devices with respect to body orifices, other than surgically invasive devices, which are intended to administer medicinal products by inhalation are classified as Class IIa, unless their mode of action has an essential impact on the efficacy and safety of the administered medicinal product or they are intended to treat life-threatening conditions, in which case they are classified as Class IIb.

Rule 21

(10) Devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body via a body orifice or applied to the skin and that are absorbed by or locally dispersed in the human body are classified as—

(a) Class III if they, or their products of metabolism, are systemically absorbed by the human body in order to achieve the intended purpose;

(b) Class III if they achieve their intended purpose in the stomach or lower gastrointestinal tract and they, or their products of metabolism, are systemically absorbed by the human body;

(c) Class IIa if they are applied to the skin or if they are applied in the nasal or oral cavity as far as the pharynx, and achieve their intended purpose on those cavities;

(d) Class IIb in all other cases.

Rule 22

(11) Active therapeutic devices with an integrated or incorporated diagnostic function which significantly determines the patient management by the device, such as closed loop systems or automated external defibrillators, are classified as Class III.

SCHEDULE 10

Regulation 1A

Conformity assessment based on quality management system on assessment of technical documentation

Chapter 1

Quality management system

1.—(1) The manufacturer must—

(a) establish, document and implement a quality management system as described in regulation 76(13);

(b) maintain the effectiveness of that system throughout the life cycle of the device concerned;

(c) ensure the application of the quality management system as specified in sub-paragraphs (2) to (6);

(d) comply with the surveillance requirements as specified in sub-paragraph (7).

Quality management system assessment

(2) The manufacturer must lodge an application for assessment of its quality management system with a notified body and that application must include—

(a) the name of the manufacturer and address of its registered place of business and any additional manufacturing site covered by the quality management system, and, if the manufacturer's application is lodged by its authorised representative, the name of the

authorised representative and the address of the authorised representative's registered place of business;

(b) all relevant information on the device or group of devices covered by the quality management system;

(c) a written declaration that no application has been lodged with any other notified body for the same device-related quality management system, or information about any previous application for the same device-related quality management system;

(d) a draft of a declaration of conformity for the device model covered by the conformity assessment procedure;

(e) the documentation on the manufacturer's quality management system;

(f) a documented description of the procedures in place to fulfil the obligations arising from the quality management system and required under Part VIII and the undertaking by the manufacturer in question to apply those procedures;

(g) the documentation on the manufacturer's post-market surveillance system and, where applicable, on the PMCF plan, and the procedures put in place to ensure compliance with the obligations resulting from the provisions on vigilance set out in regulations 125 to 129;

(h) a description of the procedures in place to keep up to date the post-market surveillance system, and, where applicable, the PMCF plan, and the procedures ensuring compliance with the obligations resulting from the provisions on vigilance set out in regulations 125 to 129, as well as the undertaking by the manufacturer to apply those procedures;

(i) documentation on the clinical evaluation plan;

(j) a description of the procedures in place to keep up to date the clinical evaluation plan, taking into account the state of the art.

(3) Implementation of the quality management system must ensure compliance with Part VIII and all the elements, requirements and provisions adopted by the manufacturer for its quality management system must be documented in a systematic and orderly manner in the form of a quality manual and written policies and procedures such as quality programmes, quality plans and quality records.

(4) The documentation to be submitted for the assessment of the quality management system must include an adequate description of, in particular—

(a) the manufacturer's quality objectives;

(b) the organisation of the business and in particular—

(i) the organisational structures with the assignment of staff responsibilities in relation to critical procedures, the responsibilities of the managerial staff and their organisational authority;

(ii) the methods of monitoring whether the operation of the quality management system is efficient and in particular the ability of that system to achieve the desired design and device quality, including control of devices which fail to conform;

(iii) where the design, manufacture, final verification and testing of the devices, or parts of any of those processes, is carried out by another party, the methods of monitoring the efficient operation of the quality management system and in particular the type and extent of control applied to the other party;

(iv) where applicable, the draft mandate for the designation of an authorised representative and a letter of intention from the authorised representative to accept the mandate;

(c) the procedures and techniques for monitoring, verifying, validating and controlling the design of devices and the corresponding documentation as well as the data and records arising from those procedures and techniques.

(d) those procedures and techniques must specifically cover—

(i) the strategy for regulatory compliance, including processes for identification of relevant legal requirements, qualification, classification, handling of equivalence, choice of and compliance with conformity assessment procedures;

(ii) risk management as referred to in paragraph 3 of Schedule 3;

(iii) the clinical evaluation, pursuant to regulation 105 and Schedule 14, including post-market clinical follow-up;

(iv) solutions for fulfilling the applicable specific requirements regarding design and construction, including appropriate pre-clinical evaluation, in particular the requirements of Part 2 of Schedule 3;

(v) solutions for fulfilling the applicable specific requirements regarding the information to be supplied with the device, in particular the requirements of Part 3 of Schedule 3;

(vi) the device identification procedures drawn up and kept up to date from drawings, specifications or other relevant documents at every stage of manufacture;

(vii) management of design or quality management system changes;

(e) the verification and quality assurance techniques at the manufacturing stage and in particular the processes and procedures which are to be used, particularly as regards sterilisation and the relevant documents;

(f) the appropriate tests and trials which are to be carried out before, during and after manufacture including—

(i) the frequency with which they are to take place;

(ii) the test equipment to be used;

(iii) a means of adequately tracing back the calibration of that test equipment.

(5) The manufacturers must grant the notified body access to the technical documentation referred to in Schedules 4 and 5.

(6) The manufacturer must inform the notified body which approved the quality management system of any plan for substantial changes to the quality management system, or the device-range covered and the approval of any substantial change to the quality management system or the device-range covered must take the form of a supplement to the quality management system certificate.

Surveillance

(7) The manufacturer must—

(a) give authorisation to the notified body to carry out all the necessary audits, including on- site audits;

(b) supply the notified body with all relevant information, in particular—

(i) the documentation on its quality management system;

(ii) documentation on any findings and conclusions resulting from the application of the post-market surveillance plan, including the PMCF plan, for a representative sample of devices, and of the provisions on vigilance set out in regulations 125 to 129;

(iii) the data stipulated in the part of the quality management system relating to design, such as the results of analyses, calculations, tests and the solutions adopted regarding the risk-management as referred to in paragraph 4 of Schedule 3;

(iv) the data stipulated in the part of the quality management system relating to manufacture, such as quality control reports and test data, calibration data, and records on the qualifications of the personnel concerned.

Chapter 2

Assessment of technical documentation

2.—(1) In addition to the obligations laid down in paragraph 1, for Class III devices and those Class IIb implantable devices specified in regulation 98(4), the manufacturer must lodge with the notified body an application for assessment of the technical documentation relating to the device which it plans to place on the market or put into service and which is covered by the quality management system referred to in paragraph 1.

(2) The application must describe the design, manufacture and performance of the device in question and must include the technical documentation as referred to in Schedules 4 and 5.

(3) Upon completing the manufacture of each batch of devices that incorporate, as an integral part, a medicinal substance which, if used separately, would be considered to be a medicinal product derived from human blood or human plasma as referred to in the first sub-paragraph of regulation 68(8), the manufacturer shall inform the notified body of the release of the batch of devices and send it the official certificate concerning the release of the batch of human blood or plasma derivative used in the device, issued by a laboratory designated for that purpose by an EU Member State in accordance with Article 114(2) of Directive 2001/83/EC or, where applicable, a laboratory provided or arranged in accordance with section 57(1)(d) of the Health and Social Care Act 2012(**6**).

Chapter 3

Administrative provisions

3.—(1) The manufacturer or, if the manufacturer is not established in the United Kingdom, the person placing the product on the market must, for a period ending no sooner than 10 years, and in the case of implantable devices no sooner than 15 years, after the last device has been placed on the market, keep at the disposal of the Secretary of State—

(a) the EU declaration of conformity;

(b) the documentation referred to in paragraph 1(2)(e) and in particular the data and records arising from the procedures referred to paragraph 1(4)(c);

(c) information on the changes referred to in paragraph 1(6);

(d) the documentation referred to in paragraph 2(2);

(e) the decisions and reports from the notified body.

(2) The documentation in sub-paragraph (1) must be kept so that it is available to the Secretary of State throughout the relevant period specified in sub-paragraph (1) irrespective of the continued

(**6**) 2012 c. 7.

status (and whether the person continues trading or not) of the manufacturer or person placing the product on the market.

SCHEDULE 11

Regulation 1A

Conformity assessment based on type examination

1. In this Schedule a "type examination" is a procedure whereby a notified body ascertains and certifies that a device, including its technical documentation and relevant life cycle processes and a corresponding representative sample of the device production envisaged, fulfils the relevant provisions.

Application

2. The manufacturer must lodge an application for assessment based on type examination with a notified body and the application must—

(a) include the name of the manufacturer and address of the registered place of business of the manufacturer and, if the application is lodged by the authorised representative, the name of the authorised representative and the address of its registered place of business;

(b) include the technical documentation referred to in Schedules 4 and 5;

(c) make available to the notified body a representative sample of the device production envisaged ('type') (and provide other samples if requested by the notified body);

(d) make a written declaration that no application has been lodged with any other notified body for the same type, or information about any previous application for the same type that was refused by another notified body or was withdrawn by the manufacturer or its authorised representative before that other notified body made its final assessment.

Assessment

3. The assessment must be carried out by a notified body in accordance with the obligations placed on such a body by Section 3 of Annex X of Regulation (EU) 2017/745.

Certificates

4. The certificate must be completed by a notified body in accordance with Section 4 of Annex X of Regulation (EU) 2017/745.

Changes to type

5.—(1) The applicant must inform the notified body which issued the type-examination certificate of any planned change to the approved type or of its intended purpose and conditions of use.

(2) Changes to the approved device including limitations of its intended purpose and conditions of use must be further approved by the notified body which issued the EU type-examination certificate where such changes may affect conformity with the general safety and performance requirements or with the conditions prescribed for use of the product.

(3) The approval of any change to the approved type must take the form of a supplement to the type-examination certificate.

(4) Changes to the intended purpose and conditions of use of the approved device, with the exception of limitations of the intended purpose and conditions of use, require a new application for a conformity assessment.

Administrative provisions

6.—(1) The manufacturer or, if the manufacturer is not established in the United Kingdom, the person placing the product on the market must, for a period ending no sooner than 10 years, and in the case of implantable devices no sooner than 15 years, after the last device has been placed on the market, keep at the disposal of the Secretary of State—

(a) the documentation referred to in paragraph 2(b);

(b) information on changes referred to in paragraph 5;

(c) copies of type-examination certificates, scientific opinions and reports (and any supplements or additions to those reports).

(2) The documentation in sub-paragraph (1) must be kept so that it is available to the Secretary of State throughout the relevant period specified in sub-paragraph (1) irrespective of the continued status (and whether the person continues trading or not) of the manufacturer or person placing the product on the market.

SCHEDULE 12

Regulation 1A

Conformity assessment based on the product conformity verification

1. A "conformity assessment based on product conformity verification" is a procedure the purpose of which is to ensure that devices conform to the type for which a type-examination certificate has been issued, and that they meet the provisions of Part VIII which apply to them.

2. Where a type-examination certificate mentioned in paragraph 4 of Schedule 11 has been issued, the manufacturer may either apply the procedure set out in Part A (production quality assurance) or the procedure set out in Part B (product verification) of this Schedule.

3. Manufacturers of Class IIa devices, may draw up the technical documentation set out in Schedules 3 and 4 and follow the conformity assessment procedure set out in this Schedule.

PART A

Production quality assurance

4. The manufacturer must ensure that the quality management system approved for the manufacture of the devices concerned is implemented, must carry out a final verification, as specified in paragraph 6, and must be subject to the surveillance referred to in paragraph 7.

5. Subject to paragraph 8, when the manufacturer fulfils the obligations laid down in paragraph 4, it must draw up and keep a declaration of conformity in accordance with regulation 86 and Schedule 6 for the device covered by the conformity assessment procedure and by issuing an EU declaration of conformity, the manufacturer is deemed to ensure and to declare that the device concerned conforms to the type described in the type-examination certificate and meets the requirements of Part VIII which apply to the device.

Quality management system

6.—(1) The manufacturer must lodge an application for assessment of its quality management system with a notified body and that application must include—

(a) all elements listed in paragraph 1(2) of Schedule 10;

(b) the technical documentation referred to in Schedules 4 and 5 for the types approved;

(c) a copy of the type-examination certificates referred to in paragraph 4 of Schedule 11 but if the type-examination certificates have been issued by the same notified body with which the application is lodged, a reference to the technical documentation and its updates and the certificates issued shall also be included in the application.

(2) Implementation of the quality management system must be such as to ensure that there is compliance with the type described in the type-examination certificate and with the provisions of Part VIII which apply to the devices at each stage.

(3) All the elements, requirements and provisions adopted by the manufacturer for its quality management system must be documented in a systematic and orderly manner in the form of a quality manual and written policies and procedures, such as quality programmes, quality plans and quality records.

(4) The documentation in sub-paragraph (3) must, in particular, include an adequate description of all elements listed in paragraphs (a), (b), (d) and (e) of paragraph 1(4) of Schedule 10.

(5) The requirement in paragraph 1(6) of Schedule 10 applies.

(6) Upon completing the manufacture of each batch of devices that incorporate, as an integral part, a medicinal substance which, if used separately, would be considered to be a medicinal product derived from human blood or human plasma referred to in regulation 68(8), the manufacturer shall inform the notified body of the release of the batch of devices and send it the official certificate concerning the release of the batch of human blood or plasma derivative used in the device, issued by a laboratory designated for that purpose by an EU Member State in accordance with Article 114(2) of Directive 2001/83/EC or, where applicable, a laboratory provided or arranged in accordance with section 57(1)(d) of the Health and Social Care Act 2012.

Administrative provisions

7.—(1) Subject to paragraph 8(3), the manufacturer or, if the manufacturer is not established in the United Kingdom, the person placing the product on the market must, for a period ending no sooner than 10 years, and in the case of implantable devices no sooner than 15 years, after the last device has been placed on the market, keep at the disposal of the Secretary of State—

(a) the declaration of conformity;

(b) the documentation referred to in paragraph (e) of paragraph 1(2) of Schedule 10;

(c) the documentation referred to in paragraph (h) of paragraph 1(2) of Schedule 10, including the type examination certificate referred to in Schedule 11;

(d) information on the changes referred to in paragraph 1(6) of Schedule 10;

(e) the decisions and reports from the notified body.

(2) The documentation in paragraphs (a) to (e) of sub-paragraph (1) must be kept so that it is available to the Secretary of State throughout the relevant period specified in sub-paragraph (1) irrespective of the continued status (and whether the person continues trading or not) of the manufacturer or person placing the product on the market.

Application to Class IIa devices

8.—(1) For Class IIa devices, by making the declaration of conformity the manufacturer is deemed to ensure and declare that those devices are manufactured in conformity with the technical documentation referred to in Schedules 4 and 5.

(2) The manufacturer must follow the procedure set down in Section 10.2 to 10.4 of Annex XI of Regulation (EU) 2017/745 and obtain the certificate relevant to that Part of that Annex.

(3) The manufacturer or, if the manufacturer is not established in the United Kingdom, the person placing the product on the market must, for a period ending no sooner than 10 years after the last device has been placed on the market, keep at the disposal of the Secretary of State—

(a) the declaration of conformity;

(b) the technical documentation referred to in Schedules 4 and 5;

(c) the certificate referred to in sub-paragraph (2).

(5) The documentation in sub-paragraph (3) must be kept so that it is available to the Secretary of State throughout the relevant period specified in sub-paragraph (3) irrespective of the continued status (and whether the person continues trading or not) of the manufacturer or person placing the product on the market.

PART B

Product Verification

9. "Product verification" means a procedure whereby, after examination of every manufactured device, the manufacturer, by issuing a declaration of conformity in accordance with regulation 84 is deemed to ensure and declare that the devices which have been subject to the procedure set out in Sections 14 and 15 of Annex XI of Regulation (EU) 2017/745 conform to the type described in the type-examination certificate and meet the requirements of Part VIII which apply to them.

10.—(1) The manufacturer must take all the measures necessary to ensure that the manufacturing process produces devices which conform to the type described in the type-examination certificate and to the requirements of Part VIII which apply to them.

(2) Prior to the start of manufacture, the manufacturer must prepare documents defining the manufacturing process, in particular, and where applicable, as regards sterilisation, together with all routine, pre-established procedures to be implemented to ensure homogeneous production and, where appropriate, conformity of the devices with the type described in the type-examination certificate and with the requirements of Part VIII which apply to them.

(3) In addition, for devices placed on the market in a sterile condition, and only for those aspects of the manufacturing process designed to secure and maintain sterility, the manufacturer must apply the provisions of paragraph 6 and comply with the surveillance obligations.

(4) The manufacturer must undertake to institute and keep up to date a post-market surveillance plan, including a PMCF plan, and the procedures ensuring compliance with the obligations of the manufacturer resulting from the provisions on vigilance and post-market surveillance system set out in regulations 122 to 125.

(5) Upon completing the manufacture of each batch of devices that incorporate, as an integral part, a medicinal substance which, if used separately, would be considered to be a medicinal product derived from human blood or human plasma referred to in the first sub-paragraph of regulation 68(8), the manufacturer shall inform the notified body of the release of the batch of devices and send it the official certificate concerning the release of the batch of human blood or

plasma derivative used in the device, issued by a laboratory designated for that purpose by an EU Member State in accordance with Article 114(2) of Directive 2001/83/EC, or, where applicable, a laboratory provided or arranged in accordance with section 57(1)(d) of the Health and Social Care Act 2012.

Administrative provisions

11.—(1) Subject to paragraph 12, the manufacturer or, if the manufacturer is not established in the United Kingdom, the person placing the product on the market must, for a period ending no sooner than 10 years and, in the case of implantable devices, 15 years after the last device has been placed on the market, keep at the disposal of the Secretary of State—

(a) the EU declaration of conformity;

(b) the documentation referred to in paragraph (2);

(c) the verification certificate referred to in Section 15.2 of Annex XI of Regulation (EU) 2017/745;

(d) the type-examination certificate referred to in Schedule 11.

(2) The documentation in sub-paragraph (1) must be kept so that it is available to the Secretary of State throughout the relevant period specified in sub-paragraph (1) irrespective of the continued status (and whether the person continues trading or not) of the manufacturer or person placing the product on the market.

Application to Class IIa devices

12.—(1) By virtue of the declaration of conformity the manufacturer is deemed to ensure and to declare that the Class IIa devices in question are manufactured in conformity with the technical documentation referred to in Schedules 4 and 5 meet the requirements of Part VIII which apply to them.

(2) The manufacturer must obtain a certificate issued in pursuance of Part B of Annex XI of Regulation (EU) 2017/745.

(3) The manufacturer or, if the manufacturer is not established in the United Kingdom, the person placing the product on the market must, for a period ending no sooner than 10 years after the last device has been placed on the market, keep at the disposal of the Secretary of State—

(a) the declaration of conformity;

(b) the technical documentation referred to Schedules 4 and 5;

(c) the certificate referred to in sub-paragraph (2).

(4) The documentation in sub-paragraph (3) must be kept so that it is available to the Secretary of State throughout the relevant period specified in sub-paragraph (3) irrespective of the continued status (and whether the person continues trading or not) of the manufacturer or person placing the product on the market.

SCHEDULE 13

Regulation 1A

Procedure for custom-made devices

1. For custom-made devices the manufacturer or its authorised representative must draw up a statement containing all of the following information—

(a) the name and address of the manufacturer, and of all manufacturing sites;

(b) if applicable, the name and address of the person placing the product on the market;

(c) data allowing identification of the device in question;

(d) a statement that the device is intended for exclusive use by a particular patient or user, identified by name, an acronym or a numerical code;

(e) the name of the person who made out the prescription and, where applicable, the name of the health institution concerned;

(f) the specific characteristics of the product as indicated by the prescription;

(g) a statement that the device in question conforms to the general safety and performance requirements set out in Schedule 3 and, where applicable, indicating which general safety and performance requirements have not been fully met, together with the grounds;

(h) where applicable, an indication that the device contains or incorporates a medicinal substance, including a human blood or plasma derivative, or tissues or cells of human origin, or of animal origin as referred to in Regulation (EU) No 722/2012.

2. The manufacturer must undertake to keep available for the Secretary of State documentation that indicates its manufacturing site or sites and allows an understanding to be formed of the design, manufacture and performance of the device, including the expected performance, so as to allow assessment of conformity with the requirements of Part VIII.

3. The manufacturer shall take all the measures necessary to ensure that the manufacturing process produces devices which are manufactured in accordance with the documentation referred to in paragraph 2.

4. The statement referred to in paragraph 1(g) must be kept for a period of at least 10 years after the device has been placed on the market and, in the case of implantable devices, the period must be at least 15 years.

5. The statement referred to in paragraph 4 must be kept so that it is available to the Secretary of State throughout the relevant period specified in paragraph 4 irrespective of the continued status (and whether the person continues trading or not) of the manufacturer or person placing the product on the market.

6. The manufacturer must—

(a) review and document experience gained in the post-production phase, including from PMCF as referred to in Part B of Schedule 14;

(b) implement appropriate means to apply any necessary corrective action;

(c) report in accordance with regulation 125 to the Secretary of State any serious incidents or field safety corrective actions or both as soon as it learns of them.

SCHEDULE 14 Regulation 1A

Clinical evaluation and post market clinical follow-up

Part A

Clinical evaluation

1. Manufacturers must plan, continuously conduct and document a clinical evaluation and must—

(a) establish and update a clinical evaluation plan, which must include at least—

(i) an identification of the general safety and performance requirements that require support from relevant clinical data;

(ii) a specification of the intended purpose of the device;

(iii) a clear specification of intended target groups with clear indications and contra-indications;

(iv) a detailed description of intended clinical benefits to patients with relevant and specified clinical outcome parameters;

(v) a specification of methods to be used for examination of qualitative and quantitative aspects of clinical safety with clear reference to the determination of residual risks and side-effects;

(vi) an indicative list and specification of parameters to be used to determine, based on the state of the art in medicine, the acceptability of the benefit-risk ratio for the various indications and for the intended purpose or purposes of the device;

(vii) an indication of how benefit-risk issues relating to specific components such as use of pharmaceutical, non- viable animal or human tissues, are to be addressed;

(viii) a clinical development plan indicating progression from exploratory investigations, such as first-in-man studies, feasibility and pilot studies, to confirmatory investigations, such as pivotal clinical investigations, and a PMCF as referred to in Part B of this Schedule with an indication of milestones and a description of potential acceptance criteria;

(b) identify available clinical data relevant to the device and its intended purpose and any gaps in clinical evidence through a systematic scientific literature review;

(c) appraise all relevant clinical data by evaluating their suitability for establishing the safety and performance of the device;

(d) generate, through properly designed clinical investigations in accordance with the clinical development plan, any new or additional clinical data necessary to address outstanding issues;

(e) analyse all relevant clinical data in order to reach conclusions about the safety and clinical performance of the device including its clinical benefits.

2. The clinical evaluation must—

(a) be thorough and objective, and take into account both favourable and unfavourable data;

(b) be proportionate and appropriate (in terms of depth and extent) to the nature, classification, intended purpose and risks of the device in question, as well as to the manufacturer's claims in respect of the device.

3.—(1) A clinical evaluation may be based on clinical data relating to a device for which equivalence to the device in question can be demonstrated.

(2) The following characteristics must be taken into consideration for the demonstration of equivalence—

(a) technical characteristics where the device—

(i) is of similar design;

(ii) is used under similar conditions of use;

(iii) has similar specifications and properties including physicochemical properties such as intensity of energy, tensile strength, viscosity, surface characteristics, wavelength and software algorithms;

(iv) where relevant, uses similar deployment methods;

(v) has similar principles of operation and critical performance requirements;

(b) biological characteristics where the device uses the same materials or substances in contact with the same human tissues or body fluids for a similar kind and duration of contact and similar release characteristics of substances, including degradation products and leachables;

(c) clinical characteristics where the device—

(i) is used for the same clinical condition or purpose, including similar severity and stage of disease, at the same site in the body, in a similar population, including as regards age, anatomy and physiology;

(ii) has the same kind of user;

(iii) has similar relevant critical performance in view of the expected clinical effect for a specific intended purpose.

(3) The characteristics listed in the sub-paragraph (2) must—

(a) be similar to the extent that there would be no clinically significant difference in the safety and clinical performance of the device;

(b) be based on proper scientific justification;

(c) be clearly demonstrated that manufacturers have sufficient levels of access to the data relating to devices with which they are claiming equivalence in order to justify their claims of equivalence.

(4) The results of the clinical evaluation and the clinical evidence on which it is based must be documented in a clinical evaluation report which—

(a) must support the assessment of the conformity of the device;

(b) must include any non-clinical data generated from non-clinical testing and other relevant documentation which must allow the manufacturer to demonstrate conformity with the general safety and performance requirements and which must be part of the technical documentation for the device in question;

(c) must include as part of the technical documentation favourable and unfavourable data considered in the clinical evaluation.

PART B

Post –market clinical follow-up (PMCF)

4.—(1) PMCF must be addressed in the manufacturer's post-market surveillance plan.

(2) When conducting PMCF, the manufacturer must proactively collect and evaluate clinical data from the use in or on humans of a device which bears the CE marking and is placed on the market or put into service within its intended purpose as referred to in the relevant conformity assessment procedure, with the aim of confirming the safety and performance throughout the expected lifetime of the device, of ensuring the continued acceptability of identified risks and of detecting emerging risks on the basis of factual evidence.

5.—(1) PMCF must be performed pursuant to a documented method laid down in a PMCF plan.

(2) The PMCF plan must specify the methods and procedures for proactively collecting and evaluating clinical data with the aim of—

(a) confirming the safety and performance of the device throughout its expected lifetime;

(b) identifying previously unknown side-effects and monitoring the identified side-effects and contraindications;

(c) identifying and analysing emergent risks on the basis of factual evidence;

(d) ensuring the continued acceptability of the benefit-risk ratio referred to in paragraph 1 and 9 of Schedule 3;

(e) identifying possible systematic misuse or off-label use of the device, with a view to verifying that the intended purpose is correct.

(3) The PMCF plan must include at least—

(a) the general methods and procedures of the PMCF to be applied, such as gathering of clinical experience gained, feedback from users, screening of scientific literature and of other sources of clinical data;

(b) the specific methods and procedures of PMCF to be applied, such as evaluation of suitable registers or PMCF studies;

(c) a rationale for the appropriateness of the methods and procedures referred to in paragraphs (3)(a) and (b);

(d) a reference to the relevant parts of the clinical evaluation report referred to in paragraph 3(4) and to the risk management referred to in paragraph 3 of Schedule 3;

(e) the specific objectives to be addressed by the PMCF;

(f) an evaluation of the clinical data relating to equivalent or similar devices;

(g) reference to any relevant standards when used by the manufacturer, and relevant guidance on PMCF;

(h) a detailed and adequately justified time schedule for PMCF activities (e.g. analysis of PMCF data and reporting) to be undertaken by the manufacturer.

6. The manufacturer must analyse the findings of the PMCF and document the results in a PMCF evaluation report that must be part of the clinical evaluation report and the technical documentation.

7.—(1) The conclusions of the PMCF evaluation report must be taken into account —

(i) for the clinical evaluation referred to in regulation 102 and Part A of this Schedule;

(ii) in the risk management referred to in paragraph 3 of Schedule 3;

(2) If, through the PMCF, the need for preventive or corrective measures has been identified, the manufacturer must implement them.

SCHEDULE 15 Regulation 1A

Clinical investigations

Chapter I

General requirements

Ethical principles

1. Each step in a clinical investigation, from the initial consideration of the need for and justification of the study, to the publication of the results, must be carried out in accordance with recognised ethical principles.

Methods

2.—(1) Clinical investigations must—

(a) be performed on the basis of an appropriate plan of investigation reflecting the latest scientific and technical knowledge and defined in such a way as to confirm or refute the manufacturer's claims regarding the safety, performance and aspects relating to benefit-risk of devices as referred to in regulation 103(1);

(b) include an adequate number of observations to guarantee the scientific validity of the conclusions;

(c) be presented as described in paragraph 3(2)(i) of Chapter II of this Schedule with the rationale for the design and chosen statistical methodology.

(2) The procedures used to perform the clinical investigation must be appropriate to the device under investigation.

(3) The research methodologies used to perform the clinical investigation must be appropriate to the device under investigation.

(4) Clinical investigations must—

(a) be performed in accordance with the clinical investigation plan by a sufficient number of intended users and in a clinical environment that is representative of the intended normal conditions of use of the device in the target patient population;

(b) be in line with the clinical evaluation plan as referred to in Part A of Schedule 14.

(5) All the appropriate technical and functional features of the device must be appropriately addressed in the investigational design, in particular—

(a) those features involving safety and performance, and their expected clinical outcomes;

(b) a list of the technical and functional features of the device and the related expected clinical outcomes must be provided.

(6) The endpoints of the clinical investigation—

(a) must address the intended purpose, clinical benefits, performance and safety of the device;

(b) be determined and assessed using scientifically valid methodologies;

(c) must be appropriate to the device and clinically relevant.

(7) The following apply in relation to those involved in the clinical investigation—

(a) investigators must have access to the technical and clinical data regarding the device;

(b) personnel involved in the conduct of an investigation must be adequately instructed and trained in the proper use of the investigational device;

(c) this training must be verified and where necessary arranged by the sponsor and documented appropriately.

(8) The clinical investigation report, signed by the investigator, must contain a critical evaluation of all the data collected during the clinical investigation, and must include any negative findings.

Chapter II

Documentation regarding the application for clinical investigation

For investigational devices covered by regulation 103, the sponsor must draw up and submit the application in accordance with regulation 110 accompanied by the following documents—

Application form

1. An application form, duly filled in, containing the following information—

(a) name, address and contact details of the sponsor and, the name, address and contact details of its contact person or legal representative in accordance with regulation 103;

(b) if different from those in paragraph (a), name, address and contact details of the manufacturer of the device intended for clinical investigation and, if applicable, of its authorised representative;

(c) title of the clinical investigation;

(d) status of the clinical investigation application (that is, whether it is the first submission, resubmission, significant amendment);

(e) details or reference to the clinical evaluation plan;

(f) if the application is a resubmission with regard to a device for which an application has been already submitted—

(i) the date and reference number of the earlier application or in the case of significant amendment, reference to the original application;

(ii) information from the sponsor regarding all of the changes from the previous application together with a rationale for those changes, in particular, whether any changes have been made to address conclusions of previous reviews;

(g) if the application is submitted in parallel with an application for a clinical trial on a medicinal product for human use, reference to the official registration number of the clinical trial;

(h) identification of the countries in which the clinical investigation is to be conducted as part of a multicentre or multinational study at the time of application;

(i) a brief description of the investigational device, its classification and other information necessary for the identification of the device and device type;

(j) information as to whether the device incorporates a medicinal substance, including a human blood or plasma derivative or whether it is manufactured utilising non-viable tissues or cells of human or animal origin, or their derivatives;

(k) summary of the clinical investigation plan including the objective or objectives of the clinical investigation, the number and gender of subjects, criteria for subject selection, whether there are subjects under 18 years of age, design of the investigation such as

controlled or randomised studies, planned dates of commencement and of completion of the clinical investigation;

(l) if applicable, information regarding a comparator device, its classification and other information necessary for the identification of the comparator device;

(m) evidence from the sponsor that the clinical investigator and the investigational site are capable of conducting the clinical investigation in accordance with the clinical investigation plan;

(n) details of the anticipated start date and duration of the investigation;

(o) details to identify the notified body, if already involved at the stage of application for a clinical investigation;

(p) confirmation that the sponsor is aware that the Secretary of State may contact the ethics committee that is assessing or has assessed the application;

(q) the statement referred to in paragraph 4(1).

Investigator's brochure

2.—(1) An investigator's brochure (IB) must contain the clinical and non-clinical information on the investigational device that is relevant for the investigation and available at the time of application.

(2) Any updates to the IB or other relevant information that is newly available must be brought to the attention of the investigators in a timely manner.

(3) The IB must be clearly identified and contain in particular the following information—

(a) identification and description of the device, including information on the intended purpose, the risk classification and applicable classification rule pursuant to Schedule 9, design and manufacturing of the device and reference to previous and similar generations of the device;

(b) the manufacturer's—

(i) instructions for installation, maintenance, maintaining hygiene standards and for use, including storage and handling requirements, as well as, to the extent that such information is available, information to be placed on the label;

(ii) instructions for use to be provided with the device when placed on the market; and

(iii) information relating to any relevant training required.

(c) pre-clinical evaluation based on relevant pre-clinical testing and experimental data, in particular regarding in-design calculations, in vitro tests, ex vivo tests, animal tests, mechanical or electrical tests, reliability tests, sterilisation validation, software verification and validation, performance tests, evaluation of biocompatibility and biological safety, as applicable.

(d) existing clinical data, in particular—

(i) from relevant scientific literature available relating to the safety, performance, clinical benefits to patients, design characteristics and intended purpose of the device or of equivalent or similar devices;

(ii) other relevant clinical data available relating to the safety, performance, clinical benefits to patients, design characteristics and intended purpose of equivalent or similar devices of the same manufacturer, including length of time on the market and a review of performance, clinical benefit and safety-related issues and any corrective actions taken;

(e) a summary of the benefit-risk analysis and the risk management, including information regarding known or foreseeable risks, any undesirable effects, contraindications and warnings;

(f) in the case of devices that incorporate a medicinal substance, including a human blood or plasma derivative or devices manufactured utilising non-viable tissues or cells of human or animal origin, or their derivatives, detailed information on the medicinal substance or on the tissues, cells or their derivatives, and on the compliance with the relevant general safety and performance requirements and the specific risk management in relation to the substance or tissues, cells or their derivatives, as well as evidence for the added value of incorporation of such constituents in relation to the clinical benefit or safety of the device;

(g) a list detailing the fulfilment of the relevant general safety and performance requirements set out in Schedule 3, including the standards applied, in full or in part, as well as a description of the solutions for fulfilling the relevant general safety and performance requirements, in so far as those standards have not or have only been partly fulfilled or are lacking;

(h) a detailed description of the clinical procedures and diagnostic tests used in the course of the clinical investigation and in particular information on any deviation from normal clinical practice.

Clinical investigation plan

3.—(1) The clinical investigation plan (CIP) must—

(a) set out the rationale, objectives, design methodology, monitoring, conduct, record-keeping and the method of analysis for the clinical investigation;

(b) contain in particular the information as laid down in this Schedule and if part of this information is submitted in a separate document, it must be referenced in the CIP.

General information

(2) The general information to be provided is as follows—

(a) identification of the sponsor—

(i) name, address and contact details of the sponsor;

(ii) where applicable, the name, address and contact details of the sponsor's contact person or legal representative in accordance with regulation 103(3);

(b) information on the principal investigator at each investigational site, the coordinating investigator for the investigation, the address details for each investigational site, the emergency contact details for the principal investigator at each site and the roles, responsibilities and qualifications of the various kinds of investigators;

(c) a brief description of how the clinical investigation is financed and a brief description of the agreement between the sponsor and the site;

(d) an overall synopsis in English of the clinical investigation;

(e) an identification and description of the device, including its intended purpose, its manufacturer, its traceability, the target population, materials coming into contact with the human body, the medical or surgical procedures involved in its use and the necessary training and experience for its use, background literature review, the current state of the art in clinical care in the relevant field of application and the proposed benefits of the new device;

(f) the risks and clinical benefits of the device to be examined, with justification of the corresponding expected clinical outcomes in the clinical investigation plan;

(g) a description of the relevance of the clinical investigation in the context of the state of the art of clinical practice;

(h) the objectives and hypotheses of the clinical investigation;

(i) design of the clinical investigation with evidence of its scientific robustness and validity and including—

(i) general information such as type of investigation with rationale for choosing it, for its endpoints and for its variables as set out in the clinical evaluation plan;

(ii) information on the investigational device, on any comparator and on any other device or medication to be used in the clinical investigation;

(iii) information on subjects, selection criteria, size of investigation population, representativeness of investigation population in relation to target population and, if applicable, information on vulnerable subjects involved such as children, pregnant women, immuno-compromised or, elderly subjects;

(iv) details of measures to be taken to minimise bias, such as randomisation, and management of potential confounding factors;

(v) description of the clinical procedures and diagnostic methods relating to the clinical investigation and in particular highlighting any deviation from normal clinical practice;

(j) the monitoring plan;

(k) statistical considerations, with justification, including a power calculation for the sample size, if applicable;

(l) data management;

(m) the information about any amendments to the CIP;

(n) the policy regarding follow-up and management of any deviations from the CIP at the investigational site and clear prohibition of use of waivers from the CIP;

(o) accountability regarding the device, in particular control of access to the device, follow-up in relation to the device used in the clinical investigation and the return of unused, expired or malfunctioning devices;

(p) a statement of compliance with the recognised ethical principles for medical research involving humans, and the principles of good clinical practice in the field of clinical investigations of devices, as well as with the applicable regulatory requirements;

(q) a description of the informed consent process;

(r) safety reporting, including definitions of adverse events and serious adverse events, device deficiencies, procedures and timelines for reporting;

(s) criteria and procedures for follow-up of subjects following the end, temporary halt or early termination of an investigation, for follow-up of subjects who have withdrawn their consent and procedures for subjects lost to follow-up and such procedures must, for implantable devices, cover as a minimum traceability;

(t) a description of the arrangements for taking care of the subjects after their participation in the clinical investigation has ended, where such additional care is necessary because of the subjects' participation in the clinical investigation and where it differs from that normally expected for the medical condition in question;

(u) the policy as regards the establishment of the clinical investigation report and publication of results in accordance with the legal requirements and the ethical principles referred to in paragraph 1 of Chapter I;

(v) a list of the technical and functional features of the device, with specific mention of those covered by the investigation;

(w) bibliography.

Other information

The other information required is as follows—

4.—(1) A signed statement by the person responsible for the manufacture of the investigational device that the device in question conforms to the general safety and performance requirements apart from the aspects covered by the clinical investigation and that, with regard to those aspects, every precaution has been taken to protect the health and safety of the subject.

(2) Where available a copy of the opinion or opinions of the ethics committee or committees concerned.

(3) Proof of insurance cover or indemnification of subjects in case of injury, pursuant to regulation 109.

(4) Documents to be used to obtain informed consent, including the patient information sheet and the informed consent document.

(5) Description of the arrangements to comply with the applicable rules on the protection and confidentiality of personal data, in particular—

(a) organisational and technical arrangements that will be implemented to avoid unauthorised access, disclosure, dissemination, alteration or loss of information and personal data processed;

(b) a description of measures that will be implemented to ensure confidentiality of records and personal data of subjects;

(c) a description of measures that will be implemented in case of a data security breach in order to mitigate the possible adverse effects.

(6) Full details of the available technical documentation, for example detailed risk analysis and management documentation or specific test reports, must upon request, be submitted to the Secretary of State.

Chapter III

Other obligations of the sponsor

5. The sponsor must undertake to keep available for the Secretary of State any documentation necessary to provide evidence for the documentation referred to in Chapter II of this Annex, but if the sponsor is not the person responsible for the manufacture of the investigational device, that obligation may be fulfilled by that person on behalf of the sponsor.

6. The Sponsor must have an agreement in place to ensure that any serious adverse events or any other event as referred to in regulation 119(2) are reported by the investigator or investigators to the sponsor in a timely manner.

7.—(1) The documentation mentioned in this Schedule must be kept for a period of at least 10 years after the clinical investigation with the device in question has ended, or, in the event that the device is subsequently placed on the market, at least 10 years after the last device has been placed on the market and in the case of implantable devices, the period shall be at least 15 years.

(2) The documentation in sub-paragraph (1) must be kept at the disposal of the Secretary of State for the period referred to in sub-paragraph (1) in case the sponsor, or its contact person or

legal representative as referred to in regulation 103(2), irrespective of the status (and whether the person continues trading or not) of that person.

8. The Sponsor must appoint a monitor that is independent from the investigational site to ensure that the investigation is conducted in accordance with the CIP, the principles of good clinical practice and Part VIII.

9. The Sponsor must complete the follow-up of investigation subjects.

10. The Sponsor must provide evidence that the investigation is being conducted in line with good clinical practice, for instance through internal or external inspection.

11. The Sponsor must prepare a clinical investigation report which includes at least the following—

(a) cover or introductory page indicating the title of the investigation, the investigational device, the single identification number, the CIP number and the details with signatures of the coordinating investigators and the principal investigators from each investigational site;

(b) details of the author and date of the report;

(c) a summary of the investigation covering the title, purpose of the investigation, description of the investigation, investigational design and methods used, the results of the investigation and conclusion of the investigation;

(d) the completion date of the investigation, and in particular details of early termination, temporary halts or suspensions of investigations;

(e) investigational device description, in particular clearly defined intended purpose;

(f) a summary of the clinical investigation plan covering objectives, design, ethical aspects, monitoring and quality measures, selection criteria, target patient populations, sample size, treatment schedules, follow-up duration, concomitant treatments, statistical plan, including hypothesis, sample size calculation and analysis methods, as well as a justification;

(g) results of the clinical investigation covering, with rationale and justification, subject demographics, analysis of results related to chosen endpoints, details of subgroup analysis, as well as compliance with the CIP, and covering follow-up of missing data and of patients withdrawing from the clinical investigation, or lost to follow-up;

(h) summary of serious adverse events, adverse device effects, device deficiencies and any relevant corrective actions;

(i) discussion and overall conclusions covering safety and performance results, assessment of risks and clinical benefits, discussion of clinical relevance in accordance with clinical state of the art, any specific precautions for specific patient populations, implications for the investigational device, limitations of the investigation.

SCHEDULE 16

Regulation 1A

List of groups of products without an intended medical purpose referred to in regulation 68(2)(b)

1. Contact lenses or other items intended to be introduced into or onto the eye.

2. Products intended to be totally or partially introduced into the human body through surgically invasive means for the purpose of modifying the anatomy or fixation of body parts with the exception of tattooing products and piercings.

3. Substances, combinations of substances, or items intended to be used for facial or other dermal or mucous membrane filling by subcutaneous, submucous or intradermal injection or other introduction, excluding those for tattooing.

4. Equipment intended to be used to reduce, remove or destroy adipose tissue, such as equipment for liposuction, lipolysis or lipoplasty.

5. High intensity electromagnetic radiation (for example infra-red, visible light and ultra-violet) emitting equipment intended for use on the human body, including coherent and non-coherent sources, monochromatic and broad spectrum, such as lasers and intense pulsed light equipment, for skin resurfacing, tattoo or hair removal or other skin treatment.

6. Equipment intended for brain stimulation that apply electrical currents or magnetic or electromagnetic fields that penetrate the cranium to modify neuronal activity in the brain.

SCHEDULE 17

Regulation 1A

General safety and performance requirements- in vitro diagnostic medical devices

PART 1

General requirements for in vitro diagnostic medical devices

1. Devices must—

(a) achieve the performance intended by their manufacturer;

(b) be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose;

(c) be safe and effective;

(d) not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art.

2. The requirement in this Schedule to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio.

3.—(1) Manufacturers must establish, implement, document and maintain a risk management system.

(2) Risk management must be understood as a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating and in carrying out risk management manufacturers must—

(a) establish and document a risk management plan for each device;

(b) identify and analyse the known and foreseeable hazards associated with each device;

(c) estimate and evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse;

(d) eliminate or control the risks referred to in sub-paragraph (c) in accordance with the requirements of paragraph 4;

(e) evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, the benefit-risk ratio and risk acceptability;

(f) based on the evaluation of the impact of the information referred to in point (e), if necessary amend control measures in line with the requirements of paragraph 4.

4.—(1) Risk control measures adopted by manufacturers for the design and manufacture of the devices must conform to safety principles, taking account of the generally acknowledged state of the art.

(2) To reduce risks, the manufacturers must manage risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable.

(3) In selecting the most appropriate solutions, manufacturers must, in the following order of priority—

(a) eliminate or reduce risks as far as possible through safe design and manufacture;

(b) where appropriate, take adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated;

(c) provide information for safety (warnings, precautions, contra-indications) and, where appropriate, training to users;

(d) inform users of any residual risks.

5. In eliminating or reducing risks related to use error, the manufacturer must—

(a) reduce as far as possible the risks related to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety);

(b) give consideration to the technical knowledge, experience, education, training and use environment, where applicable, and the medical and physical conditions of intended users (design for lay, professional, disabled or other users).

6. The characteristics and performance of a device must not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.

7. Devices must be designed, manufactured and packaged in such a way that their characteristics and performance during their intended use are not adversely affected during transport and storage, for example, through fluctuations of temperature and humidity, taking account of the instructions and information provided by the manufacturer.

8. All known and foreseeable risks, and any undesirable effects must be minimised and be acceptable when weighed against the evaluated potential benefits to the patients or the user arising from the intended performance of the device during normal conditions of use.

PART 2

Requirements regarding design and manufacture of in vitro diagnostic medical devices

Performance characteristics

9.—(1) Devices must—

(a) be designed and manufactured in such a way that they are suitable for one or more of the purposes listed in the definition of "in vitro diagnostic medical device" in regulation 137, as specified by the manufacturer, and suitable with regard to the performance they are intended to achieve, taking account of the generally acknowledged state of the art;

(b) achieve the performances, as stated by the manufacturer and in particular, where applicable—

(i) the analytical performance, such as, analytical sensitivity, analytical specificity, trueness (bias), precision (repeatability and reproducibility), accuracy (resulting from trueness and precision), limits of detection and quantitation, measuring range, linearity, cut-off, including determination of appropriate criteria for specimen collection and handling and control of known relevant endogenous and exogenous interference, cross- reactions;

(ii) the clinical performance, such as diagnostic sensitivity, diagnostic specificity, positive predictive value, negative predictive value, likelihood ratio, expected values in normal and affected populations.

(2) The performance characteristics of the device must be maintained during the lifetime of the device as indicated by the manufacturer.

(3) Where the performance of devices depends on the use of calibrators or control materials—

(a) the metrological traceability of values assigned to calibrators or control materials must be assured through suitable reference measurement procedures or suitable reference materials of a higher metrological order;

(b) where available, metrological traceability of values assigned to calibrators and control materials must be assured to certified reference materials or reference measurement procedures.

(4) The characteristics and performances of the device must be specifically checked in the event that they may be affected when the device is used for the intended use under normal conditions—

(a) for devices for self-testing, performances obtained by laypersons;

(b) for devices for near-patient testing, performances obtained in relevant environments (for example, patient home, emergency units, ambulances).

Chemical physical and biological properties

10.—(1) Devices must be designed and manufactured in such a way as to ensure that the characteristics and performance requirements referred to in Part 1 are fulfilled and, in this regard, particular attention must be paid to the possibility of impairment of analytical performance due to physical or chemical incompatibility between the materials used and the specimens, analyte or marker to be detected (such as biological tissues, cells, body fluids and micro-organisms), taking account of the intended purpose of the device.

(2) As regards substances or particles that may be released from the device—

(a) devices must be designed and manufactured in such a way as to reduce to a level as low as reasonably practicable the risks posed by these substances or particles, including wear debris, degradation products and processing residues;

(b) special attention must be given to substances—

(i) which are carcinogenic, mutagenic or toxic to reproduction ('CMR') and on the UK mandatory classification and labelling list established and maintained in accordance with Article 38A of Regulation (EC) No 1272/2008 of the European Parliament and of the Council; and

(ii) with endocrine disrupting properties for which there is scientific evidence of probable serious effects to human health and which are identified in accordance with the procedure set out in Article 59 of Regulation (EC) No 1907/2006 of the European Parliament and of the Council.

(3) Devices must be designed and manufactured in such a way as to reduce as far as possible the risks posed by the unintentional ingress of substances into the device, taking into account the device and the nature of the environment in which it is intended to be used.

Infection and microbial contamination

11. Devices and their manufacturing processes must be designed in such a way as to eliminate or reduce as far as possible the risk of infection to the user or, where applicable, other persons and the design must—

(a) allow easy and safe handling;

(b) reduce, as far as possible, any microbial leakage from the device or microbial exposure during use;

(c) where necessary, prevent microbial contamination of the device during use and, in the case of specimen receptacles, the risk of contamination of the specimen.

(2) Devices labelled either as sterile or as having a specific microbial state must be designed, manufactured and packaged to ensure that their sterile condition or microbial state is maintained under the transport and storage conditions specified by the manufacturer until that packaging is opened at the point of use, unless the packaging which maintains their sterile condition or microbial state is damaged.

(3) Devices labelled as sterile must be processed, manufactured, packaged and, sterilised by means of appropriate, validated methods.

(4) Devices intended to be sterilised must be manufactured and packaged in appropriate and controlled conditions and facilities.

(5) Packaging systems for non-sterile devices must—

(a) maintain the integrity and cleanliness of the product and, where the devices are to be sterilised prior to use, minimise the risk of microbial contamination;

(b) be suitable taking account of the method of sterilisation indicated by the manufacturer.

(6) The labelling of the device must distinguish between identical or similar devices placed on the market in both a sterile and a non-sterile condition additional to the symbol used to indicate that devices are sterile.

Devices incorporating materials of a biological origin

12. Where devices include tissues, cells and substances of animal, human or microbial origin—

(a) the selection of sources, the processing, preservation, testing and handling of tissues, cells and substances of such origin and control procedures must be carried out so as to provide safety for users or other persons;

(b) safety with regard to microbial and other transmissible agents must be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process but this requirement would not apply to devices if the activity of the microbial and other transmissible agent are integral to the intended purpose of the device or when such elimination or inactivation process would compromise the performance of the device.

Construction of devices and interaction with the environment

13.—(1) If the device is intended for use in combination with other devices or equipment, the whole combination, including the connection system, must be safe and must not impair the specified performances of the devices and any restrictions on use applying to such combinations must be indicated on the label and in the instructions for use.

(2) Devices must be designed and manufactured in such a way as to remove or reduce as far as possible—

(a) the risk of injury, in connection with their physical features, including the volume/pressure ratio, dimensional and where appropriate ergonomic features;

(b) risks connected with reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, temperature, variations in pressure and acceleration or radio signal interferences;

(c) the risks associated with the use of the device when it comes into contact with materials, liquids, and substances, including gases, to which it is exposed during normal conditions of use;

(d) the risks associated with the possible negative interaction between software and the IT environment within which it operates and interacts;

(e) the risks of accidental ingress of substances into the device;

(f) the risk of incorrect identification of specimens and the risk of erroneous results due to, for example, confusing colour or numeric or character codings on specimen receptacles, removable parts or accessories used with devices in order to perform the test or assay as intended;

(g) the risks of any foreseeable interference with other devices.

(3) Devices must be designed and manufactured in such a way as to minimise the risks of fire or explosion during normal use and in single fault condition and, in this regard, particular attention must be paid to devices the intended use of which includes exposure to or use in association with flammable or explosive substances or substances which could cause combustion.

(4) Devices must be designed and manufactured in such a way that adjustment, calibration, and maintenance can be done safely and effectively.

(5) Devices that are intended to be operated together with other devices or products must be designed and manufactured in such a way that the interoperability and compatibility are reliable and safe.

(6) Devices must be designed and manufactured in such a way as to facilitate their safe disposal and the safe disposal of related waste substances by users, or other persons and, in doing so manufacturers must—

(a) identify and test procedures and measures as a result of which their devices can be safely disposed after use;

(b) ensure that such test procedures are described in the instructions for use.

(7) The measuring, monitoring or display scale (including colour change and other visual indicators) must be designed and manufactured in line with ergonomic principles, taking account of the intended purpose, users and the environmental conditions in which the devices are intended to be used.

Devices with a measuring function

14.—(1) Devices having a primary analytical measuring function must be designed and manufactured in such a way as to provide appropriate analytical performance in accordance with paragraph 9(1), taking into account the intended purpose of the device.

(2) The measurements made by devices with a measuring function must be expressed in legal units conforming to the provisions of the Units of Measurement Regulations 1986.

Protection against radiation

15.—(1) Devices must be designed, manufactured and packaged in such a way that exposure of users or other persons to radiation (intended, unintended, stray or scattered) is reduced as far as possible and in a manner that is compatible with the intended purpose, whilst not restricting the application of appropriate specified levels for diagnostic purposes.

(2) When devices are intended to emit hazardous, or potentially hazardous, ionizing or non-ionizing radiation, they must as far as possible be—

(a) designed and manufactured in such a way as to ensure that the characteristics and the quantity of radiation emitted can be controlled or adjusted;

(b) fitted with visual displays or audible warnings of such emissions.

(3) The operating instructions for devices emitting hazardous or potentially hazardous radiation must contain—

(a) detailed information as to the nature of the emitted radiation, the means of protecting the user, and on ways of avoiding misuse and of reducing the risks inherent to installation as far as possible and appropriate;

(b) information regarding the acceptance and performance testing, the acceptance criteria, and the maintenance procedure.

Electronic programmable systems- devices that incorporate programmable systems and software that are devices in themselves

16.—(1) Devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, must—

(a) be designed to ensure repeatability, reliability and performance in line with their intended use;

(b) in the event of a single fault condition, appropriate means must be adopted to eliminate or reduce as far as possible consequent risks or impairment of performance.

(2) For devices that incorporate software or for software that is a device in itself , the software must be developed and manufactured in accordance with the state of the art taking

into account the principles of development life cycle, risk management, including information security, verification and validation.

(3) Software referred to in this paragraph that is intended to be used in combination with mobile computing platforms must be designed and manufactured taking into account the specific features of the mobile platform (e.g. size and contrast ratio of the screen) and the external factors related to their use (varying environment as regards level of light or noise).

(4) Manufacturers must set out minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorised access, necessary to run the software as intended.

Devices connected to or equipped with an energy source

17.—(1) For devices connected to or equipped with an energy source, in the event of a single fault condition, appropriate means must be adopted to eliminate or reduce as far as possible consequent risks.

(2) Devices where the safety of the patient depends on an internal power supply must be equipped with a means of determining the state of the power supply and an appropriate warning or indication for when the capacity of the power supply becomes critical and if necessary, such warning or indication shall be given prior to the power supply becoming critical.

(3) Devices must be designed and manufactured in such a way as to reduce as far as possible the risks of creating electromagnetic interference which could impair the operation of the device in question or other devices or equipment in the intended environment.

(4) Devices must be designed and manufactured in such a way as to provide a level of intrinsic immunity to electromagnetic interference such that is adequate to enable them to operate as intended.

(5) Devices must be designed and manufactured in such a way as to avoid as far as possible the risk of accidental electric shocks to the user, or other person both during normal use of the device and in the event of a single fault condition in the device, provided the device is installed and maintained as indicated by the manufacturer.

Protection against mechanical and thermal risks

18.—(1) Devices must be designed and manufactured in such a way as to protect users and other persons against mechanical risks.

(2) Devices must—

(a) be sufficiently stable under the foreseen operating conditions;

(b) be suitable to withstand stresses inherent to the foreseen working environment, and to retain this resistance during the expected lifetime of the devices, subject to any inspection and maintenance requirements as indicated by the manufacturer.

(3) Where there are risks due to the presence of moving parts, risks due to break-up or detachment, or leakage of substances, then appropriate protection means must be incorporated.

(4) Any guards or other means included with the device to provide protection, in particular against moving parts, must be secure and must not interfere with access for the normal operation of the device, or restrict routine maintenance of the device as intended by the manufacturer.

(5) Devices must be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from vibration generated by the devices, taking account of technical progress and of the means available for limiting vibrations, particularly at source, unless the vibrations are part of the specified performance.

(6) Devices must be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from the noise emitted, taking account of technical progress and of the means available to reduce noise, particularly at source, unless the noise emitted is part of the specified performance.

(7) Terminals and connectors to the electricity, gas or hydraulic and pneumatic energy supplies which the user or other person has to handle, must be designed and constructed in such a way as to minimise all possible risks.

(8) Errors likely to be made when fitting or refitting certain parts which could be a source of risk must be made impossible by the design and construction of such parts or, failing this, by information given on the parts themselves or their housings.

(9) Information must be given on moving parts or their housings where the direction of movement needs to be known in order to avoid a risk.

(10) Accessible parts of devices (excluding the parts or areas intended to supply heat or reach given temperatures) and their surroundings must not attain potentially dangerous temperatures under normal conditions of use.

Protection against the risks posed by devices intended for self-testing or near-patient testing

19.—(1) Devices intended for self-testing or near-patient testing—

(a) must be designed and manufactured in such a way that they perform appropriately for their intended purpose taking into account the skills and the means available to the intended user and the influence resulting from variation that can be reasonably anticipated in the intended user's technique and environment;

(b) the information and instructions provided by the manufacturer must be easy for the intended user to understand and apply in order to correctly interpret the result provided by the device and to avoid misleading information;

(c) in the case of near-patient testing, the information and the instructions provided by the manufacturer must make clear the level of training, qualifications or experience required by the user.

(2) Devices intended for self-testing or near-patient testing must be designed and manufactured in such a way as to—

(a) ensure that the device can be used safely and accurately by the intended user at all stages of the procedure if necessary after appropriate training or information;

(b) reduce as far as possible the risk of error by the intended user in the handling of the device and, if applicable, the specimen, and also in the interpretation of the results.

(3) Devices intended for self-testing and near-patient testing must, where feasible, include a procedure by which the intended user—

(a) can verify that, at the time of use, the device will perform as intended by the manufacturer;

(b) be warned if the device has failed to provide a valid result.

PART 3

Requirements regarding information supplied with the device

Labels and instructions for use

General requirements regarding the information supplied by the manufacturer

20.—(1) Each device must be accompanied—

(a) by the information needed to identify the device and its manufacturer;

(b) by any safety and performance information relevant to the user or any other person, as appropriate.

(2) The information in paragraph (1) may appear on the device itself, on the packaging or in the instructions for use, and must, if the manufacturer has a website, be made available and kept up to date on the website, taking into account the following—

(a) the medium, format, content, legibility, and location of the label and instructions for use must be appropriate to the particular device, its intended purpose and the technical knowledge, experience, education or training of the intended user and, in particular, instructions for use must be written in terms readily understood by the intended user and, where appropriate, supplemented with drawings and diagrams;

(b) the information required on the label must be provided on the device itself or if this is not practicable or appropriate, some or all of the information may appear on the packaging for each unit and, if individual full labelling of each unit is not practicable, the information must be set out on the packaging of multiple devices;

(c) labels must be provided in a human-readable format and may be supplemented by machine-readable information, such as radio-frequency identification or bar codes;

(d) instructions for use must be provided together with devices but, in duly justified and exceptional cases, instructions for use are not required, or may be abbreviated, if the device can be used safely and as intended by the manufacturer without any such instructions for use;

(e) where multiple devices, with the exception of devices intended for self-testing or near-patient testing, are supplied to a single user or location, a single copy of the instructions for use may be provided if so agreed by the purchaser who in any case may request further copies to be provided free of charge;

(f) when the device is intended for professional use only, instructions for use may be provided to the user in non-paper format (e.g. electronic), except when the device is intended for near-patient testing;

(g) residual risks which are required to be communicated to the user or other person shall be included as limitations, contra-indications, precautions or warnings in the information supplied by the manufacturer;

(h) where appropriate, the information supplied by the manufacturer—

(i) must take the form of internationally recognised symbols, taking into account the intended users;

(ii) must conform, in terms of any symbols or identification colour used, to the designated standards or CS;

(iii) in areas for which no designated standards or CS exist, the symbols and colours must be described in the documentation supplied with the device;

(i) in the case of devices containing a substance or a mixture which may be considered as being dangerous, taking account of the nature and quantity of its constituents and the form under which they are present—

(i) relevant hazard pictograms and labelling requirements of Regulation (EC) No 1272/2008 apply; or

(ii) where there is insufficient space to put all the information on the device itself or on its label, the relevant hazard pictograms must be put on the label and the other information required by Regulation (EC) No 1272/2008 must be given in the instructions for use;

(j) the provisions of Regulation (EC) No 1907/2006 on the safety data sheet must apply, unless all relevant information, as appropriate, is already made available in the instructions for use.

Information on the label

(3) The label must bear all of the following particulars—

(a) the name or trade name of the device;

(b) the details strictly necessary for a user to identify the device and, where it is not obvious for the user, the intended purpose of the device;

(c) the name, registered trade name or registered trade mark of the manufacturer and the address of its registered place of business;

(d) if the manufacturer has its registered place of business outside the United Kingdom, the name and address of the person placing the device on the market;

(e) an indication that the device is an in vitro diagnostic medical device, or if the device is a 'device for performance study', an indication of that fact;

(f) the lot number or the serial number of the device preceded by the words LOT NUMBER or SERIAL NUMBER or an equivalent symbol, as appropriate;

(g) the UDI carrier as referred to in regulation 157 and Part C of Schedule 22;

(h) an unambiguous indication of the time limit for using the device safely, without degradation of performance, expressed at least in terms of year and month and, where relevant, the day, in that order;

(i) where there is no indication of the date until when it may be used safely, the date of manufacture and this date of manufacture may be included as part of the lot number or serial number, provided the date is clearly identifiable;

(j) where relevant, an indication of the net quantity of contents, expressed in terms of weight or volume, numerical count, or any combination of thereof, or other terms which accurately reflect the contents of the package;

(k) an indication of any special storage or handling condition that applies;

(l) where appropriate, an indication of the sterile state of the device and the sterilisation method, or a statement indicating any special microbial state or state of cleanliness;

(m) warnings or precautions to be taken that need to be brought to the immediate attention of the user of the device or to any other person (this information may be kept to a minimum in which case more detailed information must appear in the instructions for use, taking into account the intended users);

(n) if the instructions for use are not provided in paper form in accordance with paragraph 20(2)(f), a reference to their accessibility (or availability), and where applicable the website address where they can be consulted;

(o) where applicable, any particular operating instructions;

(p) if the device is intended for single use, an indication of that fact;

(q) if the device is intended for self-testing or near-patient testing, an indication of that fact;

(r) where rapid assays are not intended for self-testing or near-patient testing, the explicit exclusion thereof;

(4) The following additional labelling requirements apply to these specific devices—

(a) for device kits which include individual reagents and articles that are made available as separate devices, the labelling requirements contained in sub-paragraph (3) and requirements of Part IX apply to each device;

(b) devices and separate components must be identified, where applicable in terms of batches, to allow all appropriate action to detect any potential risk posed by the devices and detachable components and, as far as practicable and appropriate, the information must be set out on the device itself and, where appropriate, on the sales packaging;

(c) the label for devices for self-testing must bear the following particulars—

(i) the type of specimens required to perform the test (for example blood, urine or saliva);

(ii) the need for additional materials for the test to function properly;

(iii) contact details for further advice and assistance;

(d) the name of devices for self-testing must not reflect an intended purpose other than that specified by the manufacturer.

Information on the packaging which maintains the sterile condition of a device ('sterile packaging')

(5) The following particulars must appear on the sterile packaging—

(a) an indication permitting the sterile packaging to be recognised as such;

(b) a declaration that the device is in a sterile condition;

(c) the method of sterilisation;

(d) the name and address of the manufacturer;

(e) description of the device;

(f) the month and year of manufacture;

(g) an unambiguous indication of the time limit for using the device safely, expressed at least in terms of year and month and, where relevant, the day, in that order.

Information in the instructions for use

(6) The instructions for use must contain all of the following particulars—

(a) the name or trade name of the device;

(b) the details strictly necessary for the user to uniquely identify the device;

(c) the device's intended purpose in terms of—

(i) what is detected or measured;

(ii) its function (for example screening, monitoring, diagnosis or aid to diagnosis, prognosis, prediction, companion diagnostic);

(iii) the specific information that is intended to be provided in the context of—

(aa) a physiological or pathological state;

(bb) congenital physical or mental impairments;

(cc) the predisposition to a medical condition or a disease;

(dd) the determination of the safety and compatibility with potential recipients;

(ee) the prediction of treatment response or reactions;

(ff) the definition or monitoring of therapeutic measures;

(iv) whether it is automated or not;

(v) whether it is qualitative, semi-quantitative or quantitative;

(vi) the type of specimens required;

(vii) where applicable, the testing population;

(viii) for companion diagnostics, the International Non-proprietary Name (INN) of the associated medicinal product for which it is a companion test;

(d) an indication that the device is an in vitro diagnostic medical device, or, if the device is a 'device for performance study', an indication of that fact;

(e) the intended user, as appropriate (for example self-testing, near patient and laboratory professional use, healthcare professionals);

(f) the test principle;

(g) a description of the calibrators and controls and any limitation upon their use (for example suitable for a dedicated instrument only);

(h) a description of the reagents and any limitation upon their use (for example suitable for a dedicated instrument only) and the composition of the reagent product by nature and amount or concentration of the active ingredient of the reagent or kit as well as a statement, where appropriate, that the device contains other ingredients which might influence the measurement;

(i) a list of materials provided and a list of special materials required but not provided;

(j) for devices intended for use in combination with or installed with or connected to other devices or general purpose equipment—

(i) information to identify such devices or equipment, in order to obtain a validated and safe combination, including key performance characteristics;

(ii) information on any known restrictions to combinations of devices and equipment;

(k) an indication of any special storage (for example temperature, light, humidity, etc.) or handling conditions which apply;

(l) in-use stability which may include the storage conditions, and shelf life following the first opening of the primary container, together with the storage conditions and stability of working solutions, where this is relevant;

(m) if the device is supplied as sterile, an indication of its sterile state, the sterilisation method and instructions in the event of the sterile packaging being damaged before use;

(n) information that allows the user to be informed of any warnings, precautions, measures to be taken and limitations of use regarding the device, that information must, where appropriate, cover—

(i) warnings, precautions or measures to be taken in the event of malfunction of the device or its degradation as suggested by changes in its appearance that may affect performance;

(ii) warnings, precautions or measures to be taken as regards the exposure to reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic

discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, or temperature,

(iii) warnings, precautions or measures to be taken as regards the risks of interference posed by the reasonably foreseeable presence of the device during specific diagnostic investigations, evaluations, therapeutic treatment or other procedures such as electromagnetic interference emitted by the device affecting other equipment;

(iv) precautions related to materials incorporated into the device that contain or consist of CMR substances, or endocrine disrupting substances or that could result in sensitisation or an allergic reaction by the patient or user;

(v) if the device is intended for single use, an indication of that fact;

(vi) if the device is reusable—

(aa) information on the appropriate processes to allow reuse, including cleaning, disinfection, decontamination, packaging and, where appropriate, the validated method of re-sterilisation,

(bb) information on when the device should no longer be used such as signs of material degradation or the maximum number of allowable reuses;

(o) any warnings or precautions related to potentially infectious material that is included in the device;

(p) where relevant, requirements for special facilities, such as a clean room environment, or special training, such as on radiation safety, or particular qualifications of the intended user;

(q) conditions for collection, handling, and preparation of the specimen;

(r) details of any preparatory treatment or handling of the device before it is ready for use, such as sterilisation, final assembly, calibration, etc., for the device to be used as intended by the manufacturer;

(s) the information needed to verify whether the device is properly installed and is ready to perform safely and as intended by the manufacturer, together with, where relevant—

(i) details of the nature, and frequency, of preventive and regular maintenance, including cleaning and disinfection;

(ii) identification of any consumable components and how to replace them;

(iii) information on any necessary calibration to ensure that the device operates properly and safely during its intended lifetime;

(iv) methods for mitigating the risks encountered by persons involved in installing, calibrating or servicing devices;

(t) where applicable, recommendations for quality control procedures;

(u) the metrological traceability of values assigned to calibrators and control materials, including identification of applied reference materials or reference measurement procedures of higher order and information regarding maximum (self-allowed) batch to batch variation provided with relevant figures and units of measure;

(v) assay procedure including calculations and interpretation of results and where relevant if any confirmatory testing is to be considered;

(w) where applicable, the instructions for use shall be accompanied by information regarding batch to batch variation provided with relevant figures and units of measure;

(x) analytical performance characteristics, such as analytical sensitivity, analytical specificity, trueness (bias), precision (repeatability and reproducibility), accuracy

(resulting from trueness and precision), limits of detection and measurement range, (information needed for the control of known relevant interferences, cross-reactions and limitations of the method), measuring range, linearity and information about the use of available reference measurement procedures and materials by the user;

(y) clinical performance characteristics as defined in paragraph 9(1) of this Schedule;

(z) the mathematical approach upon which the calculation of the analytical result is made;

(aa) where relevant, clinical performance characteristics, such as threshold value, diagnostic sensitivity and diagnostic specificity, positive and negative predictive value;

(bb) where relevant, reference intervals in normal and affected populations;

(cc) information on interfering substances or limitations (for example visual evidence of hyperlipidaemia or haemolysis, age of specimen) that may affect the performance of the device;

(dd) warnings or precautions to be taken in order to facilitate the safe disposal of the device, its accessories, and the consumables used with it, if any which, where appropriate, must cover—

(i) infection or microbial hazards, such as consumables contaminated with potentially infectious substances of human origin;

(ii) environmental hazards such as batteries or materials that emit potentially hazardous levels of radiation);

(iii) physical hazards such as explosion;

(ee) the name, registered trade name or registered trade mark of the manufacturer and the address of their registered place of business at which they can be contacted and their location be established, together with a telephone number or fax number or website address to obtain technical assistance;

(ff) date of issue of the instructions for use or, if they have been revised, date of issue and identifier of the latest revision of the instructions for use, with a clear indication of the introduced modifications;

(gg) a notice to the user that any serious incident that has occurred in relation to the device must be reported to the manufacturer and to the Secretary of State;

(7) The following additional requirements relating to the instructions for use apply to these specific devices—

(a) for device kits which include individual reagents and articles that may be made available as separate devices, each of these devices must comply with the instructions for use requirements contained in this sub-paragraph (6) and with the requirements of Part IX;

(b) for devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorised access, necessary to run the software as intended.

(c) the instructions for use for devices intended for self-testing must comply with all of the following principles—

(i) details of the test procedure shall be given, including any reagent preparation, specimen collection or preparation and information on how to run the test and interpret the results;

(ii) specific particulars may be omitted provided that the other information supplied by the manufacturer is sufficient to enable the user to use the device and to understand the results produced by the device;

(iii) the device's intended purpose must provide sufficient information to enable the user to understand the medical context and to allow the intended user to make a correct interpretation of the results;

(iv) the results must be expressed and presented in a way that is readily understood by the intended user;

(v) information—

(aa) must be provided with advice to the user on action to be taken (in case of positive, negative or indeterminate result), on the test limitations and on the possibility of false positive or false negative result;

(bb) must also be provided as to any factors that can affect the test result such as age, gender, menstruation, infection, exercise, fasting, diet or medication;

(vi) the information provided must include a statement clearly directing that the user should not take any decision of medical relevance without first consulting the appropriate healthcare professional, information on disease effects and prevalence, and, where available, information on where a user can obtain further advice such as helplines, websites;

(d) for devices intended for self-testing used for the monitoring of a previously diagnosed existing disease or condition, the information must specify that the patient should only adapt the treatment if he has received the appropriate training to do so.

SCHEDULE 18

Regulation 1A

Technical documentation- in vitro diagnostic medical devices

1. The technical documentation and, if applicable, the summary thereof to be drawn up by the manufacturer must be presented in a clear, organised, readily searchable and unambiguous manner and must include in particular the elements listed in this Schedule.

Device description and specification, including variants and accessories

Device description and specification

2.—(1) The description and specification of the device must contain the following—

(a) product or trade name and a general description of the device including its intended purpose and intended users;

(b) the Basic UDI-DI as referred to in Part C of Schedule 22 assigned by the manufacturer to the device in question, as soon as identification of this device becomes based on a UDI system, or otherwise a clear identification by means of product code, catalogue number or other unambiguous reference allowing traceability;

(c) the intended purpose of the device which may include information on—

(i) what is to be detected or measured;

(ii) its function such as screening, monitoring, diagnosis or aid to diagnosis, prognosis, prediction, companion diagnostic;

(iii) the specific disorder, condition or risk factor of interest that it is intended to detect, define or differentiate;

(iv) whether it is automated or not;

(v) whether it is qualitative, semi-quantitative or quantitative;

(vi) the type of specimen required;

(vii) where applicable, the testing population;

(viii) the intended user;

(ix) in addition, for companion diagnostics, the relevant target population and the associated medicinal products;

(d) the description of the principle of the assay method or the principles of operation of the instrument;

(e) the rationale for the qualification of the product as a device;

(f) the risk class of the device and the justification for the classification rules applied in accordance with Schedule 23;

(g) the description of the components and where appropriate, the description of the reactive ingredients of relevant components such as antibodies, antigens, nucleic acid primers;

(h) where applicable, the description of the specimen collection and transport materials provided with the device or descriptions of specifications recommended for use;

(i) where applicable, for instruments of automated assays, the description of the appropriate assay characteristics or dedicated assays;

(j) where applicable, for automated assays, a description of the appropriate instrumentation characteristics or dedicated instrumentation;

(k) where applicable, a description of any software to be used with the device;

(l) where applicable, a description or complete list of the various configurations or variants of the device that are intended to be made available on the market;

(m) where applicable, a description of the accessories for a device, other devices and other products that are not devices, which are intended to be used in combination with the device.

Reference to previous and similar generations of the device

(2) Where applicable the technical documentation must contain—

(a) an overview of the previous generation or generations of the device produced by the manufacturer, where such devices exist;

(b) an overview of identified similar devices available on international markets, where such devices exist.

Information to be supplied by the manufacturer

3. The manufacturer must supply a complete set of—

(a) the label or labels on the device and on its packaging, such as single unit packaging, sales packaging, transport packaging in the case of specific management conditions, in English;

(b) the instructions for use in English.

Design and manufacturing information

Design information

4.—(1) Information to allow the design stages applied to the device to be understood must include—

(a) a description of the critical ingredients of the device such as antibodies, antigens, enzymes and nucleic acid primers provided or recommended for use with the device;

(b) for instruments, a description of major subsystems, analytical technology such as operating principles and control mechanisms, dedicated computer hardware and software;

(c) for instruments and software, an overview of the entire system;

(d) for software, a description of the data interpretation methodology, namely the algorithm;

(e) for devices intended for self-testing or near-patient testing, a description of the design aspects that make them suitable for self-testing or near-patient testing.

Manufacturing information

(2) Manufacturing information must include—

(a) information to allow the manufacturing processes such as production, assembly, final product testing, and packaging of the finished device to be understood (more detailed information must be provided for the audit of the quality management system or other applicable conformity assessment procedures);

(b) identification of all sites, including suppliers and sub-contractors, where manufacturing activities are performed.

General safety and performance requirements

5.—(1) The documentation must contain information for the demonstration of conformity with the general safety and performance requirements set out in Schedule 17 that are applicable to the device taking into account its intended purpose, and must include a justification, validation and verification of the solutions adopted to meet those requirements.

(2) The demonstration of conformity must also include—

(a) the general safety and performance requirements that apply to the device and an explanation as to why others do not apply;

(b) the method or methods used to demonstrate conformity with each applicable general safety and performance requirement;

(c) the designated standards, CS or other solutions applied;

(d) the precise identity of the controlled documents offering evidence of conformity with each designated standard, CS or other method applied to demonstrate conformity with the general safety and performance requirements.

(e) the information referred to in paragraph (d) must incorporate a cross-reference to the location of such evidence within the full technical documentation and, if applicable, the summary technical documentation.

Benefit-risk analysis and risk management

6. The documentation must contain information on—

(a) the benefit-risk analysis referred to in paragraphs 1 and 8 of Schedule 17,

(b) the solutions adopted and the results of the risk management referred to in paragraph 3 of Schedule 17.

Product verification and validation

7. The documentation must contain the results and critical analyses of all verifications and validation tests or studies undertaken to demonstrate conformity of the device with the requirements Part IX and Schedules 17 to 28 and in particular the applicable general safety and performance requirements in Schedule 17.

Performance of the device

8.—(1) The documentation must include the information on the performance of the device listed in sub-paragraphs (2) and (3).

(2) The specimen type which must describe the different specimen types that can be analysed, including their stability such as storage, where applicable specimen transport conditions and, with a view to time-critical analysis methods, information on the timeframe between taking the specimen and its analysis and storage conditions such as duration, temperature limits and freeze/thaw cycles;

(3) The accuracy of the measurement consisting of—

(a) the trueness of the measurement which must provide information on the trueness of the measurement procedure and summarise the data in sufficient detail to allow an assessment of the adequacy of the means selected to establish the trueness whilst noting that trueness measures apply to both quantitative and qualitative assays only when a certified reference material or certified reference method is available;

(b) the precision of the measurement which must describe the repeatability and reproducibility studies;

(c) the analytical sensitivity which must include—

(i) information about the study design and results;

(ii) a description of specimen type and preparation including matrix, analyte levels, and how levels were established;

(ii) the number of replicates tested at each concentration must also be provided as well as a description of the calculation used to determine assay sensitivity;

(d) analytical specificity which must include—

(i) a description of interference and cross reactivity studies performed to determine the analytical specificity in the presence of other substances/agents in the specimen;

(ii) information on the evaluation of potentially interfering and cross-reacting substances or agents on the assay, on the tested substance or agent type and its concentration, specimen type, analyte test concentration, and results;

(iii) information on interferents and cross-reacting substances or agents, which vary greatly depending on the assay type and design and could derive from exogenous or endogenous sources such as—

(aa) substances used for patient treatment such as medicinal products;

(bb) substances ingested by the patient such as alcohol, foods;

(cc) substances added during specimen preparation such as preservatives, stabilisers;

(dd) substances encountered in specific specimen types such as haemoglobin, lipids, bilirubin, proteins;

(ee) analytes of similar structure such as precursors, metabolites or medical conditions unrelated to the test condition including specimens negative for the assay but positive for a condition that can mimic the test condition;

(iv) the metrological traceability of calibrator and control material values;

(v) the measuring range of the assay which must include information—

(vi) on the measuring range regardless of whether the measuring systems are linear or non-linear, including the limit of detection and describe information on how the range and detection limit were established;

(vii) including a description of specimen type, number of specimens, number of replicates, and specimen preparation including information on the matrix, analyte levels and how levels were established;

(viii) applicable, a description of any high dose hook effect and the data supporting the mitigation such as dilution steps shall be added;

(ix) a definition of the assay cut-off including—

(x) a summary of analytical data with a description of the study design including methods for determining the assay cut-off, such as—

(aa) the populations studied including demographics, selection, inclusion and exclusion criteria, number of individuals included;

(bb) the method or mode of characterisation of specimens;

(cc) statistical methods such as Receiver Operator Characteristic (ROC) to generate results and if applicable, define grey-zone/equivocal zone;

(xi) the analytical performance report referred to in Schedule 27.

Performance evaluation report

9. The documentation—

(a) must contain the performance evaluation report, which includes the reports on the scientific validity, the analytical and the clinical performance, as referred to in Schedule 27, together with an assessment of those reports;

(b) must include, or fully reference, the clinical performance study documents referred to in paragraph 2 of Part A of Schedule 27.

Shelf life, in-use stability and shipping stability studies

10. The documentation must describe claimed shelf life, in use stability and shipping stability studies.

11. For claimed shelf life the documentation must—

(a) provide information on stability testing studies to support the shelf life that is claimed for the device;

(b) confirm that testing has been performed on at least 3 different (but not necessarily consecutive) lots manufactured under conditions that are essentially equivalent to routine production conditions;

(c) describe whether accelerated studies or extrapolated data from real time data are used for initial shelf life claims and that these studies will be followed up with real time stability studies;

(d) include the detailed information in paragraphs (b) to (c) which must include—

(i) the study report including the protocol, number of lots, acceptance criteria and testing intervals;

(ii) where accelerated studies have been performed in anticipation of the real time studies, the method used for accelerated studies must be described;

(iii) the conclusions and claimed shelf life.

12. For in-use stability the documentation must—

(a) provide information on in-use stability studies for one lot reflecting actual routine use of the device, regardless of whether real or simulated which may include open vial stability or, for automated instruments, on board stability;

(b) provide supporting data in cases of automated instrumentation where calibration stability is claimed;

(c) include—

(i) the study report (including the protocol, acceptance criteria and testing intervals);

(ii) the conclusions and claimed in-use stability.

13. For shipping stability the documentation must—

(a) provide information on shipping stability studies for one lot of devices to evaluate the tolerance of devices to the anticipated shipping conditions;

(b) provide information on whether the shipping studies were done under real or simulated conditions and must include variable shipping conditions such as extreme heat and/or cold;

(c) include—

(i) the study report (including the protocol, acceptance criteria);

(ii) the method used for simulated conditions;

(iii) conclusion and recommended shipping conditions.

Software verification and validation

14. The documentation must—

(a) contain evidence of the validation of the software, as it is used in the finished device;

(b) typically include the summary results of all verification, validation and testing performed in-house and applicable in an actual user environment prior to final release;

(c) also address all of the different hardware configurations and, where applicable, operating systems identified in the labelling.

Additional information required in specific cases

15. The additional information required in specific cases is as follows—

(a) in the case of devices placed on the market in a sterile or defined microbiological condition, a description of the environmental conditions for the relevant manufacturing steps;

(b) in the case of devices placed on the market in a sterile condition, a description of the methods used, including the validation reports, with regard to packaging, sterilisation and maintenance of sterility and the validation report must address bioburden testing, pyrogen testing and, if applicable, testing for sterilant residues;

(c) in the case of devices containing tissues, cells and substances of animal, human or microbial origin, information on the origin of such material and on the conditions in which it was collected;

(d) in the case of devices placed on the market with a measuring function, a description of the methods used in order to ensure the accuracy as given in the specifications;

(e) if the device is to be connected to other equipment in order to operate as intended, a description of the resulting combination including proof that it conforms to the general safety and performance requirements set out in Schedule 17 when connected to any such equipment having regard to the characteristics specified by the manufacturer.

SCHEDULE 19

Regulation 1A

Technical documentation on post-market surveillance for in vitro diagnostic medical devices

1. The technical documentation on post-market surveillance to be drawn up by the manufacturer in accordance with regulations 186 to 189 must be presented in a clear, organised, readily searchable and unambiguous manner and must include in particular the elements described in this Schedule.

2. In the post market surveillance plan drawn up in accordance with regulation 187 the manufacturer must prove that the plan complies with the obligation in regulation 186.

3. The post-market surveillance plan must address the collection and utilisation of available information, in particular—

(a) information concerning serious incidents, including information from PSURs, and field safety corrective actions;

(b) records referring to non-serious incidents and data on any undesirable side-effects,

(c) information from trend reporting;

(d) relevant specialist or technical literature, databases and/or registers;

(e) information, including feedbacks and complaints, provided by users, distributors and importers;

(f) publicly-available information about similar medical devices.

4. The post-market surveillance plan must cover at least—

(a) a proactive and systematic process to collect any information referred to in paragraph 3 which must allow a correct characterisation of the performance of the devices and must also allow a comparison to be made between the device and similar products available on the market;

(b) effective and appropriate methods and processes to assess the collected data;

(c) suitable indicators and threshold values that must be used in the continuous reassessment of the benefit-risk analysis and of the risk management as referred to in paragraph 3 of Schedule 3;

(d) effective and appropriate methods and tools to investigate complaints and analyse market-related experience collected in the field;

(e) methods and protocols to manage the events subject to the trend report as provided for in regulation 191, including the methods and protocols to be used to establish any statistically significant increase in the frequency or severity of incidents as well as the observation period;

(f) methods and protocols to communicate effectively with the Secretary of State, notified bodies, economic operators and users;

(g) reference to procedures to fulfil the manufacturers obligations laid down in regulations 186, 187 and 189;

(h) systematic procedures to identify and initiate appropriate measures including corrective actions;

(i) effective tools to trace and identify devices for which corrective actions might be necessary; and

(j) PMPF plan as referred to in Part B of Schedule 27 or a justification as to why a PMPF is not applicable.

5. The PSUR referred to in Article 81 and the post-market surveillance report referred to in Article 80.

SCHEDULE 20

Regulation 1A

Declaration of conformity for in vitro diagnostic medical devices

The declaration of conformity must contain the following information—

(a) name, registered trade name or registered trade mark and, if applicable, the authorised representative, and the address of their registered place of business where they can be contacted and their location be established;

(b) a statement that the declaration of conformity is issued under the sole responsibility of the manufacturer;

(c) the Basic UDI-DI as referred to in Part C of Schedule 22;

(d) the product or trade name along with—

(i) the product code;

(ii) the catalogue number; or

(iii) other unambiguous reference allowing identification and traceability of the device covered by the declaration of conformity, such as a photograph; and

(iv) the product's intended purpose;

but, except for the product or trade name, the information allowing identification and traceability may be provided by the Basic UDI-DI referred to in paragraph (c);

(e) the risk class of the device in accordance with the rules set out in Schedule 23;

(f) a statement that the device, covered by the present declaration is in conformity with Part IX or Regulation (EU) 2017/746 and, if applicable, with any other relevant legislation that provides for the issuing of a declaration of conformity;

(g) references to any CS used and in relation to which conformity is declared;

(h) where applicable, the name and identification number of the notified body, a description of the conformity assessment procedure performed and identification of the certificate or certificates issued;

(i) where applicable, additional information;

(j) the place and date of issue of the declaration, the name and function of the person who signed it as well as an indication for, and on behalf of whom, that person signed;

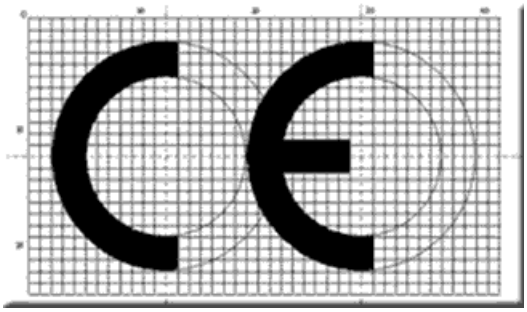
(k) signature.

SCHEDULE 21

Regulation 1A

CE marking of conformity

1. The CE marking must consist of the initials 'CE' taking the following form—



2. If the CE marking is reduced or enlarged the proportions given in the above graduated drawing shall be respected.

3. The various components of the CE marking must have substantially the same vertical dimension, which may not be less than 5 mm but this minimum dimension may be waived for small-scale devices.

SCHEDULE 22

Regulation 1A

Information to be submitted upon registration of in vitro diagnostic medical devices and economic operators in accordance with regulations 158 and 160, core data elements to be provided to the UDI database together with the UDI-DI in accordance with regulations

Part A

Information to be submitted upon the registration of devices and economic operators in accordance with regulations 158 and 160

1. The information relating to the economic operator is as follows—

(a) type of economic operator (manufacturer, authorised representative, UK responsible person or importer);

(b) name, address and contact details of the economic operator;

(c) where submission of information is carried out by another person on behalf of any of the economic operators mentioned in paragraph (a), the name, address and contact details of that person.

2. The information relating to the device is as follows—

(a) basic UDI;

(b) type, number and expiry date of the certificate issued by the notified body and the name or identification number of that notified body and the link to the information that appears on the certificate;

(c) if the device has been placed on the market of a state other than the United Kingdom before being placed on the United Kingdom market, the name of that state;

(d) in the case of Class B, Class C or Class D devices, the name of the state other than the United Kingdom, where the device is or is to be made available;

(e) presence of tissues, cells, or their derivatives of human origin;

(f) presence of tissues, cells or their derivatives of animal origin;

(g) presence of cells or substances of microbial origin;

(h) risk class of the device;

(i) where applicable, the single identification number of the performance study;

(j) in the case of devices designed and manufactured by another legal or natural person as referred in regulation 145(22), the name, address and contact details of that legal or natural person;

(k) in the case of Class C or D devices, the summary of safety and performance;

(l) status of the device (whether it is on the market, no longer placed on the market, recalled, field safety corrective Action initiated);

(m) indication as to whether the device is a "new device" and a device is to be considered "new device" if—

(i) there has been no such device continuously available on the United Kingdom or European Union market during the previous 3 years for the relevant analyte or other parameter; or

(ii) the procedure involves analytical technology not continuously used in connection with a given analyte or other parameter on the United Kingdom market or European Union market during the previous 3 years;

(n) indication as to whether the device is intended for self-testing or near-patient testing.

PART B

Core data elements to be provided to the UDI database together with the UDI-DI in accordance with regulations 157 and 158

3. The person placing the product on the market must provide to the UDI database the UDI-DI and the following information relating to the manufacturer and the device—

(a) quantity per package configuration;

(b) the Basic UDI-DI as referred to in regulation 157(6) and any additional UDI-DIs;

(c) the manner in which production of the device is controlled (expiry date or manufacturing date, lot number, serial number);

(d) if applicable, the 'unit of use' UDI-DI (where a UDI is not labelled on the device at the level of its 'unit of use', a 'unit of use' UDI-DI shall be assigned so as to associate the use of a device with a patient);

(e) name and address of the manufacturer, as indicated on the label;

(f) if applicable, name and address of the authorised representative (as indicated on the label);

(g) the medical device nomenclature code as provided for in regulation 156;

(h) risk class of the device;

(i) if applicable, name or trade name;

(j) if applicable, device model, reference, or catalogue number;

(k) any additional product description;

(l) if applicable, storage and/or handling conditions (as indicated on the label or in the instructions for use);

(m) if applicable, additional trade names of the device;

(n) whether the device is, and is labelled as, a single use device;

(o) if applicable, the maximum number of reuses;

(p) device labelled sterile;

(q) URL for additional information, such as electronic instructions for use (optional);

(r) if applicable, critical warnings or contra-indications;

(s) status of the device (on the market, no longer placed on the market, recalled, field safety action initiated).

PART C

The UDI System

Definitions

4. In this Part of this Schedule—

"automated identification and data capture" or "AIDC" means a technology used to automatically capture data for example bar codes, smart cards, biometrics and RFID;

"Basic UDI" is—

(a) the primary identifier of a device model which is assigned at the level of the device unit of use;

(b) the main key for records in the UDI database;

(c) referenced in relevant certificates and EU declarations of conformity;

"unit of Use DI" means a device identifier used to associate the use of a device with a patient in instances in which a UDI is not labelled on the individual device at the level of its unit of use, for example in the event of several units of the same device being packaged together;

"configurable device" means a device that consists of several components which can be assembled by the manufacturer in multiple configurations and those individual components may be devices in themselves;

"configuration" means a combination of items of equipment, as specified by the manufacturer, that operate together as a device to achieve an intended purpose and which may be modified, adjusted or customised to meet specific needs;

"UDI-DI" means unique numeric or alphanumeric code specific to a model of device and that is also used as the 'access key' to information stored in a UDI database;

"Human readable interpretation" or "HRI" is a legible interpretation of the data characters encoded in the UDI carrier;

"packaging levels" means the various levels of device packaging that contain a fixed quantity of devices, such as a carton or case;

"product identifier" or "UDI-PI" means a numeric or alphanumeric code that identifies the unit of device production examples of which include serial number, lot number, software identification and manufacturing or expiry date or both types of date;

"Radio Frequency Identification" or "RFID" means a technology that uses communication through the use of radio waves to exchange data between a reader and an electronic tag attached to an object, for the purpose of identification;

"shipping container" means a container in relation to which traceability is controlled by a process specific to logistics systems;

"unique device identifier" or "UDI", which is comprised of the UDI-DI and the UDI-PI, means a series of numeric or alphanumeric characters that is created through a globally accepted device identification and coding standard and which allows the unambiguous identification of a specific device on the market;

"UDI carrier" means the method of conveying (by for example ID/linear bar code, 2D/ Matrix bar code or RFID) the UDI by using AIDC, and if applicable, its HRI.

General requirements

5.—(1) The affixing of the UDI does not replace any other marking or labelling requirements laid down in Schedule 17 to these regulations.

(2) The manufacturer must assign and maintain unique UDIs for its devices.

(3) Only the manufacturer may place the UDI on the device or its packaging.

(4) Only coding standards provided by issuing entities may be used.

The UDI

6.—(1) A UDI must be assigned to the device itself or its packaging and higher levels of packaging must have their own UDI.

(2) Shipping containers must be exempted from the requirement in sub-paragraph (1), for example, a UDI is not be required on a logistics unit so that where a healthcare provider orders multiple devices using the UDI or model number of individual devices and the manufacturer places those devices in a container for shipping or to protect the individually packaged devices, the container (logistics unit) is not be subject to UDI requirements.

(3) The UDI must contain two parts, a UDI-DI and a UDI-PI.

(4) The UDI-DI must be unique at each level of device packaging.

(5) Where on the label there is—

(a) a lot number, serial number, software identification or expiry date, it must be part of the UDI-PI; or

(b) only a manufacturing date, this must be used as the UDI-PI;

but where there is both a lot number, serial number, software identification or expiry date and a manufacturing date, the manufacturing date does not need to be included in the UDI-PI.

(6) Each component that is considered to be a device and is commercially available on its own must be assigned a separate UDI unless the components are part of a configurable device that is marked with its own UDI.

(7) Kits shall be assigned and bear their own UDI.

(8) The manufacturer must assign the UDI to a device following the relevant coding standard.

(9) A new UDI-DI is required whenever there is a change that could lead to misidentification of the device or ambiguity in its traceability and in particular, any change of one of the following UDI database data elements requires a new UDI-DI—

(a) name or trade name;

(b) device version or model;

(c) labelled as single use;

(d) packaged sterile;

(e) need for sterilization before use;

(f) quantity of devices provided in a package;

(g) critical warnings or contra-indications.

(10) Manufacturers that repackage or relabel devices with their own label must retain a record of the original device manufacturer's UDI.

UDI carrier

7.—(1) The UDI carrier (AIDC and HRI representation of the UDI) must be placed on the label and on all higher levels of device packaging other than shipping containers.

(2) Where there are significant space constraints on the unit of use packaging the UDI carrier may be placed on the next higher packaging level.

(3) Subject to sub-paragraph (4) for single use Class A and Class B devices packaged and labelled individually, the UDI carrier is not be required to appear on the packaging but it must appear on a higher level of packaging, for example a carton containing several packages.

(4) However, when the healthcare provider is not expected to have access, in cases such as in home healthcare settings, to the higher level of device packaging, the UDI must be placed on the packaging.

(5) For devices exclusively intended for retail point of sale, the UDI-PIs in AIDC is not be required to appear on the point of sale packaging.

(6) When AIDC carriers, other than the UDI carrier, are part of the product labelling, the UDI carrier must be readily identifiable.

(7) If linear bar codes are used, the UDI-DI and UDI-PI may be concatenated or non-concatenated in two or more bar codes but all parts and elements of the linear bar code must be distinguishable and identifiable.

(8) Subject to sub-paragraph (9), there are significant constraints limiting the use of both AIDC and HRI on the label, only the AIDC format is be required to appear on the label.

(9) For devices intended to be used outside healthcare facilities, such as devices for home care, the HRI must appear on the label even if this results in there being no space for the AIDC.

(10) The HRI format must follow the rules of the UDI code-issuing entity.

(11) If the manufacturer is using RFID technology, a linear or 2D bar code in line with the standard provided by the issuing entities must also be provided on the label.

(12) Devices that are reusable—

(a) must bear a UDI carrier on the device itself;

(b) for reusable devices that require disinfection, sterilisation or refurbishing between patient uses, the UDI carrier must be permanent and readable after each process performed to make the device ready for the subsequent use throughout the intended lifetime of the device.

(13) The UDI carrier must be readable during normal use and throughout the intended lifetime of the device.

(14) If the UDI carrier is readily readable or scannable through the device's packaging, the placing of the UDI carrier on the packaging is not required.

(15) In the case of single finished devices made up of multiple parts that must be assembled before first use, it shall be sufficient to place the UDI carrier on only one part of each device.

(16) The UDI carrier must be placed in a manner such that the AIDC can be accessed during normal operation or storage.

(17) Bar code carriers that include both a UDI-DI and a UDI-PI may also include essential data for the device to operate or other data.

General principles of the UDI database

8.—(1) The UDI database must support the use of all core UDI database data elements referred to in Part B of this Schedule.

(2) Manufacturers must be responsible for the initial submission and updates of the identifying information and other device data elements in the UDI database.

(3) Appropriate methods or procedures for validation of the data provided must be implemented.

(4) Manufacturers must periodically verify the correctness of all of the data relevant to devices they have placed on the market, except for devices that are no longer available on the market.

(5) The presence of the device UDI-DI in the UDI database must not be assumed to mean that the device is in conformity with Part IX.

(6) The database must allow for the linking of all the packaging levels of the device.

(7) The data for new UDI-DIs must be available at the time the device is placed on the market.

(8) Manufacturers must update the relevant UDI database record within 30 days of a change being made to an element, which does not require a new UDI-DI.

(9) Internationally accepted standards for data submission and updates must, wherever possible, be used by the UDI database.

(10) The user interface of the UDI database must be available in English.

Rules for specific device types

Reusable devices that are part of kits and that require cleaning, sterilisation or refurbishing between uses

9.—(1) For reusable devices that are part of kits and that require cleaning, sterilisation or refurbishing between uses—

(a) the UDI must be placed on the device and must be readable after each procedure to make the device ready for the next use;

(b) the UDI-PI characteristics such as the lot or serial number must be defined by the manufacturer.

Device software

(2) The UDI assignment criteria for device software are—

(a) the UDI must be assigned at the system level of the software but only software which is commercially available on its own and software which constitutes a device in itself is subject to that requirement;

(b) the software identification must be considered to be the manufacturing control mechanism and must be displayed in the UDI-PI.

(3) A new UDI-DI is required whenever there is a modification that changes—

(a) the original performance;

(b) the safety or the intended use of the software;

(c) interpretation of data;

and such modifications include new or modified algorithms, database structures, operating platform, architecture or new user interfaces or new channels for interoperability.

(4) Minor software revisions—

(a) require a new UDI-PI and not a new UDI-DI;

(b) are generally associated with bug fixes, usability enhancements that are not for safety purposes, security patches or operating efficiency;

(c) must be identified by a manufacturer-specific form of identification.

UDI placement criteria for software

(5) The UDI placement criteria for software are as follows—

(a) where the software is delivered on a physical medium, for example via a CD or DVD, each packaging level must bear the human readable and AIDC representation of the complete UDI and the UDI that is applied to the physical medium containing the software and its packaging must be identical to the UDI assigned to the system level software;

(b) the UDI must be provided on a readily accessible screen for the user in an easily-readable plain-text format such as an 'about' file, or included on the start-up screen;

(c) software lacking a user interface such as middleware for image conversion, must be capable of transmitting the UDI through an application programming interface (API);

(d) only the human readable portion of the UDI is required in electronic displays of the software and the marking of UDI using AIDC is not required in the electronic displays such as 'about' menu, splash screen (a window consisting of an image or logo typically used to notify the user that a programme is in the process of loading;

(e) the human readable format of the UDI for the software must include the application identifiers (AI) for the standard used by the issuing entities, so as to assist the user in identifying the UDI and determining which standard is being used to create the UDI.

SCHEDULE 23

Regulation 1A

Classification Rules for in vitro diagnostic medical devices

Implementation rules

1.—(1) Application of the classification rules must be governed by the intended purpose of the devices.

(2) If the device in question is intended to be used in combination with another device, the classification rules must apply separately to each of the devices.

(3) Accessories for an in vitro diagnostic medical device must be classified in their own right separately from the device with which they are used.

(4) Software which—

(a) drives a device or influences the use of a device, must fall within the same class as the device;

(b) is independent of any other device, must be classified in its own right.

(5) Calibrators intended to be used with a device must be classified in the same class as the device.

(6) Control materials with quantitative or qualitative assigned values intended for one specific analyte or multiple analytes must be classified in the same class as the device.

(7) The manufacturer must take into consideration all classification and implementation rules in order to establish the proper classification for the device.

(8) Where a manufacturer states multiple intended purposes for a device, and as a result the device falls into more than one class, it must be classified in the higher class.

(9) If several classification rules apply to the same device, the rule resulting in the higher classification must apply.

(10) Each of the classification rules must apply to first line assays, confirmatory assays and supplemental assays.

Classification rules

Rule 1

2.—(1) Devices intended to be used for the following purposes are classified as Class D—

(a) detection of the presence of, or exposure to, a transmissible agent in blood, blood components, cells, tissues or organs, or in any of their derivatives, in order to assess their suitability for transfusion, transplantation or cell administration;

(b) detection of the presence of, or exposure to, a transmissible agent that causes a life-threatening disease with a high or suspected high risk of propagation;

(c) determining the infectious load of a life-threatening disease where monitoring is critical in the process of patient management.

Rule 2

(2) Devices intended to be used for blood grouping, or tissue typing to ensure the immunological compatibility of blood, blood components, cells, tissue or organs that are intended for transfusion or transplantation or cell administration, are classified as class C, except when intended to determine any of the following markers—

(a) ABO system [A (ABO1), B (ABO2), AB (ABO3)];

(b) Rhesus system [RH1 (D), RHW1, RH2 (C), RH3 (E), RH4 (c), RH5 (e)];

(c) Kell system [Kel1 (K)];

(d) Kidd system [JK1 (Jka), JK2 (Jkb)];

(e) Duffy system [FY1 (Fya), FY2 (Fyb)];

in which case they are classified as Class D.

Rule 3

(3) Devices are classified as Class C if they are intended—

(a) for detecting the presence of, or exposure to, a sexually transmitted agent;

(b) for detecting the presence in cerebrospinal fluid or blood of an infectious agent without a high or suspected high risk of propagation;

(c) for detecting the presence of an infectious agent, if there is a significant risk that an erroneous result would cause death or severe disability to the individual, foetus or embryo being tested, or to the individual's offspring;

(d) for pre-natal screening of women in order to determine their immune status towards transmissible agents;

(e) for determining infective disease status or immune status, where there is a risk that an erroneous result would lead to a patient management decision resulting in a life-threatening situation for the patient or for the patient's offspring;

(f) to be used as companion diagnostics;

(g) to be used for disease staging, where there is a risk that an erroneous result would lead to a patient management decision resulting in a life-threatening situation for the patient or for the patient's offspring;

(h) to be used in screening, diagnosis, or staging of cancer;

(i) for human genetic testing;

(j) for monitoring of levels of medicinal products, substances or biological components, when there is a risk that an erroneous result will lead to a patient management decision resulting in a life-threatening situation for the patient or for the patient's offspring;

(k) for management of patients suffering from a life-threatening disease or condition;

(l) for screening for congenital disorders in the embryo or foetus;

(m) for screening for congenital disorders in new-born babies where failure to detect and treat such disorders could lead to life-threatening situations or severe disabilities.

Rule 4

(4) Devices intended for self-testing are classified as Class C, except for devices testing the following which are classified in Class D—

(a) the detection of pregnancy;

(b) fertility testing;

(c) for determining cholesterol level;

(d) for the detection of glucose, *erythrocytes*, *leucocytes* and bacteria in urine.

(5) Devices intended for near-patient testing are classified in their own right.

Rule 5

(6) The following devices are classified as Class A—

(a) products for general laboratory use, accessories which possess no critical characteristics, buffer solutions, washing solutions, and general culture media and histological stains, intended by the manufacturer to make them suitable for in vitro diagnostic procedures relating to a specific examination;

(b) instruments intended by the manufacturer specifically to be used for in vitro diagnostic procedures;

(c) specimen receptacles.

Rule 6

Devices not covered by the above-mentioned classification rules are classified as Class B.

Rule 7

Devices which are controls without a quantitative or qualitative assigned value are classified as Class B.

SCHEDULE 24 Regulation 1A

Conformity assessment based on quality management system and on assessment of technical documentation- in vitro diagnostic medical devices

PART 1

Quality management system

1.—(1) The manufacturer must—

(a) establish, document and implement a quality management system as described in regulation 145(12);

(b) maintain its effectiveness throughout the life cycle of the devices concerned;

(c) ensure the application of the quality management system as specified in sub-paragraph (2);

(d) comply with the surveillance requirements as specified in sub-paragraph (7).

Quality management system assessment

(2) The manufacturer must lodge an application for assessment of its quality management system with a notified body and the application must include—

(a) the name of the manufacturer and address of its registered place of business and any additional manufacturing site covered by the quality management system, and, if the manufacturer's application is lodged by its authorised representative the name of the authorised representative and the address of the authorised representative's registered place of business;

(b) all relevant information on the device or group of devices covered by the quality management system;

(c) a written declaration that no application has been lodged with any other notified body for the same device-related quality management system, or information about any previous application for the same device- related quality management system;

(d) a draft of a declaration of conformity for the device model covered by the conformity assessment procedure;

(e) the documentation on the manufacturer's quality management system,

(f) a documented description of the procedures in place to fulfil the obligations arising from the quality management system and required under Part IX and of the undertaking by the manufacturer in question to apply those procedures;

(g) a description of the procedures in place to ensure that the quality management system remains adequate and effective, and the undertaking by the manufacturer to apply those procedures;

(h) the documentation on the manufacturer's post-market surveillance system, and, where applicable, on the PMPF plan, and the procedures put in place to ensure compliance with the obligations resulting from the provisions on vigilance set out in regulations 190 to 194;

(i) a description of the procedures in place to keep up to date the post-market surveillance system and, where applicable, the PMPF plan, and the procedures ensuring compliance with the obligations resulting from the provisions on vigilance set out in regulations 190 to 194, as well as the undertaking by the manufacturer to apply those procedures;

(j) documentation on the performance evaluation plan;

(k) a description of the procedures in place to keep up to date the performance evaluation plan, taking into account the state of the art.

(3) Implementation of the quality management system must ensure compliance with Part IX and all the elements, requirements and provisions adopted by the manufacturer for its quality management system must be documented in a systematic and orderly manner in the form of a quality manual and written policies and procedures, such as quality programmes, quality plans and quality records.

(4) The documentation to be submitted for the assessment of the quality management system must include an adequate description of, in particular—

(a) the manufacturer's quality objectives;

(b) the organisation of the business and in particular—

(i) the organisational structures with the assignment of staff responsibilities in relation to critical procedures, the responsibilities of the managerial staff and their organisational authority;

(ii) the methods of monitoring whether the operation of the quality management system is efficient and in particular the ability of that system to achieve the desired design and device quality, including control of devices which fail to conform;

(iii) where the design, manufacture, or final verification and testing of the devices, or parts of any of those processes, is carried out by another party, the methods of monitoring the efficient operation of the quality management system and in particular the type and extent of control applied to the other party;

(iv) where applicable, the draft mandate for the designation of an authorised representative and a letter of intention from the authorised representative to accept the mandate;

(c) the procedures and techniques for monitoring, verifying, validating and controlling the design of the devices, and the corresponding documentation as well as the data and records arising from those procedures and techniques and those procedures and techniques must specifically cover—

(i) the strategy for regulatory compliance, including processes for identification of relevant legal requirements, qualification, classification, handling of equivalence, choice of, and compliance with, conformity assessment procedures;

(ii) identification of applicable general safety and performance requirements and solutions to fulfil those requirements, taking applicable CS into account and, where opted for, designated standards;

(iii) risk management as referred to in paragraph 3 of Schedule 17;

(iv) the performance evaluation, pursuant to regulation 167 and Schedule 27, including PMPF;

(v) solutions for fulfilling the applicable specific requirements regarding design and construction, including appropriate pre-clinical evaluation, in particular the requirements of Part 2 of Schedule 17;

(vi) solutions for fulfilling the applicable specific requirements regarding the information to be supplied with the device, in particular the requirements of Part 3 of Schedule 17;

(vii) the device identification procedures drawn up and kept up to date from drawings, specifications or other relevant documents at every stage of manufacture; and

(viii) management of design or quality management system changes;

(d) the verification and quality assurance techniques at the manufacturing stage and in particular the processes and procedures which are to be used, particularly as regards sterilisation, and the relevant documents;

(e) the appropriate tests and trials which are to be carried out before, during and after manufacture, the frequency with which they are to take place, and the test equipment to be used and it must be possible to trace back adequately the calibration of that test equipment.

(5) The manufacturer must grant the notified body access to the technical documentation referred to in Schedules 18 and 19.

(6) The manufacturer must inform the notified body which approved the quality management system of any plan for substantial changes to the quality management system, or the device-range covered and the approval of any substantive change to the quality management system or the device-range covered must take the form of a supplement to the quality management system certificate.

Surveillance applicable to Class C and Class D devices

(7) The manufacturer of Class C and D devices must give authorisation to the notified body to carry out all the necessary audits, including on-site audits, and supply it with all relevant information, in particular—

(a) the documentation on its quality management system;

(b) the documentation on any findings and conclusions resulting from the application of the post-market surveillance plan, including the PMPF plan, for a representative sample of devices, and of the provisions on vigilance set out in regulations 190 to 194;

(c) the data stipulated in the part of the quality management system relating to design, such as the results of analyses, calculations, tests and the solutions adopted regarding the risk-management as referred to in paragraph 4 of Schedule 17;

(d) the data stipulated in the part of the quality management system relating to manufacture, such as quality control reports and test data, calibration data, and records on the qualifications of the personnel concerned.

PART 2

Assessment of technical documentation

Assessment of the technical documentation of class B, C and D devices and batch verification applicable to class D devices

2.—(1) In addition, to the obligation laid down in paragraph 1, the manufacturer of Class B, C and D devices must lodge with the notified body an application for the assessment of the technical documentation relating to the device which it plans to place on the market or put into service and which is covered by the quality management system referred to in paragraph 1.

(2) The application must describe the design, manufacture and performance of the device in question and must include the technical documentation as referred to in Schedules 18 and 19.

(3) In the case of devices for self-testing or near-patient testing, the application must also include the aspects referred to in paragraph 3(b).

Assessment of technical documentation of specific types of devices

3. For Class B, C and D devices for self-testing and near-patient testing the assessment of the technical documentation must be carried out as follows—

(a) the manufacturer of Class B, C and D devices for self-testing and near-patient testing must lodge with the notified body an application for the assessment of the technical documentation;

(b) the application must enable the design of the device characteristics and performance to be understood and must enable conformity with the design-related requirements of this Part to be assessed and must include—

(i) test reports, including results of studies carried out with intended users;

(ii) where practicable, an example of the device and, if required, the device must be returned on completion of the technical documentation assessment;

(iii) data showing the suitability of the device in view of its intended purpose for self-testing or near patient- testing;

(iv) the information to be provided with the device on its label and its instructions for use.

Assessment of the technical documentation of companion diagnostics

4.—(1) The manufacturer of a companion diagnostic must lodge with the notified body an application for the assessment of the technical documentation and the notified body will assess that application in accordance with the procedure laid down in Sections 4.1 to 4.8 of this Annex IX to Regulation (EU) 2017/746.

(2) The application must enable the characteristics and performance of the device to be understood, and must enable conformity with the design-related requirements of this Part to be assessed, in particular, with regard to the suitability of the device in relation to the medicinal product concerned.

PART 3

Administrative Provisions

5. The manufacturer or, where the manufacturer does not have a registered place of business in the United Kingdom, the person placing the product on the market must, for a period ending no sooner than 10 years after the last device has been placed on the market, keep at the disposal of the Secretary of State—

(a) the declaration of conformity;

(b) the documentation referred to in the fifth indent of paragraph 1(2) and, in particular, the data and records arising from the procedures referred to in paragraph 1(4)(c);

(c) information on the changes referred to in paragraph 1(6);

(d) the documentation referred to in paragraph 2(2) and paragraph 3(b); and

(e) the decisions and reports from the notified body.

6. The documentation in paragraph 5 must be kept available to the Secretary of State throughout the 10 year period specified in paragraph 5 irrespective of the continued status (and whether the person continues trading or not) of the manufacturer or person placing the product on the market.

SCHEDULE 25

Regulation 1A

Conformity assessment based on the type-examination

1. In this Schedule a "type-examination" is the procedure whereby a notified body ascertains and certifies that a device, including its technical documentation and relevant life cycle processes and a corresponding representative sample of the device production envisaged, fulfils the relevant provisions.

Application

2. The manufacturer must lodge an application for assessment with a notified body and the application must—

(a) include the name of the manufacturer and the address of its registered place of business and, if the application is lodged by the authorised representative, the name of the authorised representative and the address of its registered place of business;

(b) include the technical documentation referred to in Schedules 18 and 19;

(c) provide to or make available, a representative sample of the device production envisaged ('type'), to the notified body (the notified body may request other samples as necessary);

(d) in the case of devices for self-testing or near-patient testing, provide test reports, including results of studies carried out with intended users, and data showing the handling suitability of the device in relation to its intended purpose for self-testing or near patient-testing;

(e) where practicable, provide an example of the device which, if required, must be returned on completion of the technical documentation assessment;

(f) include data showing the suitability of the device in relation to its intended purpose for self-testing or near-patient testing;

(g) the information to be provided with the device on its label and its instructions for use; and

(h) a written declaration that no application has been lodged with any other notified body for the same type, or information about any previous application for the same type that was refused by another notified body or was withdrawn by the manufacturer or its authorised representative before that other notified body made its final assessment.

Assessment

3. The assessment must be carried out by a notified body in accordance with the obligations placed on such a body by Section 3 of Annex X to Regulation (EU) 2017/746.

Changes to the type

4.—(1) The applicant must inform the notified body which issued the type-examination certificate of any planned change to the approved type or of its intended purpose and conditions of use.

(2) Changes to the approved device including limitations of its intended purpose and conditions of use must be further approved by the notified body which issued the type-examination certificate where such changes may affect conformity with the general safety and performance requirements or with the conditions prescribed for use of the product.

(3) The approval of any change to the approved type must take the form of a supplement to the type-examination certificate.

(4) Changes to the intended purpose and conditions of use of the approved device, with the exception of limitations of the intended purpose and conditions of use, require a new application for a conformity assessment.

Administrative provisions

5.—(1) The manufacturer or, where the manufacturer does not have a registered place of business in a United Kingdom, the person placing the product on the market must, for a period ending no sooner than 10 years, after the last device has been placed on the market, keep at the disposal of the Secretary of State—

(a) the documentation referred to in paragraph 2(b);

(b) information on the changes referred to in paragraph 4;

(c) copies of type-examination certificates, scientific opinions and reports and their additions/supplements.

(2) The documentation in sub-paragraph (1) must be kept available to the Secretary of State throughout the period specified in sub-paragraph (1) irrespective of the continued status (and whether the person continues trading or not) of the person placing the product on the market.

SCHEDULE 26

Regulation 1A

Conformity assessment based on production quality assurance

1.—(1) The manufacturer must—

(a) ensure that the quality management system approved for the manufacture of the devices concerned is implemented;

(b) carry out final verification, as specified in paragraph 2(3);

(c) be subject to the surveillance referred to in paragraph 4.

(2) When the manufacturer fulfils the obligations laid down in sub-paragraph (1), the manufacturer must draw up and keep a declaration of conformity in accordance with regulation 151 for the device covered by the conformity assessment procedure.

(3) By issuing a declaration of conformity, the manufacturer must be deemed to ensure, and to declare, that the device concerned meets the requirements of this Part which apply to the device, and in the case of Class C and Class D devices that undergo a type examination, conforms to the type described in the type-examination certificate.

Quality management system

2.—(1) The manufacturer must lodge an application for assessment of its quality management system with a notified body.

(2) The application in sub-paragraph (1) must include—

(a) all elements listed in paragraph 1(2) of Schedule 24;

(b) the technical documentation referred to in Schedules 18 and 19 for the types approved;

(c) a copy of the type-examination certificates and, if the type-examination certificates have been issued by the same notified body with which the application is lodged, a reference to the technical documentation and its updates and the certificates issued must also be included in the application.

(3) Implementation of the quality management system must be such as to ensure that there is compliance with the type described in the type-examination certificate and with the provisions of this Part which apply to the devices at each stage.

(4) All the elements, requirements and provisions adopted by the manufacturer for its quality management system must be documented in a systematic and orderly manner in the form of a quality manual and written policies and procedures, such as quality programmes, quality plans and quality records and that documentation must, in particular, include an adequate description of all elements listed in paragraphs (a), (b), (d) and (e) of paragraph 1(4).

(5) The manufacturer must inform the notified body which approved the quality management system of any plan for substantial changes to the quality management system, or the device-range covered and the approval of any substantial change to the quality management system or device-range covered must take the form of a supplement to the quality management system certificate.

Surveillance

3. The manufacturer of Class C and D devices must give authorisation to the notified body to carry out all the necessary audits, including on-site audits, and supply it with all relevant information, in particular—

(a) the documentation on its quality management system;

(b) the documentation on any findings and conclusions resulting from the application of the post-market surveillance plan, including the PMPF plan, for a representative sample of devices, and of the provisions on vigilance set out in regulations 190 to 194;

(c) the data stipulated in the part of the quality management system relating to design, such as the results of analyses, calculations, tests and the solutions adopted regarding the risk-management as referred to in paragraph 4 of Schedule 17;

(d) the data stipulated in the part of the quality management system relating to manufacture, such as quality control reports and test data, calibration data, and records on the qualifications of the personnel concerned.

Verification of manufactured Class D devices

4.—(1) In the case of Class D devices, the manufacturer must carry out tests on each manufactured batch of devices.

(2) After the conclusion of the controls and tests, the manufacturer must forward to the notified body without delay the relevant reports on those tests.

(3) The manufacturer must make samples of manufactured devices or batches of devices available to the notified body in accordance with pre-agreed conditions and detailed arrangements.

(4) The manufacturer may place the devices on the market, unless the notified body communicates to the manufacturer within the agreed timeframe, but not later than 30 days after reception of the samples, any other decision, including in particular any condition of validity of delivered certificates.

Administrative provisions

5.—(1) The manufacturer or, where the manufacturer does not have a registered place of business in the United Kingdom, the person placing the product on the market must, for a period ending no sooner than 10 years after the last device has been placed on the market, keep at the disposal of the Secretary of State—

(a) the declaration of conformity;

(b) the documentation referred to in the paragraph 1(2)(e) of Schedule 24;

(c) the documentation referred to in paragraph 1(2)(i) of Schedule 24, including the type-examination certificate referred to in Schedule 25;

(d) information on the changes referred to in paragraph 1(6) of Schedule 24;

(e) the decisions and reports from the notified body.

(2) The documentation listed in sub-paragraph (1) must be kept available to the Secretary of State throughout the period specified in sub-paragraph (1) irrespective of the continued status (and whether the person continues trading or not) of the manufacturer or person placing the product on the market.

SCHEDULE 27 Regulation 1A

Performance evaluation, performance studies and post-market performance follow-up

PART A

Performance evaluation and performance studies

Performance evaluation

1.—(1) Performance evaluation of a device is a continuous process by which data are assessed and analysed to demonstrate the scientific validity, analytical performance and clinical performance of that device for its intended purpose as stated by the manufacturer.

(2) The performance evaluation must—

(a) be thorough and objective, considering both favourable and unfavourable data;

(b) be proportionate in terms of its depth and extent and appropriate to the characteristics of the device including the risks, risk class, performance and its intended purpose.

(3) To plan, continuously conduct and document a performance evaluation, the manufacturer must establish and update a performance evaluation plan which must specify the characteristics and the performance of the device and the process and criteria applied to generate the necessary clinical evidence.

Performance evaluation plan

(4) As a general rule the performance evaluation plan must include at least—

(a) a specification of the intended purpose of the device;

(b) a specification of the characteristics of the device as described in paragraph 9 of Part 2 of Schedule 17 and in paragraph 20(6)(c) of Part 3 of Schedule 17;

(c) a specification of the analyte or marker to be determined by the device;

(d) a specification of the intended use of the device;

(e) identification of certified reference materials or reference measurement procedures to allow for metrological traceability;

(f) a clear identification of specified target patient groups with clear indications, limitations and contra-indications;

(g) an identification of the general safety and performance requirements as laid down in paragraphs 1 to 9 of Schedule 17 that require support from relevant scientific validity and analytical and clinical performance data;

(h) a specification of methods, including the appropriate statistical tools, used for the examination of the analytical and clinical performance of the device and of the limitations of the device and information provided by it;

(i) a description of the state of the art, including an identification of existing relevant standards, CS, guidance or best practices documents;

(j) an indication and specification of parameters to be used to determine, based on the state of the art in medicine, the acceptability of the benefit-risk ratio for the intended purpose or purposes and for the analytical and clinical performance of the device;

(k) for software qualified as a device, an identification and specification of reference databases and other sources of data used as the basis for its decision making;

(l) an outline of the different development phases including the sequence and means of determination of the scientific validity, the analytical and clinical performance, including an indication of milestones and a description of potential acceptance criteria;

(m) the PMPF planning as referred to in Part B of this Schedule.

(5) Where any of the elements set out in sub-paragraph (4) are not deemed appropriate in the performance evaluation plan due to the specific device characteristics a justification must be provided in the plan.

Demonstration of the scientific validity and the analytical and clinical performance

(6) As a general methodological principle the manufacturer must—

(a) identify through a systematic scientific literature review the available data relevant to the device and its intended purpose and identify any remaining unaddressed issues or gaps in the data;

(b) appraise all relevant data by evaluating their suitability for establishing the safety and performance of the device;

(c) generate any new or additional data necessary to address outstanding issues.

Demonstration of scientific validity

(7) The manufacturer must demonstrate the scientific validity based on one or a combination of the following sources—

(a) relevant information on the scientific validity of devices measuring the same analyte or marker;

(b) scientific (peer-reviewed) literature;

(c) consensus expert opinions/positions from relevant professional associations;

(d) results from proof of concept studies;

(e) results from clinical performance studies.

(8) The scientific validity of the analyte or marker must be demonstrated and documented in the scientific validity report.

Demonstration of the analytical performance

(9) The manufacturer must demonstrate the analytical performance of the device in relation to all the parameters described in paragraph 9(b)(i) of Schedule 17, unless any omission can be justified as not applicable.

(10) As a general rule, the analytical performance shall always be demonstrated on the basis of analytical performance studies.

(11) For novel markers or other markers without available certified reference materials or reference measurement procedures where it is not possible to demonstrate trueness and where there are no comparable methods—

(a) different approaches may be used if demonstrated to be appropriate, such as comparison to some other well-documented methods or the composite reference standard;

(b) in the absence of such approaches, a clinical performance study comparing performance of the novel device to the current clinical standard practice is required.

(12) Analytical performance must be demonstrated and documented in the analytical performance report.

Demonstration of the clinical performance

(13) The manufacturer shall demonstrate the clinical performance of the device in relation to all the parameters described in paragraph 9(b)(ii) of Schedule 17, unless any omission can be justified as not applicable.

(14) Demonstration of the clinical performance of a device must be based on one or a combination of the following sources—

(a) clinical performance studies;

(b) scientific peer-reviewed literature;

(c) published experience gained by routine diagnostic testing.

(15) Clinical performance studies must be performed unless due justification is provided for relying on other sources of clinical performance data.

(16) Clinical performance must be demonstrated and documented in the clinical performance report.

Clinical evidence and performance evaluation report

(17) The manufacturer must assess all relevant scientific validity, analytical and clinical performance data to verify the conformity of its device with the general safety and performance requirements as referred to in Schedule 17.

(18) The amount and quality of that data must allow the manufacturer to make a qualified assessment whether the device will achieve the intended clinical benefit or benefits and safety, when used as intended by the manufacturer.

(19) The data and conclusions drawn from this assessment constitute the clinical evidence for the device.

(20) The clinical evidence must scientifically demonstrate that the intended clinical benefit or benefits and safety will be achieved according to the state of the art in medicine.

Performance evaluation report

(21) The clinical evidence must be documented in a performance evaluation report and this report must include the scientific validity report, the analytical performance report, the clinical performance report and an assessment of those reports allowing demonstration of the clinical evidence.

(22) The performance evaluation report shall in particular include—

(a) the justification for the approach taken to gather the clinical evidence;

(b) the literature search methodology and the literature search protocol and literature search report of a literature review;

(c) the technology on which the device is based, the intended purpose of the device and any claims made about the device's performance or safety;

(d) the nature and extent of the scientific validity and the analytical and clinical performance data that has been evaluated;

(e) the clinical evidence as the acceptable performances against the state of the art in medicine;

(f) any new conclusions derived from PMPF reports in accordance with Part B of this Schedule.

(23) The clinical evidence and its assessment in the performance evaluation report must be updated throughout the life cycle of the device concerned with data obtained from the implementation of the manufacturer's PMPF plan in accordance with Part B of this Schedule, as part of the performance evaluation and the post-market surveillance system referred to in regulation 145(14).

(24) The performance evaluation report must be part of the technical documentation and both favourable and unfavourable data considered in the performance evaluation must be included in the technical documentation.

Clinical performance studies

Purpose of clinical performance studies

2.—(1) The purpose of clinical performance studies is to establish or confirm aspects of device performance which cannot be determined by analytical performance studies, literature or previous experience gained by routine diagnostic testing.

(2) This information from a clinical performance study is used to demonstrate compliance with the relevant general safety and performance requirements with respect to clinical performance.

(3) When clinical performance studies are conducted, the data obtained must be used in the performance evaluation process and be part of the clinical evidence for the device.

Ethical considerations for clinical performance studies

(4) Each step in the clinical performance study, from the initial consideration of the need for and justification of the study to the publication of the results, must be carried out in accordance with recognised ethical principles.

Methods for clinical performance studies

(5) Clinical performance studies must be designed in such a way as to maximize the relevance of the data while minimising potential bias.

(6) Clinical performance studies must be performed on the basis of a clinical performance study plan (CPSP).

(7) The CPSP must define the rationale, objectives, design and proposed analysis, methodology, monitoring, conduct and record-keeping of the clinical performance study and must contain in particular the following information—

(a) identification of the sponsor, including the name, address of the registered place of business and contact details of the sponsor and, if applicable, the name, address of the registered place of business and contact details of its contact person or legal representative pursuant regulation 169(5);

(b) information on the investigator or investigators, namely principal, coordinating or other investigator; qualifications, contact details, and investigation site or sites, such

as number, qualification, contact details and, in the case of devices for self-testing, the location and number of lay persons involved;

(c) the starting date and scheduled duration for the clinical performance study;

(d) identification and description of the device, its intended purpose, the analyte or analytes or marker or markers, the metrological traceability, and the manufacturer;

(e) information about the type of specimens under investigation;

(f) overall synopsis of the clinical performance study, its design type, such as observational, interventional, together with the objectives and hypotheses of the study, reference to the current state of the art in diagnosis or medicine;

(g) a description of the expected risks and benefits of the device and of the clinical performance study in the context of the state of the art in clinical practice, and with the exception of studies using left-over samples, the medical procedures involved and patient management;

(h) the instructions for use of the device or test protocol, the necessary training and experience of the user, the appropriate calibration procedures and means of control, the indication of any other devices, medical devices, medicinal product or other articles to be included or excluded and the specifications on any comparator or comparative method used as reference;

(i) a description of and justification for the design of the clinical performance study, its scientific robustness and validity, including the statistical design, and details of measures to be taken to minimise bias, such as randomisation, and management of potential confounding factors;

(j) the analytical performance in accordance with paragraph 9(b)(i) of Schedule 17 with justification for any omission;

(k) parameters of clinical performance in accordance with paragraph 9(b)(ii) of Schedule 17 to be determined, with justification for any omission and with the exception of studies using left-over samples the specified clinical outcomes/endpoints (primary/secondary) used with a justification and the potential implications for individual health or public health management decisions;

(l) information on the performance study population: specifications of the subjects, selection criteria, size of performance study population, representativity of target population and, if applicable, information on vulnerable subjects involved, such as children, pregnant women, immuno-compromised or elderly subjects;

(m) information on use of data out of left over specimens banks, genetic or tissue banks, patient or disease registries etc. with description of reliability and representativity and statistical analysis approach; assurance of relevant method for determining the true clinical status of patient specimens;

(n) the monitoring plan;

(o) data management;

(p) decision algorithms;

(q) policy regarding any amendments, including those in accordance with regulation 182, to or deviations from the CPSP, with a clear prohibition of use of waivers from the CPSP;

(r) accountability regarding the device, in particular control of access to the device, follow-up in relation to the device used in the clinical performance study and the return of unused, expired or malfunctioning devices;

(s) statement of compliance with the recognised ethical principles for medical research involving humans and the principles of good clinical practice in the field of clinical performance studies as well as with the applicable regulatory requirements;

(t) description of the informed consent process, including a copy of the patient information sheet and consent forms;

(u) procedures for safety recording and reporting, including definitions of recordable and reportable events, and procedures and timelines for reporting;

(v) criteria and procedures for suspension or early termination of the clinical performance study;

(w) criteria and procedures for follow up of subjects following completion of a performance study, procedures for follow up of subjects in the case of suspension or early termination, procedures for follow up of subjects who have withdrawn their consent and procedures for subjects lost to follow up;

(x) procedures for communication of test results outside the study, including communication of test results to the performance study subjects;

(y) policy as regards the establishment of the clinical performance study report and publication of results in accordance with the legal requirements and the ethical principles referred to in sub-paragraph (4);

(z) list of the technical and functional features of the device indicating those that are covered by the performance study;

(aa) bibliography.

(8) Sub-paragraph (7) applies subject to the following—

(a) if part of the information referred to in sub-paragraph (7) is submitted in a separate document, it must be referenced in the CPSP;

(b) for studies using left-over samples, paragraphs (u), (x), (y)and (z) do not apply.

(9) Where any of the elements referred to in the second paragraph are not deemed appropriate for inclusion in the CPSP due to the specific study design chosen, such as use of left-over samples versus interventional clinical performance studies, a justification must be provided.

Clinical performance study report

(10) A clinical performance study report, signed by a medical practitioner or any other authorised person responsible, must contain documented information on the clinical performance study protocol plan, results and conclusions of the clinical performance study, including negative findings.

(11) The results and conclusions of the clinical performance study must be transparent, free from bias and clinically relevant.

(12) The clinical performance study report must—

(a) contain sufficient information to enable it to be understood by an independent party without reference to other documents;

(b) include as appropriate any protocol amendments or deviations, and data exclusions with the appropriate rationale.

Other performance studies

3. The performance study plan and the performance study report must be documented for performance studies other than clinical performance studies.

PART B

Post–market performance follow-up (PMPF)

4.—(1) PMPF must be specifically addressed in the manufacturer's post-market surveillance plan.

(2) When conducting PMPF, the manufacturer must proactively collect and evaluate performance and relevant scientific data from the use of a device which bears the CE marking and is placed on the market or put into service within its intended purpose as referred to in the relevant conformity assessment procedure, with the aim of confirming the safety, performance and scientific validity throughout the expected lifetime of the device, of ensuring the continued acceptability of the benefit-risk ratio and of detecting emerging risks on the basis of factual evidence.

5.—(1) PMPF shall be performed pursuant to a documented method laid down in a PMPF plan.

(2) The PMPF plan must specify the methods and procedures for proactively collecting and evaluating safety, performance and scientific data with the aim of—

(a) confirming the safety and performance of the device throughout its expected lifetime;

(b) identifying previously unknown risks or limits to performance and contra-indications;

(c) identifying and analysing emergent risks on the basis of factual evidence;

(d) ensuring the continued acceptability of the clinical evidence and of the benefit-risk ratio referred to in paragraphs 1 and 8 of Part 1 of Schedule 17; and

(e) identifying possible systematic misuse.

(3) The PMPF plan shall include at least—

(a) the general methods and procedures of the PMPF to be applied, such as gathering of clinical experience gained, feedback from users, screening of scientific literature and of other sources of performance or scientific data;

(b) the specific methods and procedures of PMPF to be applied, such as ring trials and other quality assurance activities, epidemiological studies, evaluation of suitable patient or disease registers, genetic databanks or post-market clinical performance studies;

(c) rationale for the appropriateness of the methods and procedures referred to in paragraphs (a) and (b);

(d) reference to the relevant parts of the performance evaluation report referred to in sub-paragraphs (17) to (20) of paragraph 1 of this Schedule and to the risk management referred to in paragraph 3 of Schedule 17;

(e) the specific objectives to be addressed by the PMPF;

(f) an evaluation of the performance data relating to equivalent or similar devices, and the current state of the art;

(g) reference to any relevant CS, designated standards when used by the manufacturer, and relevant guidance on PMPF;

(h) a detailed and adequately justified time schedule for PMPF activities, such as analysis of PMPF data and reporting, to be undertaken by the manufacturer.

6. The manufacturer must analyse the findings of the PMPF and document the results in a PMPF evaluation report that shall update the performance evaluation report and be part of the technical documentation.

7. The conclusions of the PMPF evaluation report must be taken into account for the performance evaluation referred to in regulation 167 and Part A of this Schedule and in the risk management referred to in paragraph 3 of Schedule 17 and if, through the PMPF, the need for preventive or corrective measures has been identified, the manufacturer must implement them.

8. If PMPF is not deemed appropriate for a specific device then a justification shall be provided and documented within the performance evaluation report.

SCHEDULE 28

Regulation 1A

Interventional clinical performance studies and certain other performance studies

PART 1

Documentation regarding the application for interventional clinical performance studies and other performance studies involving risks for the subjects of the studies

Application form

1. For devices intended to be used in the context of interventional clinical performance studies or other performance studies involving risks for the subjects of the studies, the sponsor must draw up and submit the application in accordance with regulation 169 accompanied by the following documents—

(a) The application form, filled in and containing the following information—

(i) name, address and contact details of the sponsor and, if applicable, name, address and contact details of its contact person or legal representative in accordance with regulation 169(5) established in the United Kingdom;

(ii) if different from those in sub-paragraph (i), name, address and contact details of the manufacturer of the device intended for performance evaluation and, if applicable, of the manufacturer's authorised representative;

(iii) the title of the performance study;

(iv) status of the performance study, such as the first submission, resubmission, significant amendment;

(v) details or reference to the performance study plan, such as including details of the design phase of the performance study;

(vi) if the application is a resubmission with regard to a device for which an application has been already submitted—

(aa) the date or dates and reference number or numbers of the earlier application or in the case of significant amendment, reference to the original application;

(bb) all of the changes from the previous application together with a rationale for those changes, in particular, whether any changes have been made to address conclusions of previous Secretary of State or ethics committee reviews;

(vii) if the application is submitted in parallel with an application for a clinical trial in accordance with Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16th April 2014 on clinical trials on medicinal products for human

use(**7**) as it applies in European Union law, reference to the official registration number of the clinical trial;

(viii) identification of the other countries outside the United Kingdom in which the clinical performance study is to be conducted as part of a multicentre or multinational study at the time of application;

(ix) brief description of the device for performance study, its classification and other information necessary for the identification of the device and device type;

(x) summary of the performance study plan;

(xi) if applicable, information regarding a comparator device, its classification and other information necessary for the identification of the comparator device;

(xii) evidence from the sponsor that the clinical investigator and the investigational site are capable of conducting the clinical performance study in accordance with the performance study plan;

(xiii) details of the anticipated start date and duration of the performance study;

(xiv) details to identify the notified body, if already involved at the stage of application for the performance study;

(xv) confirmation that the sponsor is aware that the Secretary of State may contact the ethics committee that is assessing or has assessed the application;

(xvi) the statement referred to in paragraph 3(a).

Investigator's brochure

2.—(1) The following requirements apply to the investigator's brochure (IB)—

(a) The IB must contain the information on the device for performance study that is relevant for the study and available at the time of application;

(b) any updates to the IB or other relevant information that is newly available must be brought to the attention of the investigators in a timely manner.

(2) The IB must be clearly identified and contain in particular the following information—

(a) identification and description of the device, including information on the intended purpose, the risk classification and applicable classification rule pursuant to Schedule 23, design and manufacturing of the device and reference to previous and similar generations of the device;

(b) manufacturer's instructions for installation, maintenance, maintaining hygiene standards and for use, including storage and handling requirements, as well as, to the extent that such information is available, information to be placed the label, and instructions for use to be provided with the device when placed on the market;

(c) information relating to any relevant training required;

(d) analytical performance;

(e) existing clinical data, in particular—

(i) from relevant peer-reviewed scientific literature and available consensus expert opinions or positions from relevant professional associations relating to the safety, performance, clinical benefits to patients, design characteristics, scientific validity, clinical performance and intended purpose of the device and/or of equivalent or similar devices;

(**7**) OJNo. L 158, 27.5.2014, p.1.

(ii) other relevant clinical data available relating to the safety, scientific validity, clinical performance, clinical benefits to patients, design characteristics and intended purpose of similar devices, including details of their similarities and differences with the device in question;

(f) summary of the benefit-risk analysis and the risk management, including information regarding known or foreseeable risks and warnings;

(g) in the case of devices that include tissues, cells and substances of human, animal or microbial origins detailed information on the tissues, cells and substances, and on the compliance with the relevant general safety and performance requirements and the specific risk management in relation to those tissues, cells and substances;

(h) a list detailing the fulfilment of the relevant general safety and performance requirements set out in Schedule 17, including the standards and CS applied, in full or in part, as well as a description of the solutions for fulfilling the relevant general safety and performance requirements, in so far as those standards and CS have not or have only been partly fulfilled or are lacking;

(i) a detailed description of the clinical procedures and diagnostic tests used in the course of the performance study and in particular information on any deviation from normal clinical practice.

(j) the Performance study plan as referred to in paragraphs 2 and 3 of Schedule 27.

Other information

3. The following other information consisting of—

(a) a signed statement by the person responsible for the manufacture of the device for performance study that the device in question conforms to the general safety and performance requirements laid down in Schedule 17 apart from the aspects covered by the clinical performance study and that, with regard to those aspects, every precaution has been taken to protect the health and safety of the subject;

(b) where applicable, a copy of the opinion or opinions of the ethics committee or committees concerned;

(c) proof of insurance cover or indemnification of subjects in case of injury, pursuant to regulation 175;

(d) documents to be used to obtain informed consent, including the patient information sheet and the informed consent document;

(e) documents to be used to obtain informed consent, including the patient information sheet and the informed consent document;

(f) description of the arrangements to comply with the applicable rules on the protection and confidentiality of personal data, in particular—

(i) organisational and technical arrangements that will be implemented to avoid unauthorised access, disclosure, dissemination, alteration or loss of information and personal data processed;

(ii) a description of measures that will be implemented to ensure confidentiality of records and personal data of subjects;

(iii) a description of measures that will be implemented in case of a data security breach in order to mitigate the possible adverse effects;

(g) full details of the available technical documentation, for example detailed risk analysis/ management documentation or specific test reports must be submitted to the Secretary of State reviewing an application upon request.

PART 2

Other obligations of the sponsor

4.—(1) The sponsor must undertake to keep available for the Secretary of State any documentation necessary to provide evidence for the documentation referred to in Part 1 of this Schedule but, if the sponsor is not the person responsible for the manufacture of the device intended for performance study, that obligation may be fulfilled by that person on behalf of the sponsor.

(2) The sponsor must have an agreement in place to ensure that any serious adverse events or any other event as referred to in regulation 185(2) are reported by the investigator or investigators to the sponsor in a timely manner.

(3) The documentation mentioned in this Schedule must be kept for a period of time of at least 10 years after the clinical performance study with the device in question has ended, or, in the event that the device is subsequently placed on the market, for at least 10 years after the last device has been placed on the market.

(4) The documentation referred to in this Schedule must be kept at the disposal of the Secretary of State for the period indicated in sub-paragraph (3) irrespective of the continued status (and whether the person continues trading or not) of the sponsor or the sponsor's legal representative.

(5) The sponsor must appoint a monitor that is independent of the investigation site to ensure that the clinical performance study is conducted in accordance with the Clinical Performance Study Plan, the principles of good clinical practice and Part IX of these Regulations."