Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU (Text with EEA relevance)

ANNEXES

ANNEX I

GENERAL SAFETY AND PERFORMANCE REQUIREMENTS

CHAPTER I

GENERAL REQUIREMENTS

1. Devices shall achieve the performance intended by their manufacturer and shall be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose. They shall be safe and effective and shall 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 Annex to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio.

3. Manufacturers shall establish, implement, document and maintain a risk management system.

Risk management shall be understood as a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating. In carrying out risk management manufacturers shall:

(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 point (c) in accordance with the requirements of Section 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; and

(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 Section 4.

4. Risk control measures adopted by manufacturers for the design and manufacture of the devices shall conform to safety principles, taking account of the generally acknowledged state of the art. To reduce risks, the manufacturers shall manage risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable. In selecting the most appropriate solutions, manufacturers shall, 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.

Manufacturers shall inform users of any residual risks.

5. In eliminating or reducing risks related to use error, the manufacturer shall:

(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), and

(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 shall 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 shall 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 shall be minimised and be acceptable when weighed against the evaluated potential benefits to the patients and/or the user arising from the intended performance of the device during normal conditions of use.

CHAPTER II

REQUIREMENTS REGARDING PERFORMANCE, DESIGN AND MANUFACTURE

9. Performance characteristics

9.1. Devices shall be designed and manufactured in such a way that they are suitable for the purposes referred to in point (2) of Article 2, 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. They shall achieve the performances, as stated by the manufacturer and in particular, where applicable:

(a) 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; and

(b) the clinical performance, such as diagnostic sensitivity, diagnostic specificity, positive predictive value, negative predictive value, likelihood ratio, expected values in normal and affected populations.

9.2. The performance characteristics of the device shall be maintained during the lifetime of the device as indicated by the manufacturer.

9.3. Where the performance of devices depends on the use of calibrators and/or control materials, the metrological traceability of values assigned to calibrators and/or control materials shall be assured through suitable reference measurement procedures and/or suitable reference materials of a higher metrological order. Where available, metrological traceability of values assigned to calibrators and control materials shall be assured to certified reference materials or reference measurement procedures.

9.4. The characteristics and performances of the device shall 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).

10. Chemical, physical and biological properties

10.1. Devices shall be designed and manufactured in such a way as to ensure that the characteristics and performance requirements referred to in Chapter I are fulfilled.

Particular attention shall be paid to the possibility of impairment of analytical performance due to physical and/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.

10.2. Devices shall be designed, manufactured and packaged in such a way as to minimise the risk posed by contaminants and residues to patients, taking account of the intended purpose of the device, and to the persons involved in the transport, storage and use of the devices. Particular attention shall be paid to tissues exposed to those contaminants and residues and to the duration and frequency of exposure.

10.3. Devices shall be designed and manufactured in such a way as to reduce to a level as low as reasonably practicable the risks posed by substances or particles, including wear debris, degradation products and processing residues, that may be released from the device. Special attention shall be given to substances which are carcinogenic, mutagenic or toxic to reproduction ('CMR'), in accordance with Part 3 of Annex VI to Regulation (EC) No 1272/2008 of the European Parliament and of the Council[(1)], and to 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 the procedure set out in Article 59 of Regulation (EC) No 1907/2006 of the European Parliament and of the Council[(2)].

10.4. Devices shall 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.

11. Infection and microbial contamination

11.1. Devices and their manufacturing processes shall 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. The design shall:

(a) allow easy and safe handling;

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

and, where necessary

(c) prevent microbial contamination of the device during use and, in the case of specimen receptacles, the risk of contamination of the specimen.

11.2. Devices labelled either as sterile or as having a specific microbial state shall 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.

11.3. Devices labelled as sterile shall be processed, manufactured, packaged and, sterilised by means of appropriate, validated methods.

11.4. Devices intended to be sterilised shall be manufactured and packaged in appropriate and controlled conditions and facilities.

11.5. Packaging systems for non-sterile devices shall 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; the packaging system shall be suitable taking account of the method of sterilisation indicated by the manufacturer.

11.6. The labelling of the device shall 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.

12. Devices incorporating materials of biological origin

Where devices include tissues, cells and substances of animal, human or microbial origin, the selection of sources, the processing, preservation, testing and handling of tissues, cells and substances of such origin and control procedures shall be carried out so as to provide safety for user or other person.

In particular, safety with regard to microbial and other transmissible agents shall be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process. This might not apply to certain 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.

13. Construction of devices and interaction with their environment

13.1. If the device is intended for use in combination with other devices or equipment, the whole combination, including the connection system, shall be safe and shall not impair the specified performances of the devices. Any restrictions on use applying to such combinations shall be indicated on the label and/or in the instructions for use.

13.2. Devices shall 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 and/or numeric and/or character codings on specimen receptacles, removable parts and/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.

13.3. Devices shall 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. Particular attention shall 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.

13.4. Devices shall be designed and manufactured in such a way that adjustment, calibration, and maintenance can be done safely and effectively.

13.5. Devices that are intended to be operated together with other devices or products shall be designed and manufactured in such a way that the interoperability and compatibility are reliable and safe.

13.6. Devices shall 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 person. To that end, manufacturers shall identify and test procedures and measures as a result of which their devices can be safely disposed after use. Such procedures shall be described in the instructions for use.

13.7 The measuring, monitoring or display scale (including colour change and other visual indicators) shall 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.

14. Devices with a measuring function

14.1. Devices having a primary analytical measuring function shall be designed and manufactured in such a way as to provide appropriate analytical performance in accordance with point (a) of Section 9.1 of Annex I, taking into account the intended purpose of the device.

14.2. The measurements made by devices with a measuring function shall be expressed in legal units conforming to the provisions of Council Directive 80/181/EEC[(3)].

15. Protection against radiation

15.1. Devices shall 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.

15.2. When devices are intended to emit hazardous, or potentially hazardous, ionizing and/or non-ionizing radiation, they shall 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 and/or adjusted; and

(b) fitted with visual displays and/or audible warnings of such emissions.

15.3. The operating instructions for devices emitting hazardous or potentially hazardous radiation shall contain 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. Information regarding the acceptance and performance testing, the acceptance criteria, and the maintenance procedure shall also be specified.

16. Electronic programmable systems — devices that incorporate electronic 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, shall be designed to ensure repeatability, reliability and performance in line with their intended use. In the event of a single fault condition, appropriate means shall be adopted to eliminate or reduce as far as possible consequent risks or impairment of performance.

16.2. For devices that incorporate software or for software that are devices in themselves, the software shall 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.

16.3. Software referred to in this Section that is intended to be used in combination with mobile computing platforms shall 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).

16.4. Manufacturers shall 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.

17. 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 shall be adopted to eliminate or reduce as far as possible consequent risks.

17.2. Devices where the safety of the patient depends on an internal power supply shall 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. If necessary, such warning or indication shall be given prior to the power supply becoming critical.

17.3. Devices shall 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.

17.4. Devices shall 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.

17.5. Devices shall 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.

18. Protection against mechanical and thermal risks

18.1. Devices shall be designed and manufactured in such a way as to protect users and other persons against mechanical risks.

18.2. Devices shall be sufficiently stable under the foreseen operating conditions. They shall 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.

18.3. 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 shall be incorporated.

Any guards or other means included with the device to provide protection, in particular against moving parts, shall be secure and shall not interfere with access for the normal operation of the device, or restrict routine maintenance of the device as intended by the manufacturer.

18.4. Devices shall 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.

18.5. Devices shall 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.

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

18.7. Errors likely to be made when fitting or refitting certain parts which could be a source of risk shall be made impossible by the design and construction of such parts or, failing this, by information given on the parts themselves and/or their housings.

The same information shall be given on moving parts and/or their housings where the direction of movement needs to be known in order to avoid a risk.

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

19. 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 shall 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. The information and instructions provided by the manufacturer shall 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. In the case of near-patient testing, the information and the instructions provided by the manufacturer shall make clear the level of training, qualifications and/or experience required by the user.

19.2. Devices intended for self-testing or near-patient testing shall 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 and/or information; and

(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.

19.3. Devices intended for self-testing and near-patient testing shall, 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; and

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

CHAPTER III

REQUIREMENTS REGARDING INFORMATION SUPPLIED WITH THE DEVICE

20. Label and instructions for use

20.1. General requirements regarding the information supplied by the manufacturer

Each device shall be accompanied by the information 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. Such information may appear on the device itself, on the packaging or in the instructions for use, and shall, 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 shall be appropriate to the particular device, its intended purpose and the technical knowledge, experience, education or training of the intended user(s). In particular, instructions for use shall 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 shall be provided on the device itself. If this is not practicable or appropriate, some or all of the information may appear on the packaging for each unit. If individual full labelling of each unit is not practicable, the information shall be set out on the packaging of multiple devices.

(c) Labels shall 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 shall be provided together with devices. However, in duly justified and exceptional cases instructions for use shall not be 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 and/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 and/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 shall take the form of internationally recognised symbols, taking into account the intended users. Any symbol or identification colour used shall conform to the harmonised standards or CS. In areas for which no harmonised standards or CS exist, the symbols and colours shall 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, relevant hazard pictograms and labelling requirements of Regulation (EC) No 1272/2008 shall apply. Where there is insufficient space to put all the information on the device itself or on its label, the relevant hazard pictograms shall be put on the label and the other information required by Regulation (EC) No 1272/2008 shall be given in the instructions for use.

(j) The provisions of Regulation (EC) No 1907/2006 on the safety data sheet shall apply, unless all relevant information, as appropriate, is already made available in the instructions for use.

20.2. Information on the label

The label shall 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 Union, the name of its authorised representative and the address of the registered place of business of the authorised representative;

(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 Article 24 and Part C of Annex VI;

(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. 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 and/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 shall 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 point (f) of Section 20.1, 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. A manufacturer's indication of single use shall be consistent across the Union;

(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 hereof;

(s) where device kits include individual reagents and articles that are made available as separate devices, each of those devices shall comply with the labelling requirements contained in this Section and with the requirements of this Regulation;

(t) the devices and separate components shall 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. As far as practicable and appropriate, the information shall be set out on the device itself and/or, where appropriate, on the sales packaging;

(u) the label for devices for self-testing shall bear the following particulars:

(i) the type of specimen(s) required to perform the test (e.g. blood, urine or saliva);

(ii) the need for additional materials for the test to function properly;

(iii) contact details for further advice and assistance.

The name of devices for self-testing shall not reflect an intended purpose other than that specified by the manufacturer.

20.3. Information on the packaging which maintains the sterile condition of a device (‘sterile packaging’):

The following particulars shall 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) a 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,

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

20.4. Information in the instructions for use

20.4.1. The instructions for use shall 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:

(i) what is detected and/or measured;

(ii) its function (e.g. 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:
- a physiological or pathological state;
- congenital physical or mental impairments;
- the predisposition to a medical condition or a disease;
- the determination of the safety and compatibility with potential recipients;
- the prediction of treatment response or reactions;
- 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 specimen(s) required;

(vii) where applicable, the testing population; and

(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 (e.g. 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 (e.g. suitable for a dedicated instrument only);

(h) a description of the reagents and any limitation upon their use (e.g. suitable for a dedicated instrument only) and the composition of the reagent product by nature and amount or concentration of the active ingredient(s) of the reagent(s) 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 and/or general purpose equipment:

— information to identify such devices or equipment, in order to obtain a validated and safe combination, including key performance characteristics, and/or

— information on any known restrictions to combinations of devices and equipment.

(k) an indication of any special storage (e.g. temperature, light, humidity, etc.) and/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 shall cover, where appropriate:

(i) warnings, precautions and/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 and/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 and/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. A manufacturer's indication of single use shall be consistent across the Union,

(vi) if the device is reusable, information on the appropriate processes to allow reuse, including cleaning, disinfection, decontamination, packaging and,

where appropriate, the validated method of re-sterilisation. Information shall be provided to identify when the device should no longer be reused, such as signs of material degradation or the maximum number of allowable reuses;

(o) any warnings and/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:

— details of the nature, and frequency, of preventive and regular maintenance, including cleaning and disinfection;

— identification of any consumable components and how to replace them;

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

— 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 and/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 shall be considered; where applicable, the instructions for use shall be accompanied by information regarding batch to batch variation provided with relevant figures and units of measure;

(w) 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;

(x) clinical performance characteristics as defined in Section 9.1 of this Annex;

(y) the mathematical approach upon which the calculation of the analytical result is made;

(z) where relevant, clinical performance characteristics, such as threshold value, diagnostic sensitivity and diagnostic specificity, positive and negative predictive value;

(aa) where relevant, reference intervals in normal and affected populations;

(ab) information on interfering substances or limitations (*e.g.* visual evidence of hyperlipidaemia or haemolysis, age of specimen) that may affect the performance of the device;

(ac) 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. This information shall cover, where appropriate:

(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.

(ad) the name, registered trade name or registered trade mark of the manufacturer and the address of its registered place of business at which he can be contacted and its location be established, together with a telephone number and/or fax number and/or website address to obtain technical assistance;

(ae) 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;

(af) a notice to the user that any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established;

(ag) where device kits include individual reagents and articles that may be made available as separate devices, each of these devices shall comply with the instructions for use requirements contained in this Section and with the requirements of this Regulation;

(ah) 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.

20.4.2 In addition, the instructions for use for devices intended for self-testing shall comply with all of the following principles:

(a) details of the test procedure shall be given, including any reagent preparation, specimen collection and/or preparation and information on how to run the test and interpret the results;

(b) 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 result(s) produced by the device;

(c) the device's intended purpose shall 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;

(d) the results shall be expressed and presented in a way that is readily understood by the intended user;

(e) information shall 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. Information shall also be provided as to any factors that can affect the test result such as age, gender, menstruation, infection, exercise, fasting, diet or medication;

(f) the information provided shall 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 specific to the Member State(s) where the device is placed on the market on where a user can obtain further advice such as national helplines, websites;

(g) for devices intended for self-testing used for the monitoring of a previously diagnosed existing disease or condition, the information shall specify that the patient should only adapt the treatment if he has received the appropriate training to do so.

ANNEX II

TECHNICAL DOCUMENTATION

The technical documentation and, if applicable, the summary thereof to be drawn up by the manufacturer shall be presented in a clear, organised, readily searchable and unambiguous manner and shall include in particular the elements listed in this Annex.

1. DEVICE DESCRIPTION AND SPECIFICATION, INCLUDING VARIANTS AND ACCESSORIES

1.1. Device description and specification

(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 Annex VI 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 and/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(s) 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 product(s).

(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 rule(s) applied in accordance with Annex VIII;

(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;

and where applicable:

(h) the description of the specimen collection and transport materials provided with the device or descriptions of specifications recommended for use;

(i) for instruments of automated assays: the description of the appropriate assay characteristics or dedicated assays;

(j) for automated assays: a description of the appropriate instrumentation characteristics or dedicated instrumentation;

(k) a description of any software to be used with the device;

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

(m) 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.

1.2. Reference to previous and similar generations of the device

(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 Union or international markets, where such devices exist.

2. INFORMATION TO BE SUPPLIED BY THE MANUFACTURER

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 the languages accepted in the Member States where the device is envisaged to be sold;

(b) the instructions for use in the languages accepted in the Member States where the device is envisaged to be sold.

3. DESIGN AND MANUFACTURING INFORMATION

3.1. Design information

Information to allow the design stages applied to the device to be understood shall 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.

3.2. Manufacturing information

(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 shall 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.

4. GENERAL SAFETY AND PERFORMANCE REQUIREMENTS

The documentation shall contain information for the demonstration of conformity with the general safety and performance requirements set out in Annex I that are applicable to the device taking into account its intended purpose, and shall include a justification, validation and verification of the solutions adopted to meet those requirements. The demonstration of conformity shall 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 harmonised standards, CS or other solutions applied;

(d) the precise identity of the controlled documents offering evidence of conformity with each harmonised standard, CS or other method applied to demonstrate conformity with the general safety and performance requirements. The information referred to under this point shall incorporate a cross-reference to the location of such evidence within the full technical documentation and, if applicable, the summary technical documentation.

5. BENFIT-RISK ANALYSIS AND RISK MANAGEMENT

The documentation shall contain information on:

(a) the benefit-risk analysis referred to in Sections 1 and 8 of Annex I, and

(b) the solutions adopted and the results of the risk management referred to in Section 3 of Annex I.

6. PRODUCT VERIFICATION AND VALIDATION

The documentation shall contain the results and critical analyses of all verifications and validation tests and/or studies undertaken to demonstrate conformity of the device with the requirements of this Regulation and in particular the applicable general safety and performance requirements.

This includes:

6.1. Information on analytical performance of the device

6.1.1. Specimen type

This Section shall 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.

6.1.2. Analytical performance characteristics

6.1.2.1. Accuracy of measurement

(a) Trueness of measurement

This Section shall 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. Trueness measures apply to both quantitative and qualitative assays only when a certified reference material or certified reference method is available.

(b) Precision of measurement

This Section shall describe repeatability and reproducibility studies.

6.1.2.2. Analytical sensitivity

This Section shall include information about the study design and results. It shall provide a description of specimen type and preparation including matrix, analyte levels, and how levels were established. The number of replicates tested at each concentration shall also be provided as well as a description of the calculation used to determine assay sensitivity.

6.1.2.3. Analytical specificity

This Section shall describe interference and cross reactivity studies performed to determine the analytical specificity in the presence of other substances/agents in the specimen.

Information shall be provided 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.

Interferents and cross-reacting substances or agents, which vary greatly depending on the assay type and design, could derive from exogenous or endogenous sources such as:

(a) substances used for patient treatment such as medicinal products;

(b) substances ingested by the patient such as alcohol, foods;

(c) substances added during specimen preparation such as preservatives, stabilisers;

(d) substances encountered in specific specimen types such as haemoglobin, lipids, bilirubin, proteins;

(e) 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.

6.1.2.4.Metrological traceability of calibrator and control material values

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6.1.2.5. Measuring range of the assay

This Section shall include information 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.

This information shall include 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. If applicable, a description of any high dose hook effect and the data supporting the mitigation such as dilution steps shall be added.

6.1.2.6. Definition of assay cut-off

This Section shall provide a summary of analytical data with a description of the study design including methods for determining the assay cut-off, such as:

(a) the population(s) studied: demographics, selection, inclusion and exclusion criteria, number of individuals included;

(b) method or mode of characterisation of specimens; and

(c) statistical methods such as Receiver Operator Characteristic (ROC) to generate results and if applicable, define grey-zone/equivocal zone.

6.1.3.The analytical performance report referred to in Annex XIII.

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6.2. Information on clinical performance and clinical evidence. Performance Evaluation Report

The documentation shall contain the performance evaluation report, which includes the reports on the scientific validity, the analytical and the clinical performance, as referred to in Annex XIII, together with an assessment of those reports.

The clinical performance study documents referred to in Section 2 of Part A of Annex XIII shall be included and/or fully referenced in the technical documentation.

6.3. Stability (excluding specimen stability)

This Section shall describe claimed shelf life, in use stability and shipping stability studies.

6.3.1. Claimed shelf-life

This Section shall provide information on stability testing studies to support the shelf life that is claimed for the device. Testing shall be performed on at least three different lots manufactured under conditions that are essentially equivalent to routine production conditions. The three lots do not need to be consecutive. Accelerated studies or extrapolated data from real time data are acceptable for initial shelf life claims but shall be followed up with real time stability studies.

Such detailed information shall include:

(a) the study report including the protocol, number of lots, acceptance criteria and testing intervals;

(b) where accelerated studies have been performed in anticipation of the real time studies, the method used for accelerated studies shall be described;

(c) the conclusions and claimed shelf life.

6.3.2. In-use stability

This Section shall provide information on in-use stability studies for one lot reflecting actual routine use of the device, regardless of whether real or simulated. This may include open vial stability and/or, for automated instruments, on board stability.

In the case of automated instrumentation, if calibration stability is claimed, supporting data shall be included.

Such detailed information shall include:

(a) the study report (including the protocol, acceptance criteria and testing intervals);

(b) the conclusions and claimed in-use stability.

6.3.3. Shipping stability

This Section shall provide information on shipping stability studies for one lot of devices to evaluate the tolerance of devices to the anticipated shipping conditions.

Shipping studies may be done under real and/or simulated conditions and shall include variable shipping conditions such as extreme heat and/or cold.

Such information shall describe:

(a) the study report (including the protocol, acceptance criteria);

(b) the method used for simulated conditions;

(c) the conclusion and recommended shipping conditions.

6.4. Software verification and validation

The documentation shall contain evidence of the validation of the software, as it is used in the finished device. Such information shall 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. It shall also address all of the different hardware configurations and, where applicable, operating systems identified in the labelling.

6.5. Additional information required in specific cases

(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. 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. The validation report shall address bioburden testing, pyrogen testing and, if applicable, testing for sterilant residues.

(b) 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.

(c) 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.

(d) 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 Annex I when connected to any such equipment having regard to the characteristics specified by the manufacturer.

ANNEX III

TECHNICAL DOCUMENTATION ON POST-MARKET SURVEILLANCE

The technical documentation on post-market surveillance to be drawn up by the manufacturer in accordance with Articles 78 to 81 shall be presented in a clear, organised, readily searchable and unambiguous manner and shall include in particular the elements described in this Annex.

1. The post-market surveillance plan drawn up in accordance with Article 79.

The manufacturer shall prove in a post-market surveillance plan that it complies with the obligation referred to in Article 78.

(a) The post-market surveillance plan shall address the collection and utilisation of available information, in particular:
- information concerning serious incidents, including information from PSURs, and field safety corrective actions,
- records referring to non-serious incidents and data on any undesirable side-effects,
- information from trend reporting,
- relevant specialist or technical literature, databases and/or registers,
- information, including feedbacks and complaints, provided by users, distributors and importers, and
- publicly-available information about similar medical devices.

(b) The post-market surveillance plan shall cover at least:
- a proactive and systematic process to collect any information referred to in point (a). The process shall allow a correct characterisation of the performance of the devices and shall also allow a comparison to be made between the device and similar products available on the market;
- effective and appropriate methods and processes to assess the collected data;
- suitable indicators and threshold values that shall be used in the continuous reassessment of the benefit-risk analysis and of the risk management as referred to in Section 3 of Annex I;
- effective and appropriate methods and tools to investigate complaints and analyse market-related experience collected in the field;
- methods and protocols to manage the events subject to the trend report as provided for in Article 83, 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;
- methods and protocols to communicate effectively with competent authorities, notified bodies, economic operators and users;

— reference to procedures to fulfil the manufacturers obligations laid down in Articles 78, 79 and 81;
— systematic procedures to identify and initiate appropriate measures including corrective actions;
— effective tools to trace and identify devices for which corrective actions might be necessary; and
— a PMPF plan as referred to in Part B of Annex XIII, or a justification as to why a PMPF is not applicable.

2.The PSUR referred to in Article 81 and the post-market surveillance report referred to in Article 80.

. . . . . .

ANNEX IV

EU DECLARATION OF CONFORMITY

The EU declaration of conformity shall contain the following information:

1. Name, registered trade name or registered trade mark and, if already issued, SRN referred to in Article 28 of the manufacturer, and, if applicable, its authorised representative, and the address of their registered place of business where they can be contacted and their location be established;

2. A statement that the EU declaration of conformity is issued under the sole responsibility of the manufacturer;

3. The Basic UDI-DI as referred to in Part C of Annex VI;

4. Product and trade name, product code, catalogue number or other unambiguous reference allowing identification and traceability of the device covered by the EU declaration of conformity, such as a photograph, where appropriate, as well as its intended purpose. Except for the product or trade name, the information allowing identification and traceability may be provided by the Basic UDI-DI referred to in point 3;

5. Risk class of the device in accordance with the rules set out in Annex VIII;

6. A statement that the device that is covered by the present declaration is in conformity with this Regulation and, if applicable, with any other relevant Union legislation that provides for the issuing of an EU declaration of conformity;

7. References to any CS used and in relation to which conformity is declared;

8. 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;

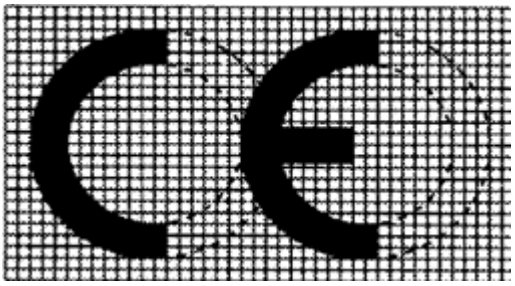
9. Where applicable, additional information;

10. 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, signature.

ANNEX V

CE MARKING OF CONFORMITY

1. The CE marking shall 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 shall have substantially the same vertical dimension, which may not be less than 5 mm. This minimum dimension may be waived for small-scale devices.

ANNEX VI

INFORMATION TO BE SUBMITTED UPON THE REGISTRATION OF DEVICES AND ECONOMIC OPERATORS IN ACCORDANCE WITH ARTICLES 26(3) AND 28, CORE DATA ELEMENTS TO BE PROVIDED TO THE UDI DATABASE TOGETHER WITH THE UDI-DI IN ACCORDANCE WITH ARTICLES 25 AND 26 AND THE UDI SYSTEM

PART A

INFORMATION TO BE SUBMITTED UPON THE REGISTRATION OF DEVICES AND ECONOMIC OPERATORS IN ACCORDANCE WITH ARTICLES 26(3) AND 28

Manufacturers or, when applicable, authorised representatives, and, when applicable, importers shall submit the information referred to in Section 1 and shall ensure that the information on their devices referred to in Section 2 is complete, correct and updated by the relevant party.

1. Information relating to the economic operator

1.1. type of economic operator (manufacturer, authorised representative, or importer),

1.2. name, address and contact details of the economic operator,

1.3. where submission of information is carried out by another person on behalf of any of the economic operators mentioned under Section 1.1, the name, address and contact details of that person,

1.4. name address and contact details of the person or persons responsible for regulatory compliance referred to in Article 15,

2. Information relating to the device

2.1. Basic UDI-DI,

2.2. 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 and was entered by the notified body in the electronic system on notified bodies and certificates,

2.3. Member State in which the device shall or has been placed on the market in the Union,

2.4. in the case of class B, class C or class D devices: Member States where the device is or is to be made available,

2.5. presence of tissues, cells, or, their derivatives, of human origin (y/n),

2.6. presence of tissues, cells or their derivatives of animal origin as referred to in Regulation (EU) No 722/2012(y/n),

2.7. presence of cells or substances of microbial origin (y/n),

2.8. risk class of the device,

2.9. where applicable, the single identification number of the performance study,

2.10. in the case of devices designed and manufactured by another legal or natural person as referred in Article 10(14), the name, address and contact details of that legal or natural person,

2.11. in the case of class C or D devices, the summary of safety and performance,

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

2.13. indication as to whether the device is a ‘new’ device.

A device shall be considered to be ‘new’ if:

(a) there has been no such device continuously available on the Union market during the previous three years for the relevant analyte or other parameter;

(b) the procedure involves analytical technology not continuously used in connection with a given analyte or other parameter on the Union market during the previous three years.

2.14. 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 ARTICLES 25 AND 26

The manufacturer shall provide to the UDI database the UDI-DI and the following information relating to the manufacturer and the device:

1. quantity per package configuration,

2. the Basic UDI-DI as referred to in Article 24(6) and any additional UDI-DIs,

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

4. 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),

5. name and address of the manufacturer, as indicated on the label,

6. the SRN issued in accordance with Article 28(2),

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

8. the medical device nomenclature code as provided for in Article 23,

9. risk class of the device,

10. if applicable, name or trade name,

11. if applicable, device model, reference, or catalogue number,

12. additional product description (optional),

13. if applicable, storage and/or handling conditions (as indicated on the label or in the instructions for use),

14. if applicable, additional trade names of the device,

15. labelled as a single use device (y/n),

16. if applicable, the maximum number of reuses,

17. device labelled sterile (y/n),

18. need for sterilisation before use (y/n),

19. URL for additional information, such as electronic instructions for use (optional),

20. if applicable, critical warnings or contra-indications,

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

PART C

THE UDI SYSTEM

1. Definitions

Automatic identification and data capture ('AIDC')

AIDC is a technology used to automatically capture data. AIDC technologies include bar codes, smart cards, biometrics and RFID.

Basic UDI-DI

The Basic UDI-DI is the primary identifier of a device model. It is the DI assigned at the level of the device unit of use. It is the main key for records in the UDI database and is referenced in relevant certificates and EU declarations of conformity.

Unit of Use DI

The Unit of Use DI serves 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

A configurable device is a device that consists of several components which can be assembled by the manufacturer in multiple configurations. Those individual components may be devices in themselves.
Configuration

Configuration is a combination of items of equipment, as specified by the manufacturer, that operate together as a device to achieve an intended purpose. The combination of items may be modified, adjusted or customised to meet specific needs.
UDI-DI

The UDI-DI is 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.
Human Readable Interpretation (HRI)

HRI is a legible interpretation of the data characters encoded in the UDI carrier.
Packaging levels

Packaging levels means the various levels of device packaging that contain a fixed quantity of devices, such as a carton or case.
Production Identifier (UDI-PI)

The UDI-PI is a numeric or alphanumeric code that identifies the unit of device production.

The different types of UDI-PI(s) include serial number, lot number, software identification and manufacturing or expiry date or both types of date.
Radio Frequency Identification ('RFID')

RFID is 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 containers

A shipping container is a container in relation to which traceability is controlled by a process specific to logistics systems.
Unique Device Identifier ('UDI')

The UDI is a series of numeric or alphanumeric characters that is created through a globally accepted device identification and coding standard. It allows the unambiguous identification of a specific device on the market. The UDI is comprised of the UDI-DI and the UDI-PI.

The word 'Unique' does not imply serialisation of individual production units.
UDI carrier

The UDI carrier is the means of conveying the UDI by using AIDC and, if applicable, its HRI.

UDI carriers include, *inter alia*, ID/linear bar code, 2D/Matrix bar code, RFID.

2. General requirements

2.1. The affixing of the UDI is an additional requirement — it does not replace any other marking or labelling requirements laid down in Annex I to this Regulation.

2.2. The manufacturer shall assign and maintain unique UDIs for its devices.

2.3. Only the manufacturer may place the UDI on the device or its packaging.

2.4. Only coding standards provided by issuing entities designated by the Commission pursuant to Article 24(2) may be used.

3. The UDI

3.1. A UDI shall be assigned to the device itself or its packaging. Higher levels of packaging shall have their own UDI.

3.2. Shipping containers shall be exempted from the requirement in Section 3.1. By way of example, a UDI shall not be required on a logistics unit; 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) shall not be subject to UDI requirements.

3.3. The UDI shall contain two parts: a UDI-DI and a UDI-PI.

3.4. The UDI-DI shall be unique at each level of device packaging.

3.5. If a lot number, serial number, software identification or expiry date appears on the label, it shall be part of the UDI-PI. If there is also a manufacturing date on the label, it does not need to be included in the UDI-PI. If there is only a manufacturing date on the label, this shall be used as the UDI-PI.

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

3.7. Kits shall be assigned and bear their own UDI.

3.8. The manufacturer shall assign the UDI to a device following the relevant coding standard.

3.9. A new UDI-DI shall be required whenever there is a change that could lead to misidentification of the device and/or ambiguity in its traceability. In particular, any change of one of the following UDI database data elements shall require 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.

3.10. Manufacturers that repackage or relabel devices with their own label shall retain a record of the original device manufacturer's UDI.

4. UDI carrier

4.1. The UDI carrier (AIDC and HRI representation of the UDI) shall be placed on the label and on all higher levels of device packaging. Higher levels do not include shipping containers.

4.2. In the event of there being significant space constraints on the unit of use packaging the UDI carrier may be placed on the next higher packaging level.

4.3. For single use class A and class B devices packaged and labelled individually, the UDI carrier shall not be required to appear on the packaging but it shall appear on a higher level of packaging e.g. a carton containing several packages. 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 shall be placed on the packaging.

4.4. For devices exclusively intended for retail point of sale, the UDI-PIs in AIDC shall not be required to appear on the point of sale packaging.

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

4.6. If linear bar codes are used, the UDI-DI and UDI-PI may be concatenated or non-concatenated in two or more bar codes. All parts and elements of the linear bar code shall be distinguishable and identifiable.

4.7. If there are significant constraints limiting the use of both AIDC and HRI on the label, only the AIDC format shall be required to appear on the label. For devices intended to be used outside healthcare facilities, such as devices for home care, the HRI shall however appear on the label even if this results in there being no space for the AIDC.

4.8. The HRI format shall follow the rules of the UDI code-issuing entity.

4.9. 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.

4.10. Devices that are reusable shall bear a UDI carrier on the device itself. The UDI carrier for reusable devices that require disinfection, sterilisation or refurbishing between patient uses shall be permanent and readable after each process performed to make the device ready for the subsequent use throughout the intended lifetime of the device.

4.11. The UDI carrier shall be readable during normal use and throughout the intended lifetime of the device.

4.12. If the UDI carrier is readily readable or scannable through the device's packaging, the placing of the UDI carrier on the packaging shall not be required.

4.13. 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.

4.14. The UDI carrier shall be placed in a manner such that the AIDC can be accessed during normal operation or storage.

4.15. 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.

5. General principles of the UDI database

5.1. The UDI database shall support the use of all core UDI database data elements referred to in Part B of this Annex.

5.2. Manufacturers shall be responsible for the initial submission and updates of the identifying information and other device data elements in the UDI database.

5.3. Appropriate methods/procedures for validation of the data provided shall be implemented.

5.4. Manufacturers shall 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.

5.5. The presence of the device UDI-DI in the UDI database shall not be assumed to mean that the device is in conformity with this Regulation.

5.6. The database shall allow for the linking of all the packaging levels of the device.

5.7. The data for new UDI-DIs shall be available at the time the device is placed on the market.

5.8. Manufacturers shall 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.

5.9. Internationally accepted standards for data submission and updates shall, wherever possible, be used by the UDI database.

5.10. The user interface of the UDI database shall be available in all official languages of the Union. The use of free-text fields shall, however, be minimised in order to reduce translations.

5.11. Data relating to devices that are no longer available on the market shall be retained in the UDI database.

6. Rules for specific device types

6.1. Reusable devices that are part of kits and that require cleaning, disinfection, sterilisation or refurbishing between uses

6.1.1. The UDI of such devices shall be placed on the device and shall be readable after each procedure to make the device ready for the next use;

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

6.2. Device software

6.2.1. UDI assignment Criteria

The UDI shall be assigned at the system level of the software. Only software which is commercially available on its own and software which constitutes a device in itself shall be subject to that requirement.

The software identification shall be considered to be the manufacturing control mechanism and shall be displayed in the UDI-PI.

6.2.2. A new UDI-DI shall be 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.

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

6.2.3. Minor software revisions shall require a new UDI-PI and not a new UDI-DI:

Minor software revisions are generally associated with bug fixes, usability enhancements that are not for safety purposes, security patches or operating efficiency.

Minor software revisions shall be identified by a manufacturer-specific form of identification.

6.2.4. UDI placement criteria for software

(a) where the software is delivered on a physical medium, for example via *a* CD or DVD, each packaging level shall bear the human readable and AIDC representation of the complete UDI. The UDI that is applied to the physical medium containing the software and its packaging shall be identical to the UDI assigned to the system level software;

(b) the UDI shall 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, shall be capable of transmitting the UDI through an application programming interface (API);

(d) only the human readable portion of the UDI shall be required in electronic displays of the software. The marking of UDI using AIDC shall not be required in the electronic displays such as 'about' menu, splash screen, etc.;

(e) the human readable format of the UDI for the software shall 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.

ANNEX VII

REQUIREMENTS TO BE MET BY NOTIFIED BODIES

1. ORGANISATIONAL AND GENERAL REQUIREMENTS

1.1. Legal status and organisational structure

1.1.1. Each notified body shall be established under the national law of a Member State, or under the law of a third country with which the Union has concluded an agreement in this respect. Its legal personality and status shall be fully documented. Such documentation shall include information about ownership and the legal or natural persons exercising control over the notified body.

1.1.2. If the notified body is a legal entity that is part of a larger organisation, the activities of that organisation as well as its organisational structure and governance, and the relationship with the notified body shall be clearly documented. In such cases, the requirements of Section 1.2 are applicable to both the notified body and the organisation to which it belongs.

1.1.3. If a notified body wholly or partly owns legal entities established in a Member State or in a third country or is owned by another legal entity, the activities and responsibilities of those entities, as well as their legal and operational relationships with the notified body, shall be clearly defined and documented. Personnel of those entities performing conformity assessment activities under this Regulation shall be subject to the applicable requirements of this Regulation.

1.1.4. The organisational structure, allocation of responsibilities, reporting lines and operation of the notified body shall be such that they ensure that there is confidence in the performance by the notified body and in the results of the conformity assessment activities it conducts.

1.1.5. The notified body shall clearly document its organisational structure and the functions, responsibilities and authority of its top-level management and of other personnel who may have an influence upon the performance by the notified body upon the results of its conformity assessment activities.

1.1.6. The notified body shall identify the persons in top-level management that have overall authority and responsibility for each of the following:

(a) provision of adequate resources for conformity assessment activities;

(b) development of procedures and policies for the operation of the notified body;

(c) supervision of implementation of the procedures, policies and quality management systems of the notified body;

(d) supervision of the notified body's finances;

(e) activities and decisions taken by the notified body, including contractual agreements;

(f) delegation of authority to personnel and/or committees, where necessary, for the performance of defined activities;

(g) interaction with the authority responsible for notified bodies and the obligations regarding communications with other competent authorities, the Commission and other notified bodies.

1.2. Independence and impartiality

1.2.1. The notified body shall be a third-party body that is independent of the manufacturer of the device in relation to which it performs conformity assessment activities. The notified body shall also be independent of any other economic operator having an interest in the device as well as of any competitors of the manufacturer. This does not preclude the notified body from carrying out conformity assessment activities for competing manufacturers.

1.2.2. The notified body shall be organised and operated so as to safeguard the independence, objectivity and impartiality of its activities. The notified body shall document and implement a structure and procedures for safeguarding impartiality and for promoting and applying the principles of impartiality throughout its organisation, personnel and assessment activities. Such procedures shall provide for the identification, investigation and resolution of any case in which a conflict of interest may arise including involvement in consultancy services in the field of devices prior to taking up employment with the notified body. The investigation, outcome and its resolution shall be documented.

1.2.3. The notified body, its top-level management and the personnel responsible for carrying out the conformity assessment tasks shall not:

(a) be the designer, manufacturer, supplier, installer, purchaser, owner or maintainer of devices which they assess, nor the authorised representative of any of those parties. Such restriction shall not preclude the purchase and use of assessed devices that are necessary for the operations of the notified body and the conduct of the conformity assessment, or the use of such devices for personal purposes;

(b) be involved in the design, manufacture or construction, marketing, installation and use, or maintenance of the devices for which they are designated, nor represent the parties engaged in those activities;

(c) engage in any activity that may conflict with their independence of judgement or integrity in relation to conformity assessment activities for which they are designated;

(d) offer or provide any service which may jeopardise the confidence in their independence, impartiality or objectivity. In particular, they shall not offer or provide consultancy services to the manufacturer, its authorised representative, a supplier or a commercial competitor as regards the design, construction, marketing or maintenance of the devices or processes under assessment; and

(e) be linked to any organisation which itself provides consultancy services as referred to in the point (d). Such restriction shall not preclude general training activities that are not client specific and that relate to regulation of devices s or to related standards.

1.2.4. Involvement in consultancy services in the field of devices prior to taking up employment with a notified body shall be fully documented at the time of employment, and potential conflicts of interests shall be monitored and resolved in accordance with this Annex. Personnel who were formerly employed by a specific client, or provided consultancy services in the field of devices to that specific client prior to taking up employment with a notified body, shall not be assigned for conformity assessment activities for that specific client or companies belonging to the same group for a period of three years.

1.2.5. The impartiality of notified bodies, of their top-level management and of the assessment personnel shall be guaranteed. The level of the remuneration of the top-level management and assessment personnel of a notified body and subcontractors involved in assessment activities shall not depend on the results of the assessments. Notified bodies shall make publicly available the declarations of interest of their top-level management.

1.2.6. If a notified body is owned by a public entity or institution, independence and absence of any conflict of interests shall be ensured and documented between, on the one hand, the authority responsible for notified bodies and/or the competent authority and, on the other hand, the notified body.

1.2.7. The notified body shall ensure and document that the activities of its subsidiaries or subcontractors or of any associated body, including the activities of its owners do not affect its independence, impartiality or the objectivity of its conformity assessment activities.

1.2.8. The notified body shall operate in accordance with a set of consistent, fair and reasonable terms and conditions, taking into account the interests of small and

medium-sized enterprises as defined in Recommendation 2003/361/EC in relation to fees.

1.2.9. The requirements laid down in this Section shall in no way preclude exchanges of technical information and regulatory guidance between a notified body and a manufacturer applying for conformity assessment.

1.3. Confidentiality

1.3.1. The notified body shall have documented procedures in place ensuring that its personnel, committees, subsidiaries, subcontractors, and any associated body or personnel of external bodies respect the confidentiality of the information which comes into its possession during the performance of the conformity assessment activities, except when disclosure is required by law.

1.3.2. The personnel of a notified body shall observe professional secrecy in carrying out their tasks under this Regulation or any provision of national law giving effect to it, except in relation to the authorities responsible for notified bodies, competent authorities for devices in the Member States or the Commission. Proprietary rights shall be protected. The notified body shall have documented procedures in place in respect of the requirement of this Section.

1.4. Liability

1.4.1. The notified body shall take out appropriate liability insurance for its conformity assessment activities, unless liability is assumed by the Member State in question in accordance with national law or that Member State is directly responsible for their conformity assessment.

1.4.2. The scope and overall financial value of the liability insurance shall correspond to the level and geographic scope of activities of the notified body and be commensurate with the risk profile of the devices certified by the notified body. The liability insurance shall cover cases where the notified body may be obliged to withdraw, restrict or suspend certificates.

1.5. Financial requirements

The notified body shall have at its disposal the financial resources required to conduct its conformity assessment activities within its scope of designation and related business operations. It shall document and provide evidence of its financial capacity and its long-term economic viability, taking into account, where relevant, any specific circumstances during an initial start-up phase.

1.6. Participation in coordination activities

1.6.1. The notified body shall participate in, or ensure that its assessment personnel is informed of any relevant standardisation activities and in the activities of the notified body coordination group referred to in Article 49 of Regulation (EU) 2017/745 and that its assessment and decision-making personnel are informed of all relevant legislation, guidance and best practice documents adopted in the framework of this Regulation.

1.6.2. The notified body shall take into consideration guidance and best practice documents.

2. QUALITY MANAGEMENT REQUIREMENTS

2.1. The notified body shall establish, document, implement, maintain and operate a quality management system that is appropriate to the nature, area and scale of its conformity assessment activities and is capable of supporting and demonstrating the consistent fulfilment of the requirements of this Regulation.

2.2. The quality management system of the notified body shall address at least the following:

(a) management system structure and documentation, including policies and objectives for its activities;

(b) policies for assignment of activities and responsibilities to personnel;

(c) assessment and decision-making processes in accordance with the tasks, responsibilities and role of the notified body's personnel and top-level management;

(d) the planning, conduct, evaluation and, if necessary, adaptation of its conformity assessment procedures;

(e) control of documents;

(f) control of records;

(g) management reviews;

(h) internal audits;

(i) corrective and preventive actions;

(j) complaints and appeals;

(k) continuous training.

Where documents are used in various languages, the notified body shall ensure and control that they have the same content.

2.3. The top-level management of the notified body shall ensure that the quality management system is fully understood, implemented and maintained throughout the notified body organisation including subsidiaries and subcontractors involved in conformity assessment activities pursuant to this Regulation.

2.4. The notified body shall require all personnel to formally commit themselves by a signature or equivalent to comply with the procedures defined by the notified body. That commitment shall cover aspects relating to confidentiality and to independence from commercial and other interests, and any existing or prior association with clients. The personnel shall be required to complete written statements indicating their compliance with confidentiality, independence and impartiality principles.

3. RESOURCE REQUIREMENTS

3.1. General

3.1.1. Notified bodies shall be capable of carrying out all the tasks falling to them under this Regulation with the highest degree of professional integrity and the requisite competence in the specific field, whether those tasks are carried out by the notified body itself or on its behalf and under its responsibility.

In particular, notified bodies shall have the necessary personnel and possess or have access to all equipment, facilities and competence needed to perform properly the technical, scientific and administrative tasks entailed in the conformity assessment activities in relation to which they have been designated. Such requirement presupposes at all times and for each conformity assessment procedure and each type of devices in relation to which they have been designated, that the notified body has permanent availability of sufficient administrative, technical and scientific personnel who possess experience and knowledge relating to the relevant devices and the corresponding technologies. Such personnel shall be in sufficient numbers to ensure that the notified body in question can perform the conformity assessment tasks, including the assessment of the medical functionality, performance evaluations and the performance and safety of devices, for which it has been designated, having regard to the requirements of this Regulation, in particular those set out in Annex I.

A notified body's cumulative competences shall be such as to enable it to assess the types of devices for which it is designated. The notified body shall have sufficient internal competence to critically evaluate assessments conducted by external expertise. Tasks which a notified body is precluded from subcontracting are set out in Section 4.1.

Personnel involved in the management of the operation of a notified body's conformity assessment activities for devices shall have appropriate knowledge to set up and operate a system for the selection of assessment and verification staff, for verification of their competence, for authorisation and allocation of their tasks, for organisation of their initial and ongoing training, and for their assignment of their duties and monitoring of those staff, in order to ensure that personnel who carry out and perform assessment and verification operations are competent to fulfil the tasks required of them.

The notified body shall identify at least one individual within its top-level management as having overall responsibility for all conformity assessment activities in relation to devices.

3.1.2. The notified body shall ensure that personnel involved in conformity assessment activities maintain their qualification and expertise by implementing a system for exchange of experience and a continuous training and education programme.

3.1.3. The notified body shall clearly document the extent and limits of duties and responsibilities and the level of authorisation of to the personnel, including any subcontractors and external experts involved in conformity assessment activities and inform those personnel accordingly.

3.2. Qualification criteria in relation to personnel

3.2.1. The notified body shall establish and document qualification criteria and procedures for selection and authorisation of persons involved in conformity assessment activities, including as regards knowledge, experience and other competence required, and the required initial and ongoing training. The qualification criteria shall address the various functions within the conformity assessment process, such as auditing, product evaluation or testing, technical documentation review, decision-making, and batch release, as well as the devices, technologies and areas, such as biocompatibility, sterilisation, self and near patient-testing, companion diagnostics and performance evaluation, covered by the scope of designation.

3.2.2. The qualification criteria referred to in Section 3.2.1 shall refer to the scope of the notified body's designation in accordance with the scope description used by the Member State for the notification referred to in Article 38(3), providing a sufficient level of detail for the required qualification within the subdivisions of the scope description.

Specific qualification criteria shall be defined at least for the assessment of:

— biological safety,
— performance evaluation,
— devices for self and near patient testing,
— companion diagnostics,
— functional safety,
— software,
— packaging, and
— the different types of sterilisation processes.

3.2.3. The personnel responsible for establishing qualification criteria and for authorising other personnel to perform specific conformity assessment activities shall be employed by the notified body itself and shall not be external experts or subcontracted. They shall have proven knowledge and experience in all of the following:

— Union devices legislation and relevant guidance documents;
— the conformity assessment procedures provided for in this Regulation;
— a broad base of knowledge of device technologies and the design and manufacture of devices;
— the notified body's quality management system, related procedures and the required qualification criteria;
— training relevant to personnel involved in conformity assessment activities in relation to devices;
— adequate experience in conformity assessments under this Regulation or previously applicable law within a notified body.

3.2.4. The notified body shall have permanent availability of personnel with relevant clinical expertise and where possible such personnel shall be employed by the notified body itself. Such personnel shall be integrated throughout the notified body's assessment and decision-making process in order to:

— identify when specialist input is required for the assessment of the performance evaluation conducted by the manufacturer and identify appropriately qualified experts;
— appropriately train external clinical experts in the relevant requirements of this Regulation, CS, guidance and harmonised standards and ensure that the external clinical experts are fully aware of the context and implications of their assessment and the advice they provide;
— be able to review and scientifically challenge the clinical data contained within the performance evaluation, and any associated performance study, and appropriately guide external clinical experts in the assessment of the performance evaluation presented by the manufacturer;
— be able to scientifically evaluate and, if necessary, challenge the performance evaluation presented, and the results of the external clinical experts' assessment of the manufacturer's performance evaluation;
— be able to ascertain the comparability and consistency of the assessments of performance evaluation conducted by clinical experts;
— be able to make an assessment of the manufacturer's performance evaluation and a clinical judgement of the opinion provided by any external expert and make a recommendation to the notified body's decision maker; and
— be able to draw up records and reports demonstrating that the relevant conformity assessment activities have been appropriately carried out.

3.2.5. The personnel responsible for carrying out product-related reviews, (product reviewers), such as technical documentation reviews or type examination, including aspects such as performance evaluation, biological safety, sterilisation and software validation, shall have all the following proven qualifications:

— successful completion of a university or a technical college degree or an equivalent qualification in relevant studies, such as medicine, pharmacy, engineering or other relevant sciences;

— four years' professional experience in the field of healthcare products or related activities, such as in manufacturing, auditing, or research, of which two years shall be in the design, manufacture, testing or use of devices or technology to be assessed or related to the scientific aspects to be assessed;

— knowledge of device legislation, including the general safety and performance requirements set out in Annex I;

— appropriate knowledge and experience of relevant harmonised standards, CS and guidance documents;

— appropriate knowledge and experience of risk management and related device standards and guidance documents;

— appropriate knowledge and experience of performance evaluation;

— appropriate knowledge of the devices which they are assessing;

— appropriate knowledge and experience of the conformity assessment procedures laid down in Annexes IX to XI, in particular of the aspects of those procedures for which they are responsible, and adequate authorisation for carrying out those assessments;

— the ability to draw up records and reports demonstrating that the relevant conformity assessment activities have been appropriately carried out.

3.2.6. The personnel responsible for carrying out audits of the manufacturer's quality management system (site auditors) shall have all of the following proven qualifications:

— successful completion of a university or a technical college degree or equivalent qualification in relevant studies, such as medicine, pharmacy, engineering or other relevant sciences;

— four years' professional experience in the field of healthcare products or related activities, such as in manufacturing, auditing or research, of which two years shall be in the area of quality management;

— appropriate knowledge of devices legislation as well as related harmonised standards, CS and guidance documents;

— appropriate knowledge and experience of risk management and related device standards and guidance documents;

— appropriate knowledge of quality management systems and related l devices standards and guidance documents;

— appropriate knowledge and experience of the conformity assessment procedures laid down in Annexes IX to XI, in particular of the aspects of those procedures for which they are responsible, and adequate authorisation for carrying out those audits;

— training in auditing techniques enabling them to challenge quality management systems;

— the ability to draw up records and reports demonstrating that the relevant conformity assessment activities have been appropriately carried out.

3.2.7. The personnel with overall responsibility for final reviews and decision-making on certification shall be employed by the notified body itself and shall not be external

experts or be subcontracted. Those personnel, as a group, shall have proven knowledge and comprehensive experience of all of the following:

— devices legislation and relevant guidance documents;

— device conformity assessments relevant to this Regulation;

— the types of qualifications, experience and expertise relevant to device conformity assessment;

— a broad base of knowledge of device technologies, including sufficient experience of the conformity assessment of devices being reviewed for certification, the device industry and the design and manufacture of devices;

— the notified body's quality system, related procedures and the required qualifications for personnel involved;

— the ability to draw up records and reports demonstrating that the conformity assessment activities have been appropriately carried out.

3.3. Documentation of qualification, training and authorisation of personnel

3.3.1. The notified body shall have a procedure in place to fully document the qualification of each member of personnel involved in conformity assessment activities and the satisfaction of the qualification criteria referred to in Section 3.2. Where, in exceptional circumstances, the fulfilment of the qualification criteria set out in Section 3.2 cannot be fully demonstrated, the notified body shall justify to the authority responsible for notified bodies the authorisation of those members of personnel to carry out specific conformity assessment activities.

3.3.2. For all of its personnel referred to in Sections 3.2.3 to 3.2.7, the notified body shall establish and maintain up to date:

— a matrix detailing the authorisations and responsibilities of the personnel in respect of conformity assessment activities;

— records attesting to the required knowledge and experience for the conformity assessment activity for which they are authorised. The records shall contain a rationale for defining the scope of the responsibilities for each of the assessment personnel and records of the conformity assessment activities carried out by each of them.

3.4. Subcontractors and external experts

3.4.1. Notified bodies may, without prejudice to Section 3.2, subcontract certain clearly defined component parts of a conformity assessment activity.

The subcontracting of the auditing of quality management systems or of product-related reviews as a whole shall not be permitted, nevertheless parts of those activities may be conducted by subcontractors and external auditors and experts working on behalf of the notified body. The notified body in question shall retain full responsibility for being able to produce appropriate evidence of the competence of subcontractors and experts to fulfil their specific tasks, for making a decision based on a subcontractor's assessment and for the work conducted by subcontractors and experts on its behalf.

The following activities may not be subcontracted by notified bodies:

— review of the qualifications and monitoring of the performance of external experts;

— auditing and certification activities where the subcontracting in question is to auditing or certification organisations;

— allocation of work to external experts for specific conformity assessment activities;

— final review and decision-making functions.

3.4.2. Where a notified body subcontracts certain conformity assessment activities either to an organisation or an individual, it shall have a policy describing the conditions under which subcontracting may take place, and shall ensure that:

— the subcontractor meets the relevant requirements of this Annex;

— subcontractors and external experts do not further subcontract work to organisations or personnel;

— the natural or legal person that applied for conformity assessment has been informed of the requirements referred to in the first and second indent.

Any subcontracting or consultation of external personnel shall be properly documented, shall not involve any intermediaries, and shall be subject to a written agreement covering, among other things, confidentiality and conflicts of interest. The notified body in question shall take full responsibility for the tasks performed by subcontractors.

3.4.3. Where subcontractors or external experts are used in the context of a conformity assessment, in particular regarding novel devices or technologies, the notified body in question shall have adequate internal competence in each product area for which it is designated that is adequate for the purpose of leading the overall conformity assessment, verifying the appropriateness and validity of expert opinions and making decisions on certification.

3.5. Monitoring of competences, training and exchange of experience

3.5.1. The notified body shall establish procedures for the initial evaluation and on-going monitoring of the competence, conformity assessment activities and performance of all internal and external personnel and subcontractors, involved in conformity assessment activities.

3.5.2. Notified bodies shall review at regular intervals, the competence of their personnel, identify training needs and draw up a training plan to maintain the required level of qualification and knowledge of individual personnel. That review shall as a minimum, verify that personnel:

— are aware of the Union and national law in force on devices, relevant harmonised standards, CS, guidance documents and the results of the coordination activities referred to in Section 1.6;

— take part in the internal exchange of experience and the continuous training and education programme referred to in Section 3.1.2.

4. PROCESS REQUIREMENTS

4.1. General

The notified body shall have in place documented processes and sufficiently detailed procedures for the conduct of each conformity assessment activity for which it is designated, comprising the individual steps from pre-application activities up to decision making and surveillance and taking into account, when necessary, the respective specificities of the devices.

The requirements laid down in Sections 4.3, 4.4, 4.7 and 4.8 shall be fulfilled as part of the internal activities of notified bodies and shall not be subcontracted.

4.2. Notified body quotations and pre-application activities

The notified body shall

(a) publish a publicly available description of the application procedure by which manufacturers can obtain certification from it. That description shall include which languages are acceptable for submission of documentation and for any related correspondence;

(b) have documented procedures relating to, and documented details about, fees charged for specific conformity assessment activities and any other financial conditions relating to notified bodies' assessment activities for devices;,

(c) have documented procedures in relation to advertising of its conformity assessment services. Those procedures shall ensure that advertising or promotional activities in no way imply or are capable of leading to an inference that their conformity assessment will offer manufacturers earlier market access or be quicker, easier or less stringent than that of other notified bodies;

(d) have documented procedures requiring the review of pre-application information including the preliminary verification that the product is covered by this Regulation and its classification prior to issuing any quotation to the manufacturer relating to a specific conformity assessment;

(e) ensure that all contracts relating to the conformity assessment activities covered by this Regulation are concluded directly between the manufacturer and the notified body and not with any other organisation.

4.3. Application review and contract

The notified body shall require a formal application signed by a manufacturer or an authorised representative containing all of the information and the manufacturer's declarations required by the relevant conformity assessment as referred to in Annexes IX to XI.

The contract between a notified body and a manufacturer shall take the form of a written agreement signed by both parties. It shall be kept by the notified body. This contract shall have clear terms and conditions and contain obligations that enable the notified body to act as required under this Regulation, including an obligation on the manufacturer to inform the notified body of vigilance reports, the right of the notified body to suspend, restrict or withdraw certificates issued and the duty of the notified body to fulfil its information obligations.

The notified body shall have documented procedures to review applications, addressing:

(a) the completeness of those applications with respect to the requirements of the relevant conformity assessment procedure, as referred to in the corresponding Annex, under which approval has been sought,

(b) the verification of the qualification of products covered by those applications as devices and their respective classifications,

(c) whether the conformity assessment procedures chosen by the applicant are applicable to the device in question under this Regulation,

(d) the ability of the notified body to assess the application based on its designation, and

(e) the availability of sufficient and appropriate resources.

The outcome of each review of an application shall be documented. Refusals or withdrawals of applications shall be notified to the electronic system referred to in Article 52 and shall be accessible to other notified bodies.

4.4. Allocation of resources

The notified body shall have documented procedures to ensure that all conformity assessment activities are conducted by appropriately authorised and qualified personnel who are sufficiently experienced in the evaluation of the devices, systems and processes and related documentation that are subject to conformity assessment.

For each application, the notified body shall determine the resources needed and identify one individual responsible for ensuring that the assessment of that application is conducted in accordance with the relevant procedures and for ensuring that the appropriate resources including personnel are utilised for each of the tasks of the assessment. The allocation of tasks required to be carried out as part of the conformity assessment and any changes subsequently made to this allocation shall be documented.

4.5. Conformity assessment activities

4.5.1. General

The notified body and its personnel shall carry out the conformity assessment activities with the highest degree of professional integrity and the requisite technical and scientific competence in the specific fields.

The notified body shall have expertise, facilities and documented procedures that are sufficient to effectively conduct the conformity assessment activities for which the notified body in question is designated, taking account of the relevant requirements set out in Annexes IX to XI and in particular the following requirements:

— to appropriately plan the conduct of each individual project,
— to ensure that the composition of the assessment teams is such that there is sufficient experience in relation to the technology concerned, and that there is continuous objectivity and independence, and to provide for rotation of the members of the assessment team at appropriate intervals,
— to specify the rationale for fixing time limits for completion of conformity assessment activities,
— to assess the manufacturer's technical documentation and the solutions adopted to meet the requirements laid down in Annex I,
— to review the manufacturer's procedures and documentation relating to performance evaluation,
— to address the interface between the manufacturer's risk management process and its appraisal and analysis of the performance evaluation and to evaluate their relevance for the demonstration of conformity with the relevant requirements in Annex I,
— to carry out the ‘specific procedures’ referred to in Section 5 of Annex IX,
— in the case of class B or C devices, to assess the technical documentation of devices selected on a representative basis,
— to plan and periodically carry out appropriate surveillance audits and assessments, to carry out or request certain tests to verify the proper functioning of the quality management system and to perform unannounced on site audits,
— relating to the sampling of devices verify that the manufactured device is in conformity with the technical documentation; such requirements shall define the relevant sampling criteria and testing procedure prior to sampling,
— to evaluate and verify a manufacturer's compliance with relevant Annexes.

The notified body shall, where relevant, take into consideration available CS, guidance and best practice documents and harmonised standards, even if the manufacturer does not claim to be in compliance.

4.5.2. Quality management system auditing

(a) As part of the assessment of the quality management system a, a notified body shall prior to an audit and in accordance with its documented procedures:

— assess the documentation submitted in accordance with the relevant conformity assessment Annex, and draw up an audit programme which clearly identifies the number and sequence of activities required to demonstrate complete coverage of a manufacturer's quality management system and to determine whether it meets the requirements of this Regulation,

— identify links between and allocation of responsibilities among, the various manufacturing sites, and identify relevant suppliers and/or subcontractors of the manufacturer, and consider the need to specifically audit any of those suppliers or subcontractors or both,

— clearly define, for each audit identified in the audit programme, the objectives, criteria and scope of the audit, and draw up an audit plan that adequately addresses and takes account of the specific requirements for the devices, technologies and processes involved,

— draw up and keep up to date, for class B and class C devices, a sampling plan for the assessment of technical documentation as referred to in Annexes II and III covering the range of such devices covered by the manufacturer's application. That plan shall ensure that all devices covered by the certificate are sampled over the period of validity of the certificate,

— select and assign appropriately qualified and authorised personnel for conducting the individual audits. The respective roles, responsibilities and authorities of the team members shall be clearly defined and documented.

(b) Based on the audit programme it has drawn up, the notified body shall, in accordance with its documented procedures:

— audit the manufacturer's quality management system in order to verify that the quality management system ensures that the devices covered conform to the relevant provisions of this Regulation which apply to devices at every stage, from design through final quality control to ongoing surveillance, and shall determine whether the requirements of this Regulation are met,

— based on relevant technical documentation, and in order to determine whether the manufacturer meets the requirements referred to in the relevant conformity assessment Annex, review and audit the manufacturer's processes and subsystems,– in particular for:

  — design and development,

  — production and process controls,

  — product documentation,

  — purchasing controls including verification of purchased devices,

  — corrective and preventive actions including for post-market surveillance, and

  — PMPF,

— and review and audit requirements and provisions adopted by the manufacturer, including those in relation to fulfilling the general safety and performance requirements set out in Annex I,

— the documentation shall be sampled in such as a manner as to reflect the risks associated with the intended use of the device, the complexity of the

manufacturing technologies, the range and classes of devices produced and any available post-market surveillance information,

— if not already covered by the audit programme, audit the control of processes on the premises of the manufacturer's suppliers, when the conformity of finished devices is significantly influenced by the activity of suppliers and, in particular when the manufacturer cannot demonstrate sufficient control over its suppliers,

— conduct assessments of the technical documentation based on its sampling plan and taking account of Section 4.5.4. for performance evaluation,

— the notified body shall ensure that audit findings are appropriately and consistently classified in accordance with the requirements of this Regulation and with relevant standards, or with best practice documents developed or adopted by the MDCG.

4.5.3. Product verification

Assessment of the technical documentation

For assessment of the technical documentation conducted in accordance with Chapter II of Annex IX, notified bodies shall have sufficient expertise, facilities and documented procedures for:

— the allocation of appropriately qualified and authorised personnel for the examination of individual aspects, such as use of the device, biocompatibility, performance evaluation, risk management and sterilisation, and

— the assessment of conformity of the design with this Regulation, and taking account of Sections 4.5.4. and 4.5.5. This assessment shall include the examination of the implementation by manufacturers of incoming, in-process and final checks and the results thereof. If further tests or other evidence is required for the assessment of conformity with the requirements of this Regulation, the notified body in question shall carry out adequate physical or laboratory tests in relation to the device or request the manufacturer to carry out such tests.

Type-examinations

The notified body shall have documented procedures, sufficient expertise and facilities for the type-examination of devices in accordance with Annex X including the capacity to:

— examine and assess the technical documentation, taking account of Sections 4.5.4. and 4.5.5, and verify that the type has been manufactured in conformity with that documentation;

— establish a test plan identifying all relevant and critical parameters which need to be tested by the notified body or under its responsibility;

— document its rationale for the selection of those parameters;

— carry out the appropriate examinations and tests in order to verify that the solutions adopted by the manufacturer meet the general safety and performance requirements set out in Annex I. Such examinations and tests shall include all tests necessary to verify that the manufacturer has in fact applied the relevant standards it has opted to use;

— agree with the applicant as to where the necessary tests will be performed if they are not to be carried out directly by the notified body;

— assume full responsibility for test results. Test reports submitted by the manufacturer shall only be taken into account if they have been issued by conformity assessment bodies which are competent and independent of the manufacturer.

Verification by examination and testing of every product batch

The notified body shall:

(a) have documented procedures, sufficient expertise and facilities for the verification by examination and testing of every product batch in accordance with Annexes IX and XI;

(b) establish a test plan identifying all relevant and critical parameters which need to be tested by the notified body or under its responsibility in order to:
- verify, for class C devices, the conformity of the device with the type described in the EU type-examination certificate and with the requirements of this Regulation which apply to those devices,
- confirm, for class B devices, the conformity with the technical documentation referred to in Annexes II and III and with the requirements of this Regulation which apply to those devices,

(c) document its rationale for the selection of the parameters referred to in point (b);

(d) have documented procedures to carry out the appropriate assessments and tests in order to verify the conformity of the device with the requirements of this Regulation by examining and testing every product batch as specified in Section 5 of Annex XI;

(e) have documented procedures providing for the reaching of an agreement with the applicant concerning when and where necessary tests that are not to be carried out by the notified body itself are to be performed;

(f) assume full responsibility for test results in accordance with documented procedures; test reports submitted by the manufacturer shall only be taken into account if they have been issued by conformity assessment bodies which are competent and independent of the manufacturer.

4.5.4. Performance evaluation assessment

The assessment by notified bodies of procedures and documentation shall address the results of literature searches and all validation, verification and testing performed and conclusions drawn, and shall typically include considering the use of alternative materials and substances and take account of the packaging, stability including shelf life of the finished device. Where no new testing has been undertaken by a manufacturer or where there have been deviations from procedures, the notified body in question shall critically examine the justification presented by the manufacturer.

The notified body shall have documented procedures in place relating to the assessment of a manufacturer's procedures and documentation relating to performance evaluation both for initial conformity assessment and on an ongoing basis. The notified body shall examine, validate and verify that the manufacturer's procedures and documentation adequately address:

(a) the planning, conduct, assessment, reporting and updating of the performance evaluation as referred to in Annex XIII,

(b) post-market surveillance and post-market performance follow up,

(c) the interface with the risk management process,

(d) the appraisal and analysis of the available data and its relevance with regard to demonstrating conformity with the relevant requirements in Annex I,

(e) the conclusions drawn with regard to the clinical evidence and drawing up of the performance evaluation report.

The procedures referred to in the second paragraph shall take into consideration available CS, guidance and best practice documents.

The notified body's assessment of performance evaluations as referred to in Annex XIII shall cover:

— the intended use specified by the manufacturer and claims for the device defined by it,
— the planning of the performance evaluation,
— the methodology for the literature search,
— relevant documentation from the literature search,
— the performance studies,
— post-market surveillance and post-market performance follow up,
— validity of equivalence claimed in relation to other devices, the demonstration of equivalence, the suitability and conclusions data from equivalent and similar devices,
— the performance evaluation report,
— justifications in relation to non-performance of performance studies or PMPF.

In relation to data from performance studies included within the performance evaluation, the notified body in question shall ensure that the conclusions drawn by the manufacturer are valid in the light of the approved performance study plan.

The notified body shall ensure that the performance evaluation adequately addresses the relevant safety and performance requirements provided for in Annex I, that it is appropriately aligned with the risk management requirements and that it is conducted in accordance with Annex XIII and that it is appropriately reflected in the information provided relating to the device.

4.5.5. Specific Procedures

The notified body shall have documented procedures, sufficient expertise and facilities for the procedures referred to in Section 5 of Annex IX, for which they are designated.

In the case of companion diagnostics, the notified body shall have documented procedures in place that aim to fulfil the requirements of this Regulation in relation to consultation of the EMA or a medicinal products competent authority during its assessment of such types of device.

4.6. Reporting

The notified body shall:

— ensure that all steps of the conformity assessment are documented so that the conclusions of the assessment are clear and demonstrate compliance with the requirements of this Regulation and can represent objective evidence of such compliance to persons that are not themselves involved in the assessment, for example personnel in designating authorities,
— ensure that records that are sufficient to provide a discernible audit trail are available for quality management system audits,
— clearly document the conclusions of its assessment of performance evaluation in a performance evaluation assessment report,
— for each specific project, provide a detailed report which shall be based on a standard format containing a minimum set of elements determined by the MDCG.

The report of the notified body shall:

— clearly document the outcome of its assessment and draw clear conclusions from the verification of the manufacturer's conformity with the requirements of this Regulation,
— make a recommendation for a final review and for a final decision to be taken by the notified body; this recommendation shall be signed off by the member of personnel responsible in the notified body,
— be provided to the manufacturer in question.

4.7. Final review

The notified body shall prior to making a final decision:

— ensure that the personnel assigned for the final review and decision making on specific projects are appropriately authorised and are different from the personnel who have conducted the assessments,

— verify that the report or reports and supporting documentation needed for decision making, including concerning resolution of non-conformities noted during assessment, are complete and sufficient with respect to the scope of the application, and

— verify whether there are any unresolved non-conformities preventing issuance of a certificate.

4.8. Decisions and certifications

The notified body shall have documented procedures for decision-making including as regards the allocation of responsibilities for the issuance, suspension, restriction and withdrawal of certificates. Those procedures shall include the notification requirements laid down in Chapter V of this Regulation. The procedures shall allow the notified body in question to:

— decide, based on the assessment documentation and additional information available whether the requirements of this Regulation are fulfilled,

— decide, based on the results of its assessment of the performance evaluation and risk management whether the post-market surveillance plan, including the PMPF plan, is adequate,

— decide on specific milestones for further review by the notified body of the up to date performance evaluation,

— decide whether specific conditions or provisions need to be defined for the certification,

— decide, based on the novelty, risk classification, performance evaluation and conclusions from the risk analysis of the device, on a period of certification not exceeding five years,

— clearly document decision making and approval steps including approval by signature of the members of personnel responsible,

— clearly document responsibilities and mechanisms for communication of decisions, in particular, where the final signatory of a certificate differs from the decision maker or decision makers or does not fulfil the requirements laid down in Section 3.2.7.,

— issue a certificate or certificates in accordance with the minimum requirements laid down in Annex XII for a period of validity not exceeding five years and shall indicate whether there are specific conditions or limitations associated with the certification,

— issue a certificate or certificates for the applicant alone and shall not issue certificates covering multiple entities,

— ensure that the manufacturer is notified of the outcome of the assessment and the resultant decision and that they are entered into the electronic system referred to in Article 52.

4.9. Changes and modifications

The notified body shall have documented procedures and contractual arrangements with manufacturers in place relating to the manufacturers' information obligations and the assessment of changes to:

— the approved quality management system or systems or to the product-range covered,

— the approved design of a device,
— the approved type of a device,
— any substance incorporated in or utilised for the manufacturing of a device and being subject to the specific procedures in accordance with Section 4.5.5.

The procedures and contractual arrangements referred to in the first paragraph shall include measures for checking the significance of the changes referred to in the first paragraph.

In accordance with its documented procedures, the notified body in question shall:
— ensure that manufacturers submit for prior approval plans for changes as referred to in the first paragraph and relevant information relating to such changes,
— assess the changes proposed and verify whether, after these changes, the quality management system, or the design of a device or type of a device, still meets the requirements of this Regulation,
— notify the manufacturer of its decision and provide a report or, as applicable, a supplementary report, which shall contain the justified conclusions of its assessment.

4.10. Surveillance activities and post-certification monitoring

The notified body shall have documented procedures:
— defining how and when surveillance activities of manufacturers are to be conducted. Those procedures shall include arrangements for unannounced on-site audits of manufacturers and, where applicable, subcontractors and suppliers carrying out product tests and the monitoring of compliance with any conditions binding manufacturers and associated with certification decisions, such as updates to clinical data at defined intervals,
— for screening relevant sources of scientific and clinical data and post-market information relating to the scope of their designation. Such information shall be taken into account in the planning and conduct of surveillance activities,
— to review vigilance data to which they have access under to Article 87 in order to estimate its impact, if any, on the validity of existing certificates. The results of the evaluation and any decisions taken shall be thoroughly documented.

The notified body in question shall, upon receipt of information about vigilance cases from a manufacturer or competent authorities, decide on which of the following options to apply:
— not to take action on the basis that the vigilance case is clearly not related to the certification granted,
— observe the manufacturer's and competent authorities' activities and the results of the manufacturer's investigation so as to determine whether the certification granted is at risk or whether adequate corrective action has been taken,
— perform extraordinary surveillance measures, such as document reviews, short-notice or unannounced audits and product testing, where it is likely that the certification granted is at risk,
— increase the frequency of surveillance audits,
— review specific products or processes on the occasion of the next audit of the manufacturer, or
— take any other relevant measure.

In relation to surveillance audits of manufacturers, the notified body shall have documented procedures to:
— conduct surveillance audits of the manufacturer on at least an annual basis which shall be planned and conducted in line with the relevant requirements in Section 4.5.,

— ensure that it adequately assesses the manufacturer's documentation on, and application of, the provisions on vigilance, the post-market surveillance and PMPF,
— sample and test devices and technical documentation, during audits, according to pre-defined sampling criteria and testing procedures to ensure that the manufacturer continuously applies the approved quality management system,
— ensure that the manufacturer complies with the documentation and information obligations laid down in the relevant Annexes and that its procedures take into account best practices in the implementation of quality management systems,
— ensure that the manufacturer does not use quality management system or device approvals in a misleading manner,
— gather sufficient information to determine if the quality management system continues to comply with the requirements of this Regulation,
— ask the manufacturer, if non-conformities are detected, for corrections, corrective actions, and where applicable preventive actions, and
— where necessary, impose specific restrictions on the relevant certificate, or suspend or withdraw it.

The notified body shall, if listed as part of the conditions for certification:
— conduct an in-depth review of the performance evaluation as most recently updated by the manufacturer based on the manufacturer's post-market surveillance, on its PMPF and on clinical literature relevant to the condition being treated with the device or on clinical literature relevant to similar devices,
— clearly document the outcome of the in-depth review and address any specific concerns to the manufacturer or impose any specific conditions on it,
— ensure that the performance evaluation as most recently updated is appropriately reflected in the instructions for use and, where applicable, the summary of safety and performance.

4.11. Re-certification

The notified body shall have documented procedures in place relating to the re-certification reviews and the renewal of certificates. Re-certification of approved quality management systems or EU technical documentation assessment certificates or EU type-examination certificates shall occur at least every five years.

The notified body shall have documented procedures relating to renewals of EU technical documentation assessment certificates and EU type-examination certificates and those procedures shall require the manufacturer in question to submit a summary of changes and scientific findings for the device, including:

(a) all changes to the originally approved device, including changes not yet notified,

(b) experience gained from post-market surveillance,

(c) experience from risk-management,

(d) experience from updating the proof of compliance with the general safety and performance requirements set out in Annex I,

(e) experience from reviews of the performance evaluation, including the results of any performance studies and PMPF,

(f) changes to the requirements, to components of the device or to the scientific or regulatory environment,

(g) changes to applied or new harmonised standards, CS or equivalent documents, and

(h) changes in medical, scientific and technical knowledge, such as:

— new treatments,

— changes in test methods,

— new scientific findings on materials and components, including findings on their biocompatibility,

— experience from studies on comparable devices,

— data from registers and registries,

— experience from performance studies with comparable devices.

The notified body shall have documented procedures to assess the information referred to in the second paragraph and shall pay particular attention to clinical data from post-market surveillance and PMPF activities undertaken since the previous certification or re-certification, including appropriate updates to manufacturers' performance evaluation reports.

For the decision on the re-certification, the notified body in question shall use the same methods and principles as for the initial certification decision. If necessary, separate forms shall be established for re-certification taking into account the steps to be taken for certification, such as application and application review.

ANNEX VIII

CLASSIFICATION RULES

1. IMPLEMENTING RULES

1.1. Application of the classification rules shall be governed by the intended purpose of the devices.

1.2. If the device in question is intended to be used in combination with another device, the classification rules shall apply separately to each of the devices.

1.3. Accessories for an *in vitro* diagnostic medical device shall be classified in their own right separately from the device with which they are used.

1.4. Software, which drives a device or influences the use of a device, shall fall within the same class as the device.

If the software is independent of any other device, it shall be classified in its own right.

1.5. Calibrators intended to be used with a device shall be classified in the same class as the device.

1.6. Control materials with quantitative or qualitative assigned values intended for one specific analyte or multiple analytes shall be classified in the same class as the device.

1.7. The manufacturer shall take into consideration all classification and implementation rules in order to establish the proper classification for the device.

1.8. Where a manufacturer states multiple intended purposes for a device, and as a result the device falls into more than one class, it shall be classified in the higher class.

1.9. If several classification rules apply to the same device, the rule resulting in the higher classification shall apply.

1.10. Each of the classification rules shall apply to first line assays, confirmatory assays and supplemental assays.

2. CLASSIFICATION RULES

2.1. Rule 1

Devices intended to be used for the following purposes are classified as class D:

— 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;

— 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;

— determining the infectious load of a life-threatening disease where monitoring is critical in the process of patient management.

2.2. Rule 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:

— ABO system [A (ABO1), B (ABO2), AB (ABO3)];

— Rhesus system [RH1 (D), RHW1, RH2 (C), RH3 (E), RH4 (c), RH5 (e)];

— Kell system [Kel1 (K)];

— Kidd system [JK1 (Jka), JK2 (Jkb)];

— Duffy system [FY1 (Fya), FY2 (Fyb)];

in which case they are classified as class D.

2.3. Rule 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.

2.4. Rule 4

(a) Devices intended for self-testing are classified as class C, except for devices for the detection of pregnancy, for fertility testing and for determining cholesterol level, and devices for the detection of glucose, *erythrocytes*, *leucocytes* and bacteria in urine, which are classified as class B.

(b) Devices intended for near-patient testing are classified in their own right.

2.5. Rule 5

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.

2.6. Rule 6

Devices not covered by the above-mentioned classification rules are classified as class B.

2.7. Rule 7

Devices which are controls without a quantitative or qualitative assigned value are classified as class B.

ANNEX IX

CONFORMITY ASSESSMENT BASED ON A QUALITY MANAGEMENT SYSTEM AND ON ASSESSMENT OF TECHNICAL DOCUMENTATION

CHAPTER I

QUALITY MANAGEMENT SYSTEM

1. The manufacturer shall establish, document and implement a quality management system, as described in Article 10(8), and maintain its effectiveness throughout the life cycle of the devices concerned. The manufacturer shall ensure the application of the quality management system as specified in Section 2, and shall be subject to audit as laid down in Sections 2.3 and 2.4 and to surveillance as specified in Section 3.

2. Quality management system assessment

2.1. The manufacturer shall lodge an application for assessment of its quality management system with a notified body. The application shall include:

— 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,

— all relevant information on the device or group of devices covered by the quality management system,

— 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,

— a draft of an EU declaration of conformity in accordance with Article 17 and Annex IV for the device model covered by the conformity assessment procedure,

— the documentation on the manufacturer's quality management system,

— a documented description of the procedures in place to fulfil the obligations arising from by the quality management system and required under this Regulation and of the undertaking by the manufacturer in question to apply those procedures,

— 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,

— 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 Articles 82 to 87,

— 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 Articles 82 to 87, as well as the undertaking by the manufacturer to apply those procedures,

— documentation on the performance evaluation plan, and

— a description of the procedures in place to keep up to date the performance evaluation plan, taking into account the state of the art.

2.2. Implementation of the quality management system shall ensure compliance with this Regulation. All the elements, requirements and provisions adopted by the manufacturer for its quality management system shall 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.

Moreover, the documentation to be submitted for the assessment of the quality management system shall include an adequate description of, in particular:

(a) the manufacturer's quality objectives;

(b) the organisation of the business and in particular:
- the organisational structures with the assignment of staff responsibilities in relation to critical procedures, the responsibilities of the managerial staff and their organisational authority,
- 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,
- where the design, manufacture, and/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,
- where the manufacturer does not have a registered place of business in a Member State, 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. Those procedures and techniques shall specifically cover:
- 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,
- identification of applicable general safety and performance requirements and solutions to fulfil those requirements, taking applicable CS into account and, where opted for, harmonised standards,
- risk management as referred to in Section 3 of Annex I,
- the performance evaluation, pursuant to Article 56 and Annex XIII, including PMPF,
- solutions for fulfilling the applicable specific requirements regarding design and construction, including appropriate pre-clinical evaluation, in particular the requirements of Chapter II of Annex I,
- solutions for fulfilling the applicable specific requirements regarding the information to be supplied with the device, in particular the requirements of Chapter III of Annex I,
- the device identification procedures drawn up and kept up to date from drawings, specifications or other relevant documents at every stage of manufacture, and

— 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, and

(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; it shall be possible to trace back adequately the calibration of that test equipment.

In addition, the manufacturer shall grant the notified body access to the technical documentation referred to in Annexes II and III.

2.3. Audit

The notified body shall audit the quality management system to determine whether it meets the requirements referred to in Section 2.2. Where the manufacturer uses a harmonised standard or CS related to a quality management system, the notified body shall assess conformity with those standards or CS. The notified body shall assume that a quality management system which satisfies the relevant harmonised standards or CS conforms to the requirements covered by those standards or CS, unless it duly substantiate not doing so.

The audit team of the notified body shall include at least one member with past experience of assessments of the technology concerned in accordance with Sections 4.3. to 4.5. of Annex VII. In circumstances where such experience is not immediately obvious or applicable, the notified body shall provide a documented rationale for the composition of that team. The assessment procedure shall include an audit on the manufacturer's premises and, if appropriate, on the premises of the manufacturer's suppliers and/or subcontractors to verify the manufacturing and other relevant processes.

Moreover, in the case of class C devices, the quality management system assessment shall be accompanied by the assessment of the technical documentation for devices selected on a representative basis in accordance with provisions in Sections 4.4 to 4.8. In choosing representative samples the notified body shall take into account the published guidance developed by the MDCG pursuant to Article 99 and in particular, the novelty of the technology, the potential impact on the patient and standard medical practice, similarities in design, technology, manufacturing and, where applicable, sterilisation methods, the intended purpose and the results of any previous relevant assessments that have been carried out in accordance with this Regulation. The notified body in question shall document its rationale for the samples taken.

If the quality management system conforms to the relevant provisions of this Regulation, the notified body shall issue an EU quality management system certificate. The notified body shall notify the manufacturer of tits decision to issue the certificate. The decision shall contain the conclusions of the audit and a reasoned report.

2.4. The manufacturer in question shall 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. The notified body shall assess the changes proposed, determine the need for additional audits and verify whether, after those changes, the quality management system still meets the requirements referred to in Section 2.2. It shall notify the manufacturer of its decision which shall contain the conclusions of the assessment, and where applicable, conclusions of additional audits. The approval of any substantial change to the quality management system

or the device-range covered shall take the form of a supplement to the EU quality management system certificate.

3. Surveillance assessment applicable to class C and class D devices

3.1. The aim of surveillance is to ensure that the manufacturer duly fulfils the obligations arising from the approved quality management system.

3.2. The manufacturer shall 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:

— the documentation on its quality management system,

— 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 Articles 82 to 87,

— 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 Section 4 of Annex I,

— 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.

3.3. Notified bodies shall periodically, at least once every 12 months, carry out appropriate audits and assessments to make sure that the manufacturer in question applies the approved quality management system and the post-market surveillance plan. Those audits and assessments shall include audits on the premises of the manufacturer and, if appropriate, of the manufacturer's suppliers and/or subcontractors. At the time of such on-site audits, the notified body shall, where necessary, carry out or ask for tests in order to check that the quality management system is working properly. It shall provide the manufacturer with a surveillance audit report and, if a test has been carried out, with a test report.

3.4. The notified body shall randomly perform at least once every five years unannounced audits on the site of the manufacturer and, where appropriate, the site of the manufacturer's suppliers and/or subcontractors, which may be combined with the periodic surveillance assessment referred to in Section 3.3 or be performed in addition to that surveillance assessment. The notified body shall establish a plan for such unannounced on-site audits but shall not disclose it to the manufacturer.

Within the context of such unannounced on-site audits, the notified body shall test an adequate sample of the devices produced or an adequate sample from the manufacturing process to verify that the manufactured device is in conformity with the technical documentation. Prior to unannounced on-site audits, the notified body shall specify the relevant sampling criteria and testing procedure.

Instead of, or in addition to, sampling referred to in the second paragraph, notified bodies shall take samples of devices from the market to verify that the manufactured device is in conformity with the technical documentation. Prior to the sampling, the notified body in question shall specify the relevant sampling criteria and testing procedure.

The notified body shall provide the manufacturer in question with an on-site audit report which shall include, if applicable, the result of the sample test.

3.5. In the case of class C devices, the surveillance assessment shall also include an assessment of the technical documentation as referred to in Sections 4.4 to 4.8 of for

the device or devices concerned on the basis of further representative samples chosen in accordance with the rationale documented by the notified body in accordance with the third paragraph of Section 2.3.

3.6. Notified bodies shall ensure that the composition of the assessment team is such that there is sufficient experience with the evaluation of the devices, systems and processes concerned, continuous objectivity and neutrality; this shall include a rotation of the members of the assessment team at appropriate intervals. As a general rule, a lead auditor shall neither lead nor attend audits for more than three consecutive years in respect of the same manufacturer.

3.7. If the notified body finds a divergence between the sample taken from the devices produced or from the market and the specifications laid down in the technical documentation or the approved design, it shall suspend or withdraw the relevant certificate or impose restrictions on it.

CHAPTER II

ASSESSMENT OF THE TECHNICAL DOCUMENTATION

4. Assessment of the technical documentation of class B, C and D devices and batch verification applicable to class D devices

4.1. In addition to the obligation laid down in Section 2, the manufacturer of devices shall 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 Section 2.

4.2. The application shall describe the design, manufacture and performance of the device in question. It shall include the technical documentation as referred to in Annexes II and III.

In the case of devices for self-testing or near-patient testing, the application shall also include the aspects referred to in point (b) of Section 5.1.

4.3. The notified body shall examine the application by using staff, employed by it, with proven knowledge and experience in the evaluation of the technology, and the devices concerned and the evaluation of clinical evidence. The notified body may require the application to be completed by having further tests carried out or requesting further evidence to be provided to allow assessment of conformity with the relevant requirements of this Regulation. The notified body shall carry out adequate physical or laboratory tests in relation to the device or request the manufacturer to carry out such tests.

4.4. The notified body shall review the clinical evidence presented by the manufacturer in the performance evaluation report and the related performance evaluation that was conducted. The notified body shall use employed device reviewers with sufficient clinical expertise and including external clinical experts with direct and current experience relating to the clinical application of the device in question for the purposes of that review.

4.5. The notified body shall, in circumstances in which the clinical evidence is based partly or totally on data from devices which are claimed to be equivalent to the device under assessment, assess the suitability of using such data, taking into account factors

such as new indications and innovation. The notified body shall clearly document its conclusions on the claimed equivalence, and on the relevance and adequacy of the data for demonstrating conformity.

4.6. The notified body shall verify that the clinical evidence and the performance evaluation are adequate and shall verify the conclusions drawn by the manufacturer on the conformity with the relevant general safety and performance requirements. That verification shall include consideration of the adequacy of the benefit-risk determination, the risk management, the instructions for use, the user training and the manufacturer's post-market surveillance plan, and include a review of the need for, and the adequacy of, the PMPF plan proposed, where applicable.

4.7. Based on its assessment of the clinical evidence, the notified body shall consider the performance evaluation and the benefit-risk determination, and whether specific milestones need to be defined to allow the notified body to review updates to the clinical evidence that result from post-market surveillance and PMPF data.

4.8. The notified body shall clearly document the outcome of its assessment in the performance evaluation assessment report.

4.9. Before issuing an EU technical documentation assessment certificate, the notified body shall request an EU reference laboratory, where designated in accordance with Article 100, to verify the performance claimed by the manufacturer and the compliance of the device with the CS, where available, or with other solutions chosen by the manufacturer to ensure a level of safety and performance that is at least equivalent. The verification shall include laboratory tests by the EU reference laboratory as referred to in Article 48(5).

In addition, the notified body shall, in the cases referred to in Article 48(6) of this Regulation, consult the relevant experts referred to in Article 106 of Regulation (EU) 2017/745 in accordance with the procedure laid down in Article 48(6) of this Regulation on the performance evaluation report of the manufacturer.

The EU reference laboratory shall provide a scientific opinion within 60 days.

The scientific opinion of the EU reference laboratory and, where applicable, the views of the experts consulted, pursuant to the procedure laid down in Article 48(6), and any possible updates shall be included in the documentation of the notified body concerning the device. The notified body shall, when making its decision, give due consideration to the views expressed in the scientific opinion of the EU reference laboratory, and, where applicable, to the views expressed by the experts consulted pursuant to Article 48(6). The notified body shall not deliver the certificate if the scientific opinion of the EU reference laboratory is unfavourable.

4.10. The notified body shall provide the manufacturer with a report on the technical documentation assessment, including a performance evaluation assessment report. If the device conforms to the relevant provisions of this Regulation, the notified body shall issue an EU technical documentation assessment certificate. The certificate shall contain the conclusions of the technical documentation assessment, the conditions of the certificate's validity, the data needed for identification of the approved device, and, where appropriate, a description of the intended purpose of the device.

4.11. Changes to the approved device shall require approval from the notified body which issued the EU technical documentation assessment certificate, where such changes could affect the safety and performance of the device or the conditions prescribed for use of the device. Where the manufacturer plans to introduce any of the above-mentioned changes it shall inform the notified body which issued the EU technical

documentation assessment certificate thereof. The notified body shall assess the planned changes and decide whether the planned changes require a new conformity assessment in accordance with Article 48 or whether they could be addressed by means of a supplement to the EU technical documentation assessment certificate. In the latter case, the notified body shall assess the changes, notify the manufacturer of its decision and, where the changes are approved, provide it with a supplement to the EU technical documentation assessment certificate.

Where the changes could affect compliance with the CS or with other solutions chosen by the manufacturer which were approved through the EU technical documentation assessment certificate, the notified body shall consult the EU reference laboratory that was involved in the initial consultation, in order to confirm that compliance with the CS or with other solutions chosen by the manufacturer, to ensure a level of safety and performance that is at least equivalent, is maintained.

The EU reference laboratory shall provide a scientific opinion within 60 days.

4.12. To verify conformity of manufactured class D devices, the manufacturer shall carry out tests on each manufactured batch of devices. After the conclusion of the controls and tests, it shall forward to the notified body, without delay, the relevant reports on those tests. Furthermore, the manufacturer shall make the samples of manufactured batches of devices available to the notified body in accordance with pre-agreed conditions and detailed arrangements which shall include that the notified body or the manufacturer shall send samples of the manufactured batches of devices to the EU reference laboratory, where such a laboratory has been designated in accordance with Article 100, to carry out appropriate tests. The EU reference laboratory shall inform the notified body about its findings.

4.13. 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.

5. Assessment of the technical documentation of specific types of devices

5.1. Assessment of the technical documentation of class B, C and D devices for self-testing and near-patient testing

(a) The manufacturer of class B, C and D devices for self-testing and near-patient testing shall lodge with the notified body an application for the assessment of the technical documentation.

(b) The application shall enable the design of the device characteristics and performance(s) to be understood and shall enable conformity with the design-related requirements of this Regulation to be assessed. It shall include:

(i) test reports, including results of studies carried out with intended users;

(ii) where practicable, an example of the device; if required, the device shall 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.

The notified body may require the application to be completed by carrying out further tests or by providing further proof to allow assessment of conformity with the requirements of this Regulation.

(c) The notified body shall verify the compliance of the device with the relevant requirements set out in Annex I of this Regulation.

(d) The notified body shall assess the application, by using staff, employed by it, with proven knowledge and experience regarding the technology concerned and the intended purpose of the device and provide the manufacturer with a technical documentation assessment report.

(e) If the device conforms to the relevant provisions of this Regulation, the notified body shall issue an EU technical documentation assessment certificate. The certificate shall contain the conclusions of the assessment, the conditions of its validity, the data needed for the identification of the approved devices and, where appropriate, a description of the intended purpose of the device.

(f) Changes to the approved device shall require approval from the notified body which issued the EU technical documentation assessment certificate, where such changes could affect the safety and performance of the device or the conditions prescribed for use of the device. Where the manufacturer plans to introduce any of the above-mentioned changes, it shall inform the notified body which issued the EU technical documentation assessment certificate thereof. The notified body shall assess the planned changes and decide whether the planned changes require a new conformity assessment in accordance with Article 48 or whether they could be addressed by means of a supplement to the EU technical documentation assessment certificate. In the latter case, the notified body shall assess the changes, notify the manufacturer of its decision and, where the changes are approved, provide it with a supplement to the EU technical documentation assessment certificate.

5.2. Assessment of the technical documentation of companion diagnostics

(a) The manufacturer of a companion diagnostic shall lodge with the notified body an application for the assessment of the technical documentation. The notified body shall assess that application in accordance with the procedure laid down in Sections 4.1 to 4.8 of this Annex.

(b) The application shall enable the characteristics and performance of the device to be understood, and shall enable conformity with the design-related requirements of this Regulation to be assessed, in particular, with regard to the suitability of the device in relation to the medicinal product concerned.

(c) The notified body shall, before issuing an EU technical documentation assessment certificate for the companion diagnostic and on the basis of the draft summary of safety and performance and the draft instructions for use, seek a scientific opinion from one of the competent authorities designated by the Member States in accordance with Directive 2001/83/EC or from the EMA, either of which to be referred to in this Section as ‘the medicinal products authority consulted’ depending on which has been consulted under this point, regarding the suitability of the device in relation to the medicinal product concerned. Where the medicinal product falls exclusively within the scope of the Annex to Regulation (EC) No 726/2004 of the European Parliament and of the Council[(4)], the notified body shall seek the opinion of the EMA. If the medicinal product concerned is already authorised, or if an application for its authorisation has

been submitted, the notified body shall consult the medicinal products authority, or the EMA, that is responsible for the authorisation.

(d) The medicinal products authority consulted shall provide its opinion, within 60 days of receipt of all the necessary documentation. This 60-day period may be extended once for a further 60 days on justified grounds. The opinion and any possible update shall be included in the documentation of the notified body concerning the device.

(e) The notified body shall give due consideration to the scientific opinion referred to in point (d) when making its decision. The notified body shall convey its final decision to the medicinal products authority consulted. The EU technical documentation assessment certificate shall be delivered in accordance with point (e) of Section 5.1.

(f) Before changes affecting the performance and/or the intended use and/or the suitability of the device in relation to the medicinal product concerned are made, the manufacturer shall inform the notified body of the changes. The notified body shall assess the planned changes and decide whether the planned changes require a new conformity assessment in accordance with Article 48 or whether they could be addressed by means of a supplement to the EU technical documentation assessment certificate. In the latter case, the notified body shall assess the changes and seek the opinion of the medicinal products authority consulted. The medicinal products authority consulted shall give its opinion within 30 days of receipt of the all the necessary documentation regarding the changes. A supplement to the EU technical documentation assessment certificate shall be issued in accordance with point (f) of Section 5.1.

CHAPTER III

ADMINISTRATIVE PROVISIONS

6. The manufacturer or, where the manufacturer does not have a registered place of business in a Member State, it's authorised representative shall, 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 competent authorities:

— the EU declaration of conformity,

— the documentation referred to in the fifth indent of Section 2.1. and, in particular, the data and records arising from the procedures referred to in point (c) of the second paragraph of Section 2.2.,

— information on the changes referred to in Section 2.4.,

— the documentation referred to in Sections 4.2. and point (b) of Section 5.1., and

— the decisions and reports from the notified body as referred to in this Annex.

7. Each Member State shall require that the documentation referred to in Section 6 is kept at the disposal of competent authorities for the period indicated in that Section in case a manufacturer, or its authorised representative, established within its territory goes bankrupt or ceases its business activity prior to the end of that period.

ANNEX X

CONFORMITY ASSESSMENT BASED ON TYPE-EXAMINATION

1. EU 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 of this Regulation.

2. Application

The manufacturer shall lodge an application for assessment with a notified body. The application shall 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,

— the technical documentation referred to in Annexes II and III. The applicant shall make a representative sample of the device production envisaged ('type') available to the notified body. The notified body may request other samples as necessary,

— in the case of devices for self-testing or near-patient testing, 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,

— where practicable, an example of the device. If required, the device shall be returned on completion of the technical documentation assessment;

— data showing the suitability of the device in relation to its intended purpose for self-testing or near-patient testing,

— the information to be provided with the device on its label and its instructions for use, and

— 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.

3. Assessment

The notified body shall:

(a) examine the application, by using staff with proven knowledge and experience in the evaluation of the technology, and the devices concerned and the evaluation of clinical evidence. The notified body may require the application to be completed by having further tests carried out or requesting further evidence to be provided to allow assessment of conformity with the relevant requirements of this Regulation. The notified body shall carry out adequate physical or laboratory tests in relation to the device or request the manufacturer to carry out such tests;

(b) examine and assess the technical documentation for conformity with the requirements of this Regulation that are applicable to the device and verify that the type has been manufactured in conformity with that documentation; it shall also record the items designed in conformity with the applicable standards referred to in Article 8 or with applicable CS, and record items not designed on the basis of the relevant standards referred to in Article 8 or of the relevant CS;

(c) review the clinical evidence presented by the manufacturer in the performance evaluation report in accordance with Section 1.3.2 of Annex XIII. The notified body shall employ device reviewers with sufficient clinical expertise and, if necessary, use external clinical experts with direct and current experience relating to the clinical application of the device in question for the purposes of that review;

(d) in circumstances in which the clinical evidence is partly or totally based on data from devices which are claimed to be similar or equivalent to the device under assessment, assess the suitability of using such data, taking into account factors such as new indications and innovation. The notified body shall clearly document its conclusions on the claimed equivalence, and on the relevance and adequacy of the data for demonstrating conformity;

(e) clearly document the outcome of its assessment in the performance evaluation assessment report referred to in Section 4.8 of Annex IX;

(f) carry out or arrange for the appropriate assessments and the physical or laboratory tests necessary to verify whether the solutions adopted by the manufacturer meet the general safety and performance requirements laid down in this Regulation in the event that the standards referred to in Article 8 or the CS have not been applied. Where the device has to be connected to another device or devices in order to operate as intended, proof shall be provided that it conforms to the general safety and performance requirements when connected to any such device or devices having the characteristics specified by the manufacturer;

(g) carry out or arrange for the appropriate assessments and the physical or laboratory tests necessary to verify whether, in the event that the manufacturer has chosen to apply the relevant harmonised standards, those standards have actually been applied;

(h) agree with the applicant on the place where the necessary assessments and tests are to be carried out;

(i) draw up an EU type-examination report on the results of the assessments and tests carried out under points (a) to (g);

(j) in the case of class D devices, request the EU reference laboratory, where designated in accordance with Article 100, to verify the performance claimed by the manufacturer and the compliance of the device with the CS, where available, or with other solutions chosen by the manufacturer to ensure a level of safety and performance that is at least equivalent. The verification shall include laboratory tests by the EU reference laboratory in accordance with Article 48(5).

In addition, the notified body shall, in the cases referred to in Article 48(6) of this Regulation, consult the relevant experts referred to in Article 106 of Regulation (EU) 2017/745 following the procedure laid down in Article 48(6) of this Regulation on the performance evaluation report of the manufacturer.

The EU reference laboratory shall provide a scientific opinion within 60 days.

The scientific opinion of the EU reference laboratory and, where the procedure laid down in Article 48(6) is applicable, the views of the experts consulted, and any possible updates shall be included in the documentation of the notified body concerning the device. The notified body shall give due consideration to the views expressed in the scientific opinion of the EU reference laboratory, and, where applicable, to the views expressed by the experts consulted in accordance with Article

48(6), when making its decision. The notified body shall not deliver the certificate if the scientific opinion of the EU reference laboratory is unfavourable;

(k) for companion diagnostics, seek the opinion, on the basis of the draft summary of safety and performance and the draft instructions for use, of one of the competent authorities designated by the Member States in accordance with Directive 2001/83/EC or the EMA (either of which to be hereinafter referred to as 'the medicinal products authority consulted' depending on which has been consulted under this point) on the suitability of the device in relation to the medicinal product concerned. Where the medicinal product falls exclusively within the scope of the Annex of Regulation (EC) No 726/2004, the notified body shall consult the EMA. If the medicinal product concerned is already authorised, or if an application for its authorisation has been submitted, the notified body shall consult the medicinal products competent authority, or the EMA, that is responsible for the authorisation. The medicinal products authority consulted shall deliver its opinion within 60 days of receipt of all the necessary documentation. This 60-day period may be extended once for a further 60 days on justified grounds. The opinion of the medicinal products authority consulted and any possible update shall be included in the documentation of the notified body concerning the device. The notified body shall give due consideration to the opinion expressed by the medicinal products authority consulted when making its decision. It shall convey its final decision to the medicinal products authority consulted; and

(l) draw up an EU type-examination report on the results of the assessments and tests carried out, and scientific opinions provided under, points (a) to (k), including a performance evaluation assessment report for class C or class D devices or covered by the third indent of Section 2.

4. Certificate

If the type conforms to this Regulation, the notified body shall issue an EU type-examination certificate. The certificate shall contain the name and address of the manufacturer, the conclusions of the type examination assessment, the conditions of certificate's validity and the data needed for identification of the type approved. The certificate shall be drawn up in accordance with Annex XII. The relevant parts of the documentation shall be annexed to the certificate and a copy kept by the notified body.

5. Changes to the type

5.1. The applicant shall inform the notified body which issued the EU type-examination certificate of any planned change to the approved type or of its intended purpose and conditions of use.

5.2. Changes to the approved device including limitations of its intended purpose and conditions of use shall require further approval from 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. The notified body shall examine the planned changes, notify the manufacturer of its decision and provide him with a supplement to the EU type-examination report. The approval of any change to the approved type shall take the form of a supplement to the EU type-examination certificate.

5.3. 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, shall necessitate a new application for a conformity assessment.

5.4. Where the changes could affect the performance claimed by the manufacturer or compliance with the CS or with other solutions chosen by the manufacturer which were approved through the EU type-examination certificate, the notified body shall consult the EU reference laboratory that was involved in the initial consultation, in order to confirm that compliance with the CS, when available, or with other solutions chosen by the manufacturer to ensure a level of safety and performance that is at least equivalent are maintained.

The EU reference laboratory shall provide a scientific opinion within 60 days.

5.5. Where the changes affect the performance or the intended use of a companion diagnostic approved through the EU type-examination certificate or its suitability in relation to a medicinal product, the notified body shall consult the medicinal products competent authority that was involved in the initial consultation or the EMA. The medicinal products authority consulted shall give its opinion, if any, within 30 days after receipt of the valid documentation regarding the changes. The approval of any change to the approved type shall take the form of a supplement to the initial EU type-examination certificate.

6. Administrative provisions

The manufacturer or, where the manufacturer does not have a registered place of business in a Member State, its authorised representative shall, 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 competent authorities:

— the documentation referred to in the second indent of Section 2,

— information on the changes referred to in Section 5,

— copies of EU type-examination certificates, scientific opinions and reports and their additions/supplements.

Section 7 of Annex IX shall apply.

ANNEX XI

CONFORMITY ASSESSMENT BASED ON PRODUCTION QUALITY ASSURANCE

1. The manufacturer shall ensure that the quality management system approved for the manufacture of the devices concerned is implemented, shall carry out final verification, as specified in Section 3, and shall be subject to the surveillance referred to in Section 4.

2. When the manufacturer fulfils the obligations laid down in Section 1, it shall draw up and keep an EU declaration of conformity in accordance with Article 17 and Annex IV for the device covered by the conformity assessment procedure. By issuing an EU declaration of conformity, the manufacturer shall be deemed to ensure, and to declare, that the device concerned meets the requirements of this Regulation 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 EU type-examination certificate.

3. Quality management system

3.1. The manufacturer shall lodge an application for assessment of its quality management system with a notified body.

The application shall include:

— all elements listed in Section 2.1 of Annex IX,

— the technical documentation referred to in Annexes II and III for the types approved,

— a copy of the EU type-examination certificates referred to in Section 4 of Annex X; if the EU 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.

3.2. Implementation of the quality management system shall be such as to ensure that there is compliance with the type described in the EU type-examination certificate and with the provisions of this Regulation which apply to the devices at each stage. All the elements, requirements and provisions adopted by the manufacturer for its quality management system shall 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.

That documentation shall, in particular, include an adequate description of all elements listed in points (a), (b), (d) and (e) of Section 2.2. of Annex IX.

3.3. The first and second paragraphs of Section 2.3 of Annex IX shall apply.

If the quality management system is such that it ensures that the devices conform to the type described in the EU type-examination certificate and conform to the relevant provisions of this Regulation, the notified body shall issue an EU production quality assurance certificate. The notified body shall notify the manufacturer of its decision to issue the certificate. That decision shall contain the conclusions of the notified body's audit and a reasoned assessment.

3.4. Section 2.4 of Annex IX shall apply.

4. Surveillance

Section 3.1, the first, second and fourth indents of Section 3.2, Sections 3.3, 3.4, 3.6 and 3.7 of Annex IX shall apply.

5. Verification of manufactured class D devices

5.1. In the case of class D devices, the manufacturer shall carry out tests on each manufactured batch of devices. After the conclusion of the controls and tests, it shall forward to the notified body without delay the relevant reports on those tests. Furthermore, the manufacturer shall make samples of manufactured devices or batches of devices available to the notified body in accordance with pre-agreed conditions and detailed arrangements which shall include that the notified body or the manufacturer, shall send samples of the manufactured devices or batches of devices to an EU reference laboratory, where such a laboratory has been designated in accordance with Article 100, to carry out appropriate laboratory tests. The EU reference laboratory shall inform the notified body about its findings.

5.2. 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.

6. Administrative provisions

The manufacturer or, where the manufacturer does not have a registered place of business in a Member State, its authorised representative shall, 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 competent authorities:

— the EU declaration of conformity,

— the documentation referred to in the fifth indent of Section 2.1 of Annex IX,

— the documentation referred to in the eighth indent of Section 2.1 of Annex IX, including the EU type-examination certificate referred to in Annex X,

— information on the changes referred to in Section 2.4 of Annex IX, and

— the decisions and reports from the notified body as referred to in Sections 2.3., 3.3. and 3.4. of Annex IX.

Section 7 of Annex IX shall apply.

ANNEX XII

CERTIFICATES ISSUED BY A NOTIFIED BODY

CHAPTER I

GENERAL REQUIREMENTS

1. Certificates shall be drawn up in one of the official languages of the Union.

2. Each certificate shall refer to only one conformity assessment procedure.

3. Certificates shall only be issued to one manufacturer. The name and address of the manufacturer included in the certificate shall be the same as that registered in the electronic system referred to in Article 27.

4. The scope of the certificates shall unambiguously describe the device or devices covered:

   (a) EU technical documentation assessment certificates and EU type-examination certificates shall include a clear identification, including the name, model and type, of the device or devices, the intended purpose as indicated by the manufacturer in the instructions for use and in relation to which the device has been assessed in the conformity assessment procedure, risk classification and the Basic UDI-DI as referred to in Article 24(6).

   (b) EU quality management system certificates and EU production quality assurance certificates shall include the identification of the devices or groups of devices, the risk classification and the intended purpose.

5. The notified body shall be able to demonstrate on request, which (individual) devices are covered by the certificate. The notified body shall set up a system that enables the determination of the devices, including their classification, covered by the certificate.

6. Certificates shall contain, if applicable, a note that, for the placing on the market of the device or devices it covers, another certificate issued in accordance with this Regulation is required.

7. EU quality management system certificates and EU production quality assurance certificates for class A sterile devices shall include a statement that the audit by the

notified body was limited to the aspects of manufacture concerned with securing and maintaining sterile conditions.

8. Where a certificate is supplemented, modified or re-issued, the new certificate shall contain a reference to the preceding certificate and its date of issue with identification of the changes.

CHAPTER II

MINIMUM CONTENT OF THE CERTIFICATES

1. name, address and identification number of the notified body;
2. name and address of the manufacturer and, if applicable, of the authorised representative;
3. unique number identifying the certificate;
4. if already issued, the SRN of the manufacturer referred to in Article 28(2);
5. date of issue;
6. date of expiry;
7. data needed for the unambiguous identification of the device or devices where applicable as specified in Section 4 of this Annex;
8. if applicable, reference to any previous certificate as specified in Section 8 of Chapter I;
9. reference to this Regulation and the relevant Annex in accordance with which the conformity assessment has been carried out;
10. examinations and tests performed, e.g. reference to relevant CS, harmonised standards, test reports and audit report(s);
11. if applicable, reference to the relevant parts of the technical documentation or other certificates required for the placing on the market of the device or devices covered;
12. if applicable, information about the surveillance by the notified body;
13. conclusions of the notified body's conformity assessment with regard to the relevant Annex;
14. conditions for or limitations to the validity of the certificate;
15. legally binding signature of the notified body in accordance with the applicable national law.

ANNEX XIII

PERFORMANCE EVALUATION, PERFORMANCE STUDIES AND POST-MARKET PERFORMANCE FOLLOW-UP

PART A

PERFORMANCE EVALUATION AND PERFORMANCE STUDIES

1. PERFORMANCE EVALUATION

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. To plan, continuously conduct and document a performance evaluation, the manufacturer shall establish and update a performance evaluation plan. The performance evaluation plan shall specify the characteristics and the performance of the device and the process and criteria applied to generate the necessary clinical evidence.

The performance evaluation shall be thorough and objective, considering both favourable and unfavourable data.

Its depth and extent shall be proportionate and appropriate to the characteristics of the device including the risks, risk class, performance and its intended purpose.

1.1. Performance evaluation plan

As a general rule, the performance evaluation plan shall include at least:

— a specification of the intended purpose of the device;
— a specification of the characteristics of the device as described in Section 9 of Chapter II of Annex I and in point (c) of Section 20.4.1. of Chapter III of Annex I;
— a specification of the analyte or marker to be determined by the device;
— a specification of the intended use of the device;
— identification of certified reference materials or reference measurement procedures to allow for metrological traceability;
— a clear identification of specified target patient groups with clear indications, limitations and contra-indications;
— an identification of the general safety and performance requirements as laid down in Sections 1 to 9 of Annex I that require support from relevant scientific validity and analytical and clinical performance data;
— 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;
— a description of the state of the art, including an identification of existing relevant standards, CS, guidance or best practices documents;
— 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;
— 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;

— 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;
— the PMPF planning as referred to in Part B of this Annex.

Where any of the above mentioned elements are not deemed appropriate in the Performance Evaluation Plan due to the specific device characteristics a justification shall be provided in the plan.

1.2. Demonstration of the scientific validity and the analytical and clinical performance:

As a general methodological principle the manufacturer shall:
— 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;
— appraise all relevant data by evaluating their suitability for establishing the safety and performance of the device;
— generate any new or additional data necessary to address outstanding issues.

1.2.1. Demonstration of the scientific validity

The manufacturer shall demonstrate the scientific validity based on one or a combination of the following sources:
— relevant information on the scientific validity of devices measuring the same analyte or marker;
— scientific (peer-reviewed) literature;
— consensus expert opinions/positions from relevant professional associations;
— results from proof of concept studies;
— results from clinical performance studies.

The scientific validity of the analyte or marker shall be demonstrated and documented in the scientific validity report.

1.2.2. Demonstration of the analytical performance

The manufacturer shall demonstrate the analytical performance of the device in relation to all the parameters described in point (a) of Section 9.1 of Annex I, unless any omission can be justified as not applicable.

As a general rule, the analytical performance shall always be demonstrated on the basis of analytical performance studies.

For novel markers or other markers without available certified reference materials or reference measurement procedures, it may not be possible to demonstrate trueness. If there are no comparative methods, different approaches may be used if demonstrated to be appropriate, such as comparison to some other well-documented methods or the composite reference standard. In the absence of such approaches, a clinical performance study comparing performance of the novel device to the current clinical standard practice is required.

Analytical performance shall be demonstrated and documented in the analytical performance report.

1.2.3. Demonstration of the clinical performance

The manufacturer shall demonstrate the clinical performance of the device in relation to all the parameters described in point (b) of Section 9.1. of Annex I, unless any omission can be justified as not applicable.

Demonstration of the clinical performance of a device shall be based on one or a combination of the following sources:

— clinical performance studies;

— scientific peer-reviewed literature;

— published experience gained by routine diagnostic testing.

Clinical performance studies shall be performed unless due justification is provided for relying on other sources of clinical performance data.

Clinical performance shall be demonstrated and documented in the clinical performance report.

1.3. Clinical evidence and performance evaluation report

1.3.1. The manufacturer shall 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 Annex I. The amount and quality of that data shall 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. The data and conclusions drawn from this assessment shall constitute the clinical evidence for the device. The clinical evidence shall scientifically demonstrate that the intended clinical benefit or benefits and safety will be achieved according to the state of the art in medicine.

1.3.2. Performance evaluation report

The clinical evidence shall be documented in a performance evaluation report. This report shall 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.

The performance evaluation report shall in particular include:

— the justification for the approach taken to gather the clinical evidence;

— the literature search methodology and the literature search protocol and literature search report of a literature review;

— 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;

— the nature and extent of the scientific validity and the analytical and clinical performance data that has been evaluated;

— the clinical evidence as the acceptable performances against the state of the art in medicine;

— any new conclusions derived from PMPF reports in accordance with Part B of this Annex.

1.3.3. The clinical evidence and its assessment in the performance evaluation report shall 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 Annex, as part of the performance evaluation and the post-market surveillance system referred to in Article 10(9). The performance evaluation report shall be part of the technical documentation. Both favourable and unfavourable data considered in the performance evaluation shall be included in the technical documentation.

2. CLINICAL PERFORMANCE STUDIES

2.1. Purpose of clinical performance studies

The purpose of clinical performance studies is to establish or confirm aspects of device performance which cannot be determined by analytical performance studies, literature and/or previous experience gained by routine diagnostic testing. This information is used to demonstrate compliance with the relevant general safety and performance requirements with respect to clinical performance. When clinical performance studies are conducted, the data obtained shall be used in the performance evaluation process and be part of the clinical evidence for the device.

2.2. Ethical considerations for clinical performance studies

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, shall be carried out in accordance with recognised ethical principles.

2.3. Methods for clinical performance studies

2.3.1. Clinical performance study design type

Clinical performance studies shall be designed in such a way as to maximize the relevance of the data while minimising potential bias.

2.3.2. Clinical performance study plan

Clinical performance studies shall be performed on the basis of a clinical performance study plan (CPSP).

The CPSP shall define the rationale, objectives, design and proposed analysis, methodology, monitoring, conduct and record-keeping of the clinical performance study. It shall contain in particular the following information:

(a) the single identification number of the clinical performance study, as referred to in Article 66(1);

(b) 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 to Article 58(4) established in the Union;

(c) 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;

(d) the starting date and scheduled duration for the clinical performance study;

(e) identification and description of the device, its intended purpose, the analyte or analytes or marker or markers, the metrological traceability, and the manufacturer;

(f) information about the type of specimens under investigation;

(g) 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 and/or medicine;

(h) 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;

(i) 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;

(j) 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;

(k) the analytical performance in accordance with point (a) of Section 9.1 of Chapter I of Annex I with justification for any omission;

(l) parameters of clinical performance in accordance with point (b) of Section 9.1 of Annex I 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 and/or public health management decisions;

(m) 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;

(n) 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;

(o) monitoring plan;

(p) data management;

(q) decision algorithms;

(r) policy regarding any amendments, including those in accordance with Article 71, to or deviations from the CPSP, with a clear prohibition of use of waivers from the CPSP;

(s) 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;

(t) 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;

(u) description of the informed consent process, including a copy of the patient information sheet and consent forms;

(v) procedures for safety recording and reporting, including definitions of recordable and reportable events, and procedures and timelines for reporting;

(w) criteria and procedures for suspension or early termination of the clinical performance study;

(x) 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;

(y) procedures for communication of test results outside the study, including communication of test results to the performance study subjects;

(z) 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 Section 2.2;

(aa) list of the technical and functional features of the device indicating those that are covered by the performance study;

(ab) bibliography.

If part of the information referred to in the second paragraph is submitted in a separate document, it shall be referenced in the CPSP. For studies using left-over samples, points (u), (x), (y) and (z) shall not apply.

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 shall be provided.

2.3.3. Clinical performance study report

A clinical performance study report, signed by a medical practitioner or any other authorised person responsible, shall contain documented information on the clinical performance study protocol plan, results and conclusions of the clinical performance study, including negative findings. The results and conclusions shall be transparent, free of bias and clinically relevant. The report shall contain sufficient information to enable it to be understood by an independent party without reference to other documents. The report shall also include as appropriate any protocol amendments or deviations, and data exclusions with the appropriate rationale.

3. OTHER PERFORMANCE STUDIES

By analogy, the performance study plan referred to in Section 2.3.2, and the performance study report, referred to in Section 2.3.3, shall be documented for other performance studies than clinical performance studies.

PART B

POST-MARKET PERFORMANCE FOLLOW-UP

4. PMPF shall be understood to be a continuous process that updates the performance evaluation referred to in Article 56 and Part A of this Annex and shall be specifically addressed in the manufacturer's post-market surveillance plan. When conducting PMPF, the manufacturer shall 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. PMPF shall be performed pursuant to a documented method laid down in a PMPF plan.

5.1. The PMPF plan shall 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 Sections 1 and 8 of Chapter I of Annex I, and

(e) identifying possible systematic misuse.

5.2. 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) a rationale for the appropriateness of the methods and procedures referred to in points (a) and (b);

(d) a reference to the relevant parts of the performance evaluation report referred to in Section 1.3 of this Annex and to the risk management referred to in Section 3 of Annex I;

(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, harmonised standards when used by the manufacturer, and relevant guidance on PMPF, and;

(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 shall 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 shall be taken into account for the performance evaluation referred to in Article 56 and Part A of this Annex and in the risk management referred to in Section 3 of Annex I. If, through the PMPF, the need for preventive and/or corrective measures has been identified, the manufacturer shall 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.

ANNEX XIV

INTERVENTIONAL CLINICAL PERFORMANCE STUDIES AND CERTAIN OTHER PERFORMANCE STUDIES

CHAPTER I

DOCUMENTATION REGARDING THE APPLICATION FOR INTERVENTIONAL CLINICAL PERFORMANCE STUDIES AND OTHER PERFORMANCE STUDIES INVOLVING RISKS FOR THE SUBJECTS OF THE STUDIES

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 shall draw up and submit the application in accordance with Article 58 accompanied by the following documents:

1. Application form

The application form shall be duly filled in, containing the following information:

1.1. 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 Article 58(4) established in the Union;

1.2. if different from those in Section 1.1, name, address and contact details of the manufacturer of the device intended for performance evaluation and, if applicable, of its authorised representative;

1.3. title of the performance study;

1.4. single identification number in accordance with Article 66(1);

1.5. status of the performance study, such as. the first submission, resubmission, significant amendment;

1.6. details and/ or reference to the performance study plan, such as including details of the design phase of the performance study;

1.7. if the application is a resubmission with regard to a device for which an application has been already submitted, 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. The sponsor shall identify 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 competent authority or ethics committee reviews;

1.8. if the application is submitted in parallel with an application for a clinical trial in accordance with Regulation (EU) No 536/2014, reference to the official registration number of the clinical trial;

1.9. identification of the Member States and third countries in which the clinical performance study is to be conducted as part of a multicentre or multinational study at the time of application;

1.10. brief description of the device for performance study, its classification and other information necessary for the identification of the device and device type;

1.11. summary of the performance study plan;

1.12. if applicable, information regarding a comparator device, its classification and other information necessary for the identification of the comparator device;

1.13. 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;

1.14. details of the anticipated start date and duration of the performance study;

1.15. details to identify the notified body, if already involved at the stage of application for the performance study;

1.16. confirmation that the sponsor is aware that the competent authority may contact the ethics committee that is assessing or has assessed the application;

1.17. the statement referred to in Section 4.1.

2. Investigator's brochure

The investigator's brochure (IB) shall contain the information on the device for performance study that is relevant for the study and available at the time of application. Any updates to the IB or other relevant information that is newly available shall be brought to the attention of the investigators in a timely manner. The IB shall be clearly identified and contain in particular the following information:

2.1. Identification and description of the device, including information on the intended purpose, the risk classification and applicable classification rule pursuant to Annex VIII, design and manufacturing of the device and reference to previous and similar generations of the device.

2.2. 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. In addition, information relating to any relevant training required.

2.3. Analytical performance.

2.4. Existing clinical data, in particular:

— 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;

— 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.

2.5. Summary of the benefit-risk analysis and the risk management, including information regarding known or foreseeable risks and warnings.

2.6. 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.

2.7. A list detailing the fulfilment of the relevant general safety and performance requirements set out in Annex I, 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.

2.8. 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.

3. Performance study plan as referred to in Sections 2 and 3 of Annex XIII.

4. Other information

4.1. A signed statement by the natural or legal 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 Annex I 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.

4.2. Where applicable according to national law, a copy of the opinion or opinions of the ethics committee or committees concerned. Where under national law the opinion or opinions of the ethics committee or committees is not required at the time of the submission of the application, a copy of the opinion or opinions shall be submitted as soon as available.

4.3. Proof of insurance cover or indemnification of subjects in case of injury, pursuant to Article 65 and the corresponding national law.

4.4. Documents to be used to obtain informed consent, including the patient information sheet and the informed consent document.

4.5 Description of the arrangements to comply with the applicable rules on the protection and confidentiality of personal data, in particular:

— organisational and technical arrangements that will be implemented to avoid unauthorised access, disclosure, dissemination, alteration or loss of information and personal data processed;

— a description of measures that will be implemented to ensure confidentiality of records and personal data of subjects;

— a description of measures that will be implemented in case of a data security breach in order to mitigate the possible adverse effects.

4.6. Full details of the available technical documentation, for example detailed risk analysis/management documentation or specific test reports shall be submitted to the competent authority reviewing an application upon request.

CHAPTER II

OTHER OBLIGATIONS OF THE SPONSOR

1. The sponsor shall undertake to keep available for the competent national authorities any documentation necessary to provide evidence for the documentation referred to in Chapter I of this Annex. If the sponsor is not the natural or legal 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 shall have an agreement in place to ensure that any serious adverse events or any other event as referred to in Article 76(2) are reported by the investigator or investigators to the sponsor in a timely manner.

3. The documentation mentioned in this Annex shall 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.

   Each Member State shall require that the documentation referred to in this Annex is kept at the disposal of the competent authorities for the period indicated in the first subparagraph in case the sponsor, or his contact person, established within its territory, goes bankrupt or ceases its activity prior to the end of this period.

4. The sponsor shall 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 this Regulation.

5. The sponsor shall complete the follow-up of investigation subjects.

ANNEX XV

CORRELATION TABLE

Directive 98/79/EC	**This Regulation**
Article 1(1)	Article 1(1)
Article 1(2)	Article 2
Article 1(3)	points (54) and (55) of Article 2
Article 1(4)	—
Article 1(5)	Article 5(4) and (5)
Article 1(6)	Article 1(9)
Article 1(7)	Article 1(5)
Article 2	Article 5(1)

Article 3	Article 5(2)
Article 4(1)	Article 21
Article 4(2)	Article 19(1) and (2)
Article 4(3)	Article 19(3)
Article 4(4)	Article 10(10)
Article 4(5)	Article 18(6)
Article 5(1)	Article 8(1)
Article 5(2)	—
Article 5(3)	Article 9
Article 6	—
Article 7	Article 107
Article 8	Articles 89 and 92
Article 9(1) first subparagraph	Article 48(10) first subparagraph
Article 9(1) second subparagraph	Article 48(3) second subparagraph, Article 48(7) second subparagraph and Article 48(9) second subparagraph
Article 9(2)	Article 48(3) to (6)
Article 9(3)	Article 48(3) to (9)
Article 9(4)	Article 5(6)
Article 9(5)	—
Article 9(6)	Article 11(3) and (4)
Article 9(7)	Article 10(7)
Article 9(8)	Article 49(1)
Article 9(9)	Article 49(4)
Article 9(10)	Article 51(2)
Article 9(11)	Article 48(12)
Article 9(12)	Article 54(1)
Article 9(13)	Article 48(2)
Article 10(1) and (2), second sentence of Article 10(3) and Article 10(4)	Articles 26(3), 27 and 28
Article 10(3), first sentence	Article 11(1)
Article 11(1)	Articles 82(1) and 84(2)
Article 11(2)	Article 82(10) and Article 82(11) first subparagraph
Article 11(3)	Article 84(7)

Article 11(4)	—
Article 11(5)	Article 86
Article 12	Article 30
Article 13	Article 93
Article 14(1)(a)	—
Article 14(1)(b)	Article 47(3) and (6)
Article 14(2)	—
Article 14(3)	—
Article 15(1)	Article 38 and Article 39
Article 15(2)	Article 32
Article 15(3)	Article 40(2) and (4)
Article 15(4)	—
Article 15(5)	Article 51(5)
Article 15(6)	Article 51(4)
Article 15(7)	Article 34(2) and Article 40(2)
Article 16	Article 18
Article 17	Articles 89 to 92
Article 18	Article 94
Article 19	Article 102
Article 20	Article 97
Article 21	—
Article 22	—
Article 23	—
Article 24	—

(**1**) 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 (OJ L 353, 31.12.2008, p. 1).

(**2**) 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) (OJ L 136, 29.5.2007, p. 3).

(**3**) Council Directive 80/181/EEC of 20 December 1979 on the approximation of the laws of the Member States relating to units of measurement and on the repeal of Directive 71/354/EEC (OJ L 39, 15.2.1980, p. 40).

(**4**) Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (OJ L 136, 30.4.2004, p. 1).