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Subject: Proposal for a Regulation of the European Parliament and of the Council
on ***in vitro*** diagnostic medical devices

Delegations will find in the Annex to this document the consolidated text of the annexes to the proposed Regulation on *in vitro* diagnostic medical devices prepared by the Luxembourg Presidency with a view to the finalisation of a General Approach, thus completing the partial General Approach reached at the meeting of the Council (EPSCO) on 19 June 2015.

New text compared to the Commission proposal is written in ***bold italics***. Deletions are marked by ~~strikethrough~~.

The text in this document was presented to delegations in documents WK 53/2015 as amended by WK 71/2015.

Proposal for a
REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
on *in vitro* diagnostic medical devices

ANNEXES

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GENERAL SAFETY AND PERFORMANCE REQUIREMENTS

I. GENERAL REQUIREMENTS

1. The devices shall achieve the performance intended by the manufacturer and be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose, ~~taking into account the generally acknowledged state of the art~~. They shall ***be safe and effective and shall*** not compromise, directly or indirectly, the clinical condition or the safety of the patients, or the safety or health of users or, where applicable, other persons, provided that any risks or limits to performance 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***.

This shall include:

- ~~reducing as far as possible the risk of error due to ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety), and~~
- ~~consideration of the technical knowledge, experience, education or training, and the medical and physical conditions of intended users (design for lay, professional, disabled or other users).~~

1aa. The requirements in this Annex to reduce risks as far as possible mean reduce risks as far as possible without adversely affecting the risk-benefit ratio.

- 1a. *The manufacturer shall establish, implement, document and maintain a risk management process.*

Risk management is a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic update. It requires a manufacturer to:

- (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 associated risks occurring during the intended use and during reasonably foreseeable misuse;*
- (d) eliminate or control these risks according to the requirements of clause 2;*
- (e) evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system on hazards and their frequency of occurrence, estimates of their associated risks, as well as on the overall risk, risk-benefit ratio and risk acceptability;*
- (f) based on the evaluation of the impact of information from the production phase or the post-market surveillance system if necessary amend control measures in line with the requirements of clause 2.*

2. The *risk control measures* ~~solutions~~ adopted by the manufacturer for the design and ~~manufacture~~ **construction** of the devices shall ~~must~~ conform to safety principles, taking account of the generally acknowledged state of the art. To reduce risks, the manufacturer shall manage the risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable. ~~The~~ ***In selecting the most appropriate solutions, the*** manufacturer shall apply the following principles in the priority order listed:
- ~~(a) identify known or foreseeable hazards and estimate the associated risks arising from the intended use and foreseeable misuse;~~
 - (b) eliminate ***or reduce*** risks as far as possible ***and appropriate*** through ~~inherently~~ safe design and ~~manufacture~~ **construction**;

- (c) *where appropriate, take* ~~reduce as far as possible the remaining risks by taking~~ adequate protection measures, including alarms, *if necessary, in relation to risks that cannot be eliminated*; and
- (d) provide *information for safety (warnings/precautions/contraindications) and, where appropriate* training to users.

The manufacturer shall ~~and/or~~ inform users of any residual risks.

2b. *In eliminating or reducing risks related to use error the manufacturer shall apply the following principles:*

- *reducing risks as far as possible related to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient and user safety), and*
- *consideration of the technical knowledge, experience, education, training, use environment and, where applicable, the medical and physical conditions of intended users (design for lay, professional, disabled or other users).*

3. The characteristics and performances of the 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. ~~When no lifetime is stated, the same applies for the lifetime reasonably to be expected of a device of that kind, having regard to the intended purpose and the anticipated use of the device.~~

4. *Devices* ~~The devices~~ shall be designed, manufactured and packaged in such a way that their characteristics and performance during their intended use will not be adversely affected by *during* transport and storage ~~conditions~~ (for example, fluctuations of temperature and humidity) taking account of the instructions and information provided by the manufacturer.

5. ~~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 of the intended performance of the device during normal conditions of use.

II. REQUIREMENTS REGARDING *PERFORMANCE, DESIGN AND CONSTRUCTION MANUFACTURING*

6. Performance characteristics

- 6.1. *Devices* ~~The devices~~ shall be designed and manufactured in such a way that *they are suitable for the purposes referred to in Article 2(2), as specified by the manufacturer, and suitable with regard to the performance taking account of the generally acknowledged state of the art* ~~the performance characteristics support the intended purpose, based on appropriate scientific and technical methods.~~ They shall achieve the performances, as stated by the manufacturer and in particular, where appropriate *applicable*:

- (a) the analytical performance, such as ~~accuracy (trueness and precision), bias,~~ 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, ~~repeatability, reproducibility,~~ 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*, ~~and~~ negative predictive value, likelihood ratio, expected values in normal ~~or~~ *and* affected populations.

- 6.2. The performance characteristics of the device need to be maintained during the lifetime of the device as indicated by the manufacturer.

6.3. Where the performance of devices depends on the use of calibrators and/or control materials, the metrological traceability of values assigned for a given analyte to such calibrators and/or control materials shall be assured through available and suitable reference measurement procedures and/or available and suitable reference materials of a higher metrological order. ~~The device shall be designed and manufactured to enable the user to provide measurement results in patient specimens metrologically traceable to available and suitable higher order~~ **Where available, metrological traceability of values assigned to calibrators and control materials shall be assured to certified** reference materials and/or reference measurement procedures following the instructions and information provided by the manufacturer.

6.4. **Characteristics and performances of the device must be specifically checked when they may be affected when used for the intended use under normal conditions:**

- **for devices for self-testing, performances obtained by laypersons;**
- **for devices for near-patient testing, performances obtained in relevant environments (for example, patient home, emergency units, ambulances).**

7. Chemical, physical and biological properties

7.1. **Devices** ~~The devices~~ shall be designed and manufactured in such a way as to ensure the characteristics and performance referred to in Chapter I 'General Requirements'.

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, and/or 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.

- 7.2. **Devices** ~~The 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 and to the duration and frequency of exposure.~~
- 7.3. **Devices** ~~The devices~~ shall be designed and manufactured in such a way as to reduce ~~as far as possible~~ **to a level as low as reasonably practicable** the risks posed by substances **or particles, including wear debris, degradation products, processing residues**, that may ~~leach or leak~~ **be released** from the device. Special attention shall be given to substances which are carcinogenic, mutagenic or toxic to reproduction, in accordance with Part 3 of Annex VI to 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 1907/2006¹, 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 of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)².
- 7.4. **Devices** ~~The devices~~ shall be designed and manufactured in such a way as to reduce as far as possible the risks posed by the unintentional ingress ~~or egress~~ of substances into ~~or from~~ the device, taking into account the device and the nature of the environment in which it is intended to be used.

¹ OJ L 353, 31.12.2008, p. 1.

² OJ L 136, 29.5.2007, p.3.

8. Infection and microbial contamination

8.1. **Devices** ~~The 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, professional or lay, or, where applicable, other persons.

The design shall:

(a) allow easy and safe handling;

~~and, where necessary~~

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

and, where necessary

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

8.2. **Devices** ~~The devices~~ labelled either as sterile or as having a *specific microbial* ~~special microbiological~~ state shall be designed, manufactured and packaged to ensure that they remain so when placed on the market, and remain so under the transport and storage conditions specified by the manufacturer, until the protective packaging is damaged or opened.

8.3. **Devices** ~~The devices~~ labelled either as sterile or as having a ~~special microbiological state~~ shall have been processed, manufactured, *packaged* and, if applicable, sterilised by appropriate validated methods.

8.4. **Devices** ~~The devices~~ intended to be sterilised shall be manufactured *and packaged* in appropriately *and* controlled (~~e.g. environmental~~) conditions *and facilities*.

8.5. Packaging systems for non-sterile devices shall maintain the integrity and cleanliness of the device indicated by the manufacturer and, if 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.

8.6. The labelling of the devices shall distinguish between identical or similar products placed on the market in both sterile and non-sterile condition *additional to the symbol used to indicate that a product is sterile.*

9. Devices incorporating materials of biological origin

9.1. Where the devices include tissues, cells and substances originating from animals *or humans*, *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 optimal safety for user, professional or lay, or other person.

In particular, safety with regard to ~~viruses~~ *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 may not apply to certain devices if the activity of the ~~virus~~ *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.

~~9.2. Where the devices include human tissues, cells or substances, the selection of sources, donors and/or substances of human origin, the processing, preservation, testing and handling of tissues, cells and substances of such origin shall be carried out so as to provide optimal safety for user, professional or lay, or other person.~~

~~In particular, safety with regard to viruses and other transmissible agents shall be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process. This may not apply to certain devices if the activity of the virus 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.~~

9.3. ~~Where the devices include cells or substances of microbial origin, the processing, preservation, testing and handling of cells and substances shall be carried out so as to provide optimal safety for user, professional or lay, or other person.~~

~~In particular, safety with regard to viruses and other transmissible agents shall be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process. This may not apply to certain devices if the activity of the virus 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.~~

10. ~~Interaction of devices with their environment~~ *Construction and environmental properties*

10.1. 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. ~~Connections which the user has to handle shall be designed and constructed in such a way as to minimise all possible risks from incorrect connection.~~

10.2. *Devices* ~~The devices~~ shall be designed and manufactured in such a way as to remove or reduce as far as possible and appropriate:

- (a) the risks of injury, ~~to user, professional or lay, or other person~~ in connection with their physical *features, including the volume/pressure ratio, dimensional* and *where appropriate* ergonomic features;
- (b) ~~the risks of use error due to the ergonomic features, human factors and the environment in which the device is intended to be used;~~
- (c) ~~the risks~~ connected with *any 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;

- (d) 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;
- (e) the risks associated with the possible negative interaction between software and the *IT* environment within which it operates and interacts;
- (f) the risks of accidental ingress of substances into the device;
- (g) the risk of incorrect identification of specimens, ***the risk of erroneous results due to confusing colour and/or numeric and/or character codings on specimen receptacles, removable parts and/or accessories used with In Vitro Diagnostic medical devices in order to perform the test or assay as intended;***
- (h) the risks of any foreseeable interference with other devices.

10.3. **Devices** ~~The 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 whose intended ~~purpose~~ ***use*** includes exposure to or use in association with flammable ***or explosive*** substances or substances which could cause combustion.

10.4. **Devices** ~~The devices~~ shall be designed and manufactured in such a way that adjustment, calibration, and maintenance, ~~where such is necessary to achieve the performances intended,~~ can be done safely ***and effectively***.

10.5. **Devices** ~~The devices~~ that are intended to be operated together with other devices or products shall be designed and manufactured in such as ***a*** way that the interoperability ***and compatibility*** ~~is~~ ***are*** reliable and safe.

10.6. **Devices** ~~The devices~~ shall be designed and manufactured in such a way as to facilitate the safe disposal of the device and/or ~~of any~~ ***related*** waste substances by the user, professional or lay, or other person. ***To that end, manufacturers shall investigate and test procedures and measures by which their devices can be safely disposed after use. These procedures shall be described in the instruction for use.***

10.7. 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 of~~ ***users and the environmental condition in which*** the devices ***are intended to be used***.

11. Devices with a measuring function

11.1. ***Devices*** ~~The devices~~ having a primary analytical measuring function shall be designed and manufactured in such a way as to provide ***appropriate analytical performance (Annex I, II 6.1 first indent)*** ~~sufficient accuracy, precision and stability of measurement within appropriate accuracy limits,~~ taking into account the intended purpose of the device ~~and of available and appropriate reference measurement procedures and materials.~~ ~~The accuracy limits shall be specified by the manufacturer.~~

11.2. The measurements made by devices with a measuring function and expressed in legal units shall conform to the provisions of Council Directive 80/181/EEC³.

12. Protection against radiation

12.1. ***Devices*** ~~The devices~~ shall be designed, manufactured and packaged in such a way that exposure of users, ~~professional or lay,~~ or other persons to the emitted radiation (intended, unintended, stray or scattered) is reduced as far as possible ***and appropriate, compatible with the intended purpose, whilst not restricting the application of appropriate specified levels for diagnostic purposes.***

12.2. When ~~the devices~~ are intended to emit ~~potentially hazardous, visible and/or invisible~~ ***ionizing and/or not 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.

³ OJ L 39, 15.2.1980.

12.3. The operating instructions for devices emitting radiation shall give detailed information as to the nature of the emitted radiation, means of protecting the user, and on ways of avoiding misuse and of ~~eliminating~~ *reducing* the risks inherent ~~in~~ *to* installation *as far as possible and appropriate*. *Information regarding the acceptance testing, the performance testing and the acceptance criteria shall also be specified, as well as the maintenance procedure.*

13. ~~Software incorporated in devices and standalone software~~ *Electronic programmable systems and devices that incorporate electronic programmable systems*

13.1. ~~The devices that incorporate~~ *Devices* ~~an electronic programmable systems, including software, or standalone software that are devices in themselves,~~ shall be designed to ensure repeatability, reliability and performance according to ~~their~~ *their* intended ~~purpose~~ *use*. In the event of a single fault condition, appropriate means shall be adopted to eliminate or reduce as far as possible ~~and appropriate~~ consequent risks *or impairment of performance*.

13.2. ~~For the devices that incorporate software or for standalone software that are devices in themselves,~~ the software shall be developed and manufactured according to the state of the art taking into account the principles of development life cycle, risk management, *including information security*, verification and validation.

13.3. ~~Software referred to in this Section that are 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 to level of light or noise).~~ *The manufacturer shall describe minimum requirements on hardware, IT networks characteristics and IT security measures, including protection against unauthorized access, necessary to run the software as intended.*

14. Devices connected to or equipped with an energy source

- 14.1. For ~~the~~ 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 and appropriate consequent risks.
- 14.2. *Devices* ~~The devices~~ where the safety of the patient depends on an internal power supply ~~in the device~~ shall be equipped with a means of determining the state of the power supply *and an appropriate warning or indication if, or if necessary before, the capacity of the power supply becomes critical.*
- 14.3. *Devices* ~~The 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 this or other devices or equipment in the intended environment.
- 14.4. *Devices* ~~The devices~~ shall be designed and manufactured in such a way as to provide an adequate level of intrinsic immunity to electromagnetic disturbance to enable them to operate as intended.
- 14.5. ~~The 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, professional or lay, 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.~~

15. Protection against mechanical and thermal risks

- 15.1. *Devices* ~~The devices~~ shall be designed and manufactured in such a way as to protect the user, professional or lay, or other person against mechanical risks.

15.2. **Devices** ~~The devices~~ shall be sufficiently stable under the foreseen operating conditions. They shall be suitable to withstand stresses inherent in 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.

15.3. 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.

15.4. **Devices** ~~The 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.

15.5. **Devices** ~~The 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.

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

15.7. Errors likely to be made when fitting or refitting, ~~or connecting or reconnecting,~~ certain parts before or during use which could be a source of risk ~~must~~ **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 ~~must~~ **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.

15.8. Accessible parts of ~~the~~ 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.

16. Protection against the risks posed by devices intended by ~~the manufacturer~~ for self-testing or near-patient testing

16.1. **Devices** ~~The 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.***

16.2. **Devices** ~~The devices~~ intended for self-testing or near-patient testing shall be designed and manufactured in such a way as to

- ensure that the device ~~is easy~~ **can be used safely and accurately** ~~to use~~ by the intended user at all stages of the procedure **if necessary after appropriate training and/or information**; and
- 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.

16.3. **Devices** ~~The devices~~ intended for self-testing and near-patient testing shall, where **feasible** ~~reasonably possible~~, include a procedure by which the intended user can:

- verify that, at the time of use, the device will perform as intended by the manufacturer; and
- be warned if the device has failed to provide a valid result.

III. REQUIREMENTS REGARDING INFORMATION SUPPLIED WITH THE DEVICE

17. Label and instructions for use

17.1. 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 communicate safety and performance related information to the user, ~~professional or lay~~, or other person, as appropriate. Such information may appear on the device itself, on the packaging or in the instructions for use, taking into account the following:

- (i) 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. ~~Some devices may include separate information for the professional user and the lay person.~~
- (ii) 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, ~~and/or~~ ***If individual full labelling of each unit is not practicable, the information shall be set out*** on the packaging of multiple devices.

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.

- (iii) In duly justified and exceptional cases instructions for use may not be needed or may be abbreviated if the device can be used safely and as intended by the manufacturer without any such instructions for use.

- (iv) Labels shall be provided in a human-readable format **and** ~~but~~ may be supplemented by machine-readable ~~forms~~ **information**, such as radio-frequency identification (RFID) or bar codes.
- (v) 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.
- (vi) Residual risks which are required to be communicated to the user and/or other person shall be included as limitations, contraindications, precautions or warnings in the information supplied by the manufacturer.
- (vii) Where appropriate, ~~this~~ **the** information **supplied by the manufacturer** ~~should~~ **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 CFS. In areas for which no standards or CFS exist, the symbols and colours shall be described in the documentation supplied with the device.
- (viii) 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 that Regulation shall be given in the instructions for use.
- (ix) 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 by the instructions for use.

17.2. Labelling ~~Information on the label~~

The label shall bear the following particulars *shall appear on the device or, where this is not practicable or appropriate, on the packaging*:

- (i) The name or trade name of the device;
- (ii) The details strictly necessary for the user to identify the device and, where it is not obvious for the user, the intended purpose of the device;
- (iii) The name, registered trade name or registered trade mark of the manufacturer and the address of his registered place of business ~~at which he can be contacted and his location be established~~;
- (*iiia*) ***The Single Registration Number of the manufacturer in accordance with Article 23a***;
- (iv) ~~For imported devices~~ ***If the manufacturer has his registered place of business outside the Union, the name and address, registered trade name or registered trade mark of the authorised representative established within the Union and the address of his registered place of business at which he can be contacted and his location be established and its Single Registration Number in accordance with Article 23a***;
- (v) An indication that the device is ~~for~~ ***an in vitro diagnostic use medical device, or if the device is a 'device for performance evaluation', an indication of that fact***;
- (vi) The batch code/lot number or the serial number of the device preceded by the word LOT or SERIAL NUMBER or an equivalent symbol, as appropriate;
- (vii) ~~Where applicable,~~ the unique device identification (UDI) ***carrier according to Article 24 and Annex V Part C***;
- (viii) An unambiguous indication of the date until when the device may be used safely, without degradation of performance, expressed at least as the year, the month and, where relevant, the day, in that order;

- (ix) Where there is no indication of the date until when it may be used safely, the **year date** of manufacture. This ~~year~~ **date** of manufacture may be included as part of the batch or serial number, provided the date is clearly identifiable;
- (x) Where relevant, an indication of the net quantity of contents, expressed in terms of weight or volume, numerical count, or any combination of these, or other terms which accurately reflect the contents of the package;
- (xi) An indication of any special storage and/or handling condition that applies;
- (xii) Where appropriate, an indication of the sterile state of the device and the sterilisation method, or a statement indicating any special microbiological state or state of cleanliness;
- (xiii) Warnings or precautions to be taken that need to be brought to the immediate attention of the user, ~~professional or lay~~, or 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**;
- (xiiiia) ***If the instructions for use are not provided in paper form in accordance with Section 17.1(v), a reference to their accessibility (or availability), and where applicable the website address where they can be consulted;***
- (xiv) Where applicable, any particular operating instructions;
- (xv) 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;
- (xvi) If the device is intended for self-testing or near-patient testing, an indication of that fact;
- (xviiia) ***Where rapid assays are not intended for self-testing or near-patient testing, the explicit exclusion hereof;***
- (~~xvii~~) ~~If the device is for performance evaluation only, an indication of that fact;~~

- (xviii) Where device kits include individual reagents and articles that ~~are~~ may be made available as separate devices, each of these devices shall comply with the labelling requirements contained in this Section **and with the requirements of this Regulation;**
- (xix) ~~The~~ ~~Wherever reasonable and practicable,~~ the devices and separate components shall be identified, where appropriate **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 must be set out on the device itself and/or, where appropriate, on the sales packaging. In addition, the label for devices intended for self-testing shall bear the following particulars:**
- (a) **The type of specimen(s) required to perform the test (e.g. blood, urine or saliva);**
 - (b) **Information on disease effects and prevalence;**
 - (c) **The need for additional materials for the test to function properly;**
 - (d) **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.**

17.2a. On the sterile packaging:

The following particulars shall appear on the sterile packaging:

- (a) **an indication permitting the sterile packaging to be recognized as such,**
- (b) **a declaration that the device is in a sterile condition,**
- (c) **the method of sterilization,**
- (d) **the name and address and Single Registration Number of the manufacturer,**
- (e) **a description of the device,**
- (f) **the month and year of manufacture,**
- (g) **an indication of the time limit for using the device safely,**
- (h) **an instruction to check the Instructions For Use for what to do if the sterile packaging is damaged etc.**

17.3. Information in the instructions for use

17.3.1. The instructions for use shall contain the following particulars:

- (i) The name or trade name of the device;
- (ia) ***The details strictly necessary for the user to uniquely identify the device;***
- (ii) The device's intended purpose:
 - what is detected and/or measured;
 - ~~its function (e.g. screening, monitoring, diagnosis or aid to diagnosis);~~
 - ~~the specific disorder, condition or risk factor of interest that it is intended to detect, define or differentiate~~ ***information that is intended to be provided in the context of:***
 - = ***a physiological or pathological state;***
 - = ***a congenital abnormality;***
 - = ***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;***
 - = ***where the device may be used for reasonably foreseeable purposes other than those intended by the manufacturer, the exclusion of such unintended purpose, if a higher classification for that unintended purpose is applicable, or for rapid assays not intended for self-testing or near-patient testing, the explicit exclusion hereof;***
 - whether it is automated or not;
 - whether it is qualitative, semi-quantitative or quantitative;
 - the type of specimen(s) required; and
 - where applicable, the testing population.
 - ***for companion diagnostics, the INN (International Non-proprietary Name) of the associated drug for which it is a companion test.***
- (iii) An indication that the device is ~~for~~ ***an in vitro diagnostic medical device use, or if the device is a 'device for performance evaluation' an indication of that fact;***
- (iv) The intended user, as appropriate (e.g. ***self-testing, near patient and laboratory professional use***, healthcare professionals, ~~lay person~~);

- (v) The test principle;
- (vi) A description of the reagents, calibrators and controls and any limitation upon their use (e.g. suitable for a dedicated instrument only);
- (via) ***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;***
- (vii) A list of materials provided and a list of special materials required but not provided;
- (viii) For devices intended for use ~~together with~~ ***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.
- (ix) An indication of any special storage (e.g. temperature, light, humidity, etc.) and/or handling conditions which apply;
- (x) 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;
- (xi) 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;

- (xii) Information that allows the user to be informed of any warnings, precautions, measures to be taken and limitations of use regarding the device. This information shall cover, where appropriate:
- 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;
 - warnings, precautions and/or measures to be taken in regards to 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;
 - warnings, precautions and/or measures to be taken in regards to the risks of interference posed by the reasonably foreseeable presence of the device during specific diagnostic investigations, evaluations, therapeutic treatment or other procedures (e.g. electromagnetic interference emitted by the device affecting other equipment);
 - precautions related to materials incorporated into the device that are carcinogenic, mutagenic or toxic, or that have endocrine disrupting properties or that could result in sensitisation or allergic reaction of the patient or user;
 - 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;
 - 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-sterilization. Information shall be provided to identify when the device should no longer be reused, e.g. signs of material degradation or the maximum number of allowable reuses.
- (xiii) Any warnings and/or precautions related to potentially infectious material that is included in the device;
- (xiv) Where relevant, requirements for special facilities (e.g. clean room environment) or special training (e.g. radiation safety), or particular qualifications of the device intended user;

- (xv) Conditions for collection, handling, and preparation of the specimen;
- (xvi) Details of any preparatory treatment or handling of the device before it is ready for use (e.g. sterilisation, final assembly, calibration, etc.) **for the device to be used as intended by the manufacturer;**
- (xvii) 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 preventative 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 of mitigating the risks encountered by persons involved in installing, calibrating or servicing devices.
- (xviii) Where **applicable** ~~relevant~~, recommendations for quality control procedures;
- (xix) The metrological traceability of values assigned to calibrators and ~~trueness-control~~ materials, including identification of applicable **applied** reference materials and/or reference measurement procedures of higher order, **information regarding batch to batch variation provided with relevant figures and units of measure;**
- (xx) Assay procedure including calculations and interpretation of results and where relevant if any confirmatory testing shall be considered, **information regarding batch to batch variation provided with relevant figures and units of measure ;**
- (xxi) Analytical performance characteristics, such as sensitivity, specificity, ~~and accuracy, repeatability, reproducibility,~~ **trueness (bias), precision (repeatability and reproducibility), accuracy (resulting from trueness and precision)**, limits of detection and measurement range, ~~including~~ (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;
- (xxia) **Clinical performance characteristics as defined in Chapter II Section 6.1. of this Annex;**

- (xxib) ***The mathematical approach upon which the calculation of the analytical result is made;***
- (xxii) Where relevant, clinical performance characteristics, such as ***threshold value***, diagnostic sensitivity and diagnostic specificity, ***positive and negative predictive value***;
- (xxiii) Where relevant, reference intervals ***in normal and affected populations***;
- (xxiv) 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;
- (xxv) 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:
- infection or microbial hazards (e.g. consumables contaminated with potentially infectious substances of human origin);
 - environmental hazards (e.g. batteries or materials that emit potentially hazardous levels of radiation);
 - physical hazards (e.g. explosion).
- (xxvi) The name, registered trade name or registered trade mark of the manufacturer and the address of his registered place of business at which he can be contacted and his location be established, together with a telephone number and/or fax number and/or website address to obtain technical assistance;
- (xxvii) 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***;
- (xxviii) ~~A notice to the user, professional or lay, that any serious incident that has occurred in relation to the device should be reported to the manufacturer and the competent authority of the Member State where the user and/or patient is established;~~

- (xxix) 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.*

In the case of the following devices, other than devices for performance evaluation, the instructions for use shall also contain the clinical evidence as presented in the clinical evidence report, referred to in Section 3 of Part A of Annex XII:

- (i) companion diagnostic intended to be used to assess the patient eligibility to a treatment with a specific medicinal product;*
- (ii) devices intended to be used in screening for or in the diagnosis of cancer;*
- (iii) devices intended for human genetic testing.*

17.3.2. In addition, the instructions for use for devices intended for self-testing ~~or near-patient testing~~ shall comply with the following principles:

- (i) 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 read the results;
- (ia) 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;*
- (ib) 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, taking into account the state of the art in medicine;*
- (ii) The results ~~need to~~ *shall* be expressed and presented in a way that is readily understood by the intended user;

- (iii) Information ~~needs to~~ **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 (e.g. age, gender, menstruation, infection, exercise, fasting, diet or medication);
- (iv) for devices intended for self-testing, 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 **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 (e.g. national helplines, websites, etc.)**;
- (v) 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.

TECHNICAL DOCUMENTATION

The technical documentation and, if applicable, the summary technical documentation (STED) to be drawn up by the manufacturer *shall be presented in a clear, organized, readily searchable and unequivocal way and* shall include in particular the following elements: *described in this Annex. The STED shall summarize the elements of the technical documentation.*

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 user*;
- (b) the UDI device identifier *and the Basic UDI device identifier* as referred to in item (i) of point (a) of Article 22(1) *and in Part C of annex V* attributed by the manufacturer to the device in question, as soon as identification of this device shall be based on a UDI system, or otherwise 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:
 - (i) what is detected and/or measured;
 - (ii) its function (e.g. screening, monitoring, diagnosis or aid to diagnosis);
 - (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.

- (d) the description of the principle of the assay method or ~~instrument~~ **the** principles of operation **of the instrument**;
- (da) **the determination of the regulatory status of the device, including the rationale for qualification as a device**;
- (e) the risk class of the device and **the justification of the applicable** classification rule(s) **applied** according to Annex VII;
- (f) 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:
- (g) the description of the specimen collection and transport materials provided with the device or descriptions of specifications recommended for use;
- (h) for instruments of automated assays: the description of the appropriate assay characteristics or dedicated assays;
- (i) for automated assays: a description of the appropriate instrumentation characteristics or dedicated instrumentation;
- (j) a description of any software to be used with the device;
- (k) a description or complete list of the various configurations/variants of the device that will be made available;
- (l) a description of the accessories, other *in vitro* diagnostic medical devices and other products, 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 manufacturer's previous generation(s) of the device, if such exist;
- (b) an overview of ~~the manufacturer's~~ **identified** similar devices available on the EU or international markets, if such exist.

2. INFORMATION SUPPLIED BY THE MANUFACTURER

- (a) a complete set of
 - the label(s) on the device and on its packaging (*single unit packaging, sales packaging, transport packaging in case of specific management conditions*), *in the languages accepted in the Member States where the device is envisaged to be sold*;
 - the instructions for use *in the languages accepted in the Member States where the device is envisaged to be sold*;
- (b) ~~a list of the language variants for the Member States where the device is envisaged to be marketed.~~

3. DESIGN AND MANUFACTURING INFORMATION

3.1. Design information

Information to allow ~~a general~~ *the* understanding of the design stages applied to the device.

This shall include:

- (a) the 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, the description of major subsystems, analytical technology (e.g. operating principles, control mechanisms), dedicated computer hardware and software;
- (c) for instruments and software, the overview of the entire system;
- (d) for ~~standalone~~ software, the description of the data interpretation methodology (i.e. algorithm);
- (e) for devices intended for self-testing or near-patient testing devices the 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 a general~~ understanding of the manufacturing processes such as production, assembly, final product testing, and packaging of the finished device. More detailed information ~~needs to~~ **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 *a demonstration of conformity with* ~~information regarding the solutions adopted to meet~~ the general safety and performance requirements laid down in Annex I, *applicable to the device and taking into account its intended purpose, including the justification, validation and verification of the solutions adopted to meet those requirements*. This ~~information may take the form of a checklist identifying~~ *demonstration shall include:*

- (a) the general safety and performance requirements that apply to the device and why others do not apply;
- (b) the method(s) used to demonstrate conformity with each applicable general safety and performance requirement;
- (c) the harmonised standards or **CTS CS** applied or other method(s) employed;
- (d) the precise identity of the controlled documents offering evidence of conformity with each harmonised standard, **CTS CS** or other method employed to demonstrate conformity with the general safety and performance requirements. This information shall incorporate a cross-reference to the location of such evidence within the full technical documentation and, if applicable, the summary technical documentation.

5. RISK/BENEFIT ANALYSIS AND RISK MANAGEMENT

The documentation shall contain ~~a summary of~~

- (a) the risk/benefit analysis referred to in Section 1 and 5 of Annex I; and
- (b) the solutions adopted and the results of the risk management referred to in Section 2 of Annex I.

6. PRODUCT VERIFICATION AND VALIDATION

The documentation shall contain the results *and critical analyses* of *all* verifications and validation ~~testing~~ *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

6.1.1. Specimen type

This section shall describe the different specimen types that can be used, including their stability (e.g. storage, ~~and~~ where applicable 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 (e.g. 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 assessment of the adequacy of the means selected to establish the trueness. Trueness measures apply to both quantitative and qualitative assays only when a reference standard or 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 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/agents on the assay, on the substance/agent type and concentration tested, specimen type, analyte test concentration, and results.

Interferents and cross reacting substances/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 (e.g. medicinal products);
- (b) substances ingested by the patient (e.g. alcohol, foods);
- (c) substances added during specimen preparation (e.g. preservatives, stabilisers);
- (d) substances encountered in specific specimens types (e.g. haemoglobin, lipids, bilirubin, proteins);
- (e) analytes of similar structure (e.g. precursors, metabolites) or medical conditions unrelated to the test condition including specimens negative for the assay but positive for a condition that may mimic the test condition.

6.1.2.4. Metrological traceability of calibrator and control material values

6.1.2.5. Measuring range of the assay

This section shall include information on the measuring range (linear and non-linear measuring systems) including the limit of detection and describe information on how these were established.

This information shall include a description of specimen type, number of specimen, number of replicates, and preparation including information on matrix, analyte levels and how levels were established. If applicable, a description of high dose hook effect and the data supporting the mitigation (e.g. 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, including:

- (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 e.g. Receiver Operator Characteristic (ROC) to generate results and if applicable, define grey-zone/equivocal zone.

6.1.3. *The Analytical Performance Report according to Annex XII.*

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

~~The~~ Where applicable, the documentation shall contain data on the clinical performance of the device *evaluation report, which includes the reports on the scientific validity, the analytical and the clinical performance, according to Annex XII, together with an assessment of these reports.*

The clinical evidence report *performance study documents* referred to in *Part A*, Section 3.2 of Annex XII 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 claimed shelf life. Testing shall be performed on at least three different lots manufactured under conditions that are essentially equivalent to routine production conditions (these lots do not need to be consecutive lots). Accelerated studies or extrapolated data from real time data are acceptable for initial shelf life claim but ~~need to~~ *shall* be followed up with real time stability studies.

Such detailed information shall describe:

- (a) the study report (including the protocol, number of lots, acceptance criteria and testing intervals);
- (b) when accelerated studies have been performed in anticipation of the real time studies, the method used for accelerated studies;
- (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 (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 describe:

- (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 to evaluate the tolerance of products to the anticipated shipping conditions.

Shipping studies can 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 used in the finished device. This information shall typically include the summary results of all verification, validation and testing performed in-house and as 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 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 respect 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 this combination including proof that it conforms to the general safety and performance requirements when connected to any such equipment having regard to the characteristics specified by the manufacturer.

TECHNICAL DOCUMENTATION ON POST-MARKET SURVEILLANCE

The technical documentation on post-market surveillance to be drawn up by the manufacturer in accordance with Section 0 of Chapter VII shall be presented in a clear, organized, readily searchable and unequivocal way and shall include in particular:

1.1. The post-market surveillance plan in accordance with Article 58b.

The manufacturer shall prove in a post-market surveillance plan that it complies with the obligation referred to in Article 58a.

(a) The post-market surveillance plan shall address the collection and utilization of available information, in particular:

- *information concerning serious incidents, including information from periodic safety update reports, and field safety corrective actions,*
- *records referring to non-serious incidents and data on any undesirable side effects,*
- *information from trends reporting,*
- *relevant specialist or technical literature, databases and/or registers,*
- *information, including feedbacks and complaints, provided by users, distributors and importers,*
- *publicly available information about similar medical devices.*

(b) The post-market surveillance plan shall include at least:

- *a proactive and systematic process to collect any information referred to in point (a). The process shall allow a correct characterization of the performance of the devices also comparing the device with the 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 risk benefit analysis and of the risk management as referred to in Chapter I of Annex I;*
- *effective and appropriate methods and tools to investigate complaints or market experiences collected in the field;*
- *methods and protocols to manage the events subject to trend report as provided in Article 59a, including those 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 Article 58a, 58b and 58c;*
- *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;*
- *a post-market performance follow-up plan according to Part B of Annex XII, or a justification why a post-market performance follow-up is not deemed necessary or appropriate.*

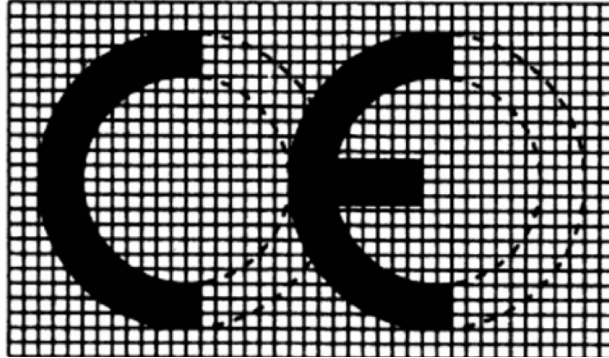
1.3. The periodic safety update report referred to in Article 58c.

EU DECLARATION OF CONFORMITY

1. Name, registered trade name or registered trade mark, **and single registration number referred to in Article 23a** of the manufacturer and, if applicable, his 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 declaration of conformity is issued under the sole responsibility of the manufacturer;
3. The **basic UDI-DI and the** UDI device identifier as referred to in item (i) of point (a) of Article 22(1) **and in Part C of Annex V** as soon as identification of the device that is covered by the declaration shall be based on a UDI system;
4. Product ~~or~~ **and** trade name, product code, catalogue number or other unambiguous reference allowing identification and traceability of the device that is covered by the declaration (it may include a photograph, where appropriate), **including its intended purpose**. Except for the product or trade name, the information allowing identification and traceability may be provided by the device identifier referred to in point 3;
5. Risk class of the device in accordance with the rules set out in Annex VII;
6. A statement that the device that is covered by the present declaration is in conformity with this Regulation and, if applicable, with other relevant Union legislation that make provision for the issuing of a declaration of conformity;
7. References to the relevant harmonised standards or ~~CTS CS~~ used in relation to which conformity is declared;
8. Where applicable, name and identification number of the notified body, description of the conformity assessment procedure performed and identification of the certificate(s) issued;
9. Where applicable, additional information;
10. Place and date of issue, name and function of the person who signs as well as indication for and on behalf of whom he/she signs, signature.

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.

**INFORMATION TO BE SUBMITTED WITH THE REGISTRATION OF
DEVICES AND ECONOMIC OPERATORS IN ACCORDANCE WITH
ARTICLE 23a**

AND

**CORE DATA ELEMENTS TO BE PROVIDED TO OF THE UDI DATA BASE
TOGETHER WITH THE DEVICE IDENTIFIER IN ACCORDANCE WITH
ARTICLE 22a**

AND

THE EUROPEAN UNIQUE DEVICE IDENTIFICATION SYSTEM

Part A

Information to be submitted with the registration of devices in accordance with Article 23a

Manufacturers or, when applicable, authorised representatives, and, when applicable, importers shall submit the following 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 related to the economic operator

- 1.1.** economic operator's role (manufacturer, authorised representative, or importer),
- 1.2.** name, address and contact details of the economic operator,
- 1.3.** where submission of information is completed by another person on behalf of any of the economic operators mentioned under point 1, the name, address and contact details of this person,
 - 1.3a.** *name address and contact details of the person responsible for regulatory compliance (qualified person) according to article 13,*
 - 1.3b.** *risk class of the device (if applicable the highest from the portfolio of the manufacturer).*

2. *Information related to the devices*

- 2.4. UDI device identifier, or where identification of the device is not yet based on a UDI system, the data elements laid down in points 5 to 18 of Part B of this Annex,
- 2.5. type, number and expiry date of certificate and name or identification number of the notified body that has issued the certificate (and link to the information on the certificate entered by the notified body in the electronic system on certificates),
- 2.6. Member State where the device shall or has been placed on the market in the Union,
- 2.7. in case of devices classified as classes B, C or D: Member States where the device is or shall be made available,
- ~~8. in case of imported device: country of origin,~~
- 2.9. presence of tissues, cells or substances of human origin (y/n),
- 2.10. presence of tissues, cells or substances of animal origin (y/n),
- 2.11. presence of cells or substances of microbial origin (y/n),
- 2.12. risk class of the device according to the rules set out in Annex VII,
- 2.13. where applicable, single identification number of the interventional clinical performance study and other clinical performance study involving risks for the subjects of the study conducted in relation to the device (or link to the clinical performance study registration in the electronic system regarding clinical performance studies),
- 2.14. in case of devices designed and manufactured by another legal or natural person as referred in Article 8(10), the name, address and contact details of that legal or natural person,
- 2.15. in case of devices classified as class C or D, the summary of safety and performance,
- 2.16. status of the device (on the market, no ***more placed on the market*** ~~longer manufactured, withdrawn from the market,~~ recalled, ***Field Safety Corrective Action initiated***),
- 2.17. indication when the device is a 'new' device.
A device shall be considered as '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.
- 2.18. Indication if the device is intended for self-testing or near-patient testing.

Part B

Data elements of the UDI device identifier in accordance with Article 22a

The *manufacturer shall provide to the UDI data base the UDI device identifier (UDI-DI) shall provide access to and* to the following information related to the manufacturer and the device model:

1. quantity per package configuration,
2. if applicable, *the Basic UDI-DI according to Article 22(4b) and alternative or* additional identifier(s),
3. the way how the device production is controlled (expiration date or manufacturing date, lot or batch number, serialisation number),
4. if applicable, the 'unit of use' device identifier (when a UDI is not assigned to the device at the level of its 'unit of use', a 'unit of use' device identifier shall be assigned to associate the use of a device with a patient),
5. name and address of the manufacturer (as indicated on the label),
- 5a. the single registration number according to Article 23a(2),**
6. if applicable, name and address of the authorised representative (as indicated on the label),
7. ~~Global Medical Device Nomenclature (GMDN)~~ code *according to Article 21a or* internationally recognised nomenclature code,
- 7a. risk class of the device,**
8. if applicable, trade/brand name,
9. if applicable, device model, reference, or catalogue number,
10. additional product description (optional),
11. if applicable, storage and/or handling conditions (as indicated on the label or in the instructions for use),
12. if applicable, additional trade names of the device,
13. labelled as single use device (y/n),
14. if applicable, restricted number of reuses,
15. device packaged sterile (y/n),
16. need for sterilisation before use (y/n),
17. URL for additional information, e.g. electronic instructions for use (optional),

18. if applicable, critical warnings or contraindications,
19. *status of the device on the market (choice box, ~~stop of placing~~ no more placed on the market, recalled, Field Safety Action initiated).*

PART C

The European Unique Device Identification System

1. Definitions

Automatic Identification and Data Capture (hereinafter 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 shall be referenced in relevant certificates and declarations of conformity. In instances when a UDI is not labelled at the level of the device unit of use (e.g. several units contained in a plastic bag) it is also the purpose of the Basic UDI DI to associate the use of a device to/on a patient to data related to that patient.

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 to provide an intended use or purpose as a device. The combination of items may be modified, adjusted or customized to meet a customer need.

Device Identifier (hereinafter 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 (hereinafter HRI)

Human Readable Interpretation is a legible interpretation of the data characters encoded in the UDI Carrier.

Packaging levels

Packaging levels means the various levels of device packages that contain a fixed quantity of devices, e.g. each, carton, or case.

Production Identifier (hereinafter UDI-PI)

The Production Identifier is a numeric or alphanumeric code that identifies the unit of device production.

The different types of Production Identifier(s) include serial number, lot/batch number, Software identification and/or manufacturing and/or expiration date.

Radio Frequency Identification (hereinafter 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

Shipping container is a container where the traceability is controlled by a process specific to logistics systems.

Unique Device Identification

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.

Note: The word "Unique" does not imply serialization of individual production units.

UDI Carrier

The UDI Carrier is the means to convey the UDI by using AIDC and, if applicable, its HRI.

Note: Carriers ~~can~~ include, inter alia, ID/linear bar code, 2D/Matrix bar code, RFID.

UDI database

The UDI database contains identifying information and other elements associated with the specific device.

2. UDI system - General requirements

- 2.1. The marking of the UDI is an additional requirement – it does not replace any other marking or labelling requirements described in Annex I of this regulation.***
- 2.2. The manufacturer shall create and maintain unique UDIs on his devices.***
- 2.3. Only the manufacturer may establish the UDI on the device or its packaging.***
- 2.4. Only coding standards offered by assigning entities designated by the European Commission according to article 22(2) may be used by the manufacturers.***

3. The UDI

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

- 3.2. *Shipping containers shall be exempted. As an example, UDI is not required on a logistics unit; when a healthcare provider orders multiple devices using the UDI or model number of individual devices and the manufacturer places these devices in a container for shipping or to protect the individually packaged devices, the container (logistics unit) is not subject to UDI requirements.*
- 3.3. *The UDI shall contains two parts: an UDI-DI and an UDI-PI.*
- 3.4. *The UDI-DI shall be unique at all levels of device packaging.*
- 3.5. *If a lot number, serial number, software identification or expiration date appears on the label, they 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 ~~should~~ shall be used as the UDI-PI.*
- 3.7. *Each component that is considered a device and is commercially available on its own ~~needs~~ shall be assigned a separate UDI unless the components are part of a configurable device that is marked with its own UDI.*
- 3.8. *Kits shall be assigned and bear their own UDI.*
- 3.9. *The manufacturer shall assigns the UDI to a device following the relevant coding standard.*
- 3.10. *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 require a new UDI-DI:*
- (a) Brand Name or Trade name,*
 - (b) Device version or model,*
 - (d) Labelled as single use,*
 - (e) Packaged sterile,*
 - (f) Need for sterilization before use,*
 - (g) Quantity of devices provided in a package,*
 - (h) Critical warnings or contraindications.*
- 3.12. *Manufacturers who repackages or relabels devices with their own label shall retain record of the Original Equipment Manufacturer's (OEM) UDI.*

4. UDI Carrier

- 4.1. The UDI Carrier (AIDC and HRI representation of the UDI) shall be placed on the label ~~or~~ and on all higher levels of device packaging. Higher levels do not include shipping containers.**
- 4.2. In case of significant space constraints on the unit of use package the UDI carrier may be placed on the next higher package level.**
- 4.3. For single use devices of class A and B packaged and labelled individually the UDI Carrier shall not be required to appear on the package 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 (home healthcare settings) to the higher level of device packaging, the UDI shall be placed on the package.**
- 4.4. For devices exclusively intended for retail Point of Sale (POS) the Production Identifiers in AIDC shall not be required to appear on the point of sale package.**
- 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 of healthcare facilities such as devices for home care, the HRI shall however appear on the label even if this means that there is no space for the ~~over~~ AIDC.**
- 4.8. The HRI format shall follow the rules of the UDI code issuing organization.**
- 4.9. If the manufacturer is using RFID technology, a linear or 2D bar code according to the standard provided by the assigning 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 of 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 next use for the intended lifetime of the device.**

- 4.11. *The UDI Carrier shall be readable during normal use and throughout the intended life of the device.*
- 4.12. *If the UDI Carrier is readily readable or scannable through the device's package, then the placing of the UDI Carrier on the package shall not be required.*
- 4.13. *A single finished device made up of multiple parts that must be assembled before first use may bear the UDI Carrier on only one part.*
- 4.14. *The UDI Carrier shall be placed so that the AIDC can be accessed during normal operation or storage.*
- 4.15. *The bar code carrier(s) that include(s) UDI data identifiers "UDI-DI" and "UDI-PI" may also include essential data for the device to operate or other data.*
5. *The UDI database - General principles of the UDI database*
- 5.1. *The UDI database shall support the use of all core UDI database data elements.*
- 5.3. *The manufacturer ~~is~~ shall be responsible for the initial submission and updates ~~to~~ of the identifying information and other device data elements in the UDI database.*
- 5.4. *Appropriate methods/procedures for validation of the provided data shall be implemented.*
- 5.5. *The manufacturers shall periodically reconfirm all the data relevant to devices he has placed on the market, except for devices that are no more available on the market.*
- 5.7. *The presence of the device UDI-DI in the UDI database does not mean that the device is in conformity with this Regulation.*
- 5.8. *The database shall allow for the linking of all the packaging levels of the device.*
- 5.9. *The data for new UDI-DI shall be available at the time device is placed on the market.*
- 5.10. *Manufacturers shall update the relevant UDI database record within 30 days when a change is made to an element that does NOT require a new UDI-DI.*
- 5.11. *The UDI database shall use internationally accepted standards for data submission and updates. Additional submission means may, however, also be accommodated.*
- 5.12. *The core elements are the minimum elements needed to identify a device throughout its distribution and use.*

5.13. The design of the UDI database shall support the languages required in the Member States where the device is placed on the market. The use of free-text fields shall, however, be minimized in order to reduce translations.

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

6. Rules for specific device types

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

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

6.2.2. The PI characteristics (e.g. lot or serial number) shall be defined by the manufacturer.

6.5. In vitro diagnostic Medical Device Software

6.5.1. UDI Assignment Criteria

The UDI shall be assigned at the system level of the Software. Only software which are commercially available on their own and software which are medical devices in themselves, shall be subject to this requirement.

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

6.5.1a. A new UDI-DI shall be required whenever there is a modification that changes:

- (a) the original performance and effectiveness,**
- (b) the safety or the intended use of the Software.**
- (c) interpretation of data.**

These changes may include new or modified algorithms, database structures, operating platform, architecture or new user interfaces or new channels for interoperability.

6.5.1b. *The following changes of a Software shall require only a new UDI-PI (not a new UDI-DI):*

Minor Software revisions shall be identified with a new UDI-PI;

Minor Software revisions are generally associated with bug fixes, usability enhancements (not for safety purpose), security patches or operating efficiency.

Minor revisions shall be identified by manufacturer-specific identification.

6.5.2. *UDI Placement Criteria for Software*

- (a) When the Software is delivered on a physical medium, e.g. CD or DVD, each package 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 must be identical to the UDI assigned to the system level Software.*
- (b) The UDI shall be provided on a readily accessible screen ~~by~~ for the user in an easily-readable plain-text format (e.g. an “about” file or included on the start-up screen).*
- (c) Software lacking a user interface (e.g. middleware for image conversion) ~~must~~ shall be capable of transmitting the UDI through an Application Programming Interface (API).*
- (d) Only the human readable portion of the UDI ~~is~~ shall be required in electronic displays of the Software. The UDI AIDC marking ~~needs~~ shall not be required ~~used~~ in the electronic displays, e.g. about menu, splash screen, etc.*
- (e) The human readable format of the UDI for the Software ~~should~~ shall include the Application Identifiers (AI) of the used standard of the assigning entities, to assist the user in identifying the UDI and determining which standard is being used to create the UDI.*

MINIMUM REQUIREMENTS TO BE MET BY NOTIFIED BODIES**1. ORGANISATIONAL AND GENERAL REQUIREMENTS****1.1. Legal status and organisational structure**

- 1.1.1. A 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, and shall have full documentation of its legal personality and status. This 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 this organisation as well as its organisational structure and governance, and the relationship with the notified body shall be clearly documented. *In this instance, the requirements of Section 1.2 of this Annex are applicable to both the notified body and the organisation to which it belongs.*
- 1.1.3. If the 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 according to this Regulation are subject to the applicable requirements of this Regulation.*
- 1.1.4. The organisational structure, *allocation* ~~distribution~~ of responsibilities, *reporting lines* and operation of the notified body shall be such that it assures confidence in the performance and results of the conformity assessment activities conducted.

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* ~~with~~ influence upon the performance and results of the conformity assessment activities ~~shall be clearly documented.~~

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

- *the provision of adequate resources for conformity assessment activities;*
- *the development of procedures and policies for the operation of the notified body;*
- *the supervision of implementation of the procedures, policies and quality management systems;*
- *the supervision of the notified body's finances;*
- *the activities and decisions taken by the notified body, including contractual agreements;*
- *the delegation of authority to personnel and/or committees, where necessary, for the performance of defined activities ; and*
- *the interaction with the national 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 product 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 product as well as of any competitors of the manufacturer.

This does not preclude 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 ~~have~~ **document and implement a structure and** procedures ~~in place that effectively ensure~~ **for safeguarding impartiality and for promoting and applying the principles of impartiality throughout its organisation, personnel and assessment activities. These procedures shall allow for the** identification, investigation and resolution of any case in which a conflict of interests may arise including involvement in consultancy services in the field of *in vitro diagnostic* medical 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
- be the designer, manufacturer, supplier, installer, purchaser, owner, ~~user~~ or maintainer of the products **which they assess**, nor the authorised representative of any of those parties. This shall not preclude the purchase and use of assessed products that are necessary for the operations of the notified body (~~e.g. measuring equipment~~), the conduct of the conformity assessment or the use of such products for personal purposes;
 - be ~~directly~~ involved in the design, manufacture or construction, the marketing, installation, **and** use or maintenance of ~~the~~ **those** products **for** which they **are designated** assess, **nor** represent the parties engaged in those activities. They shall not engage in any activity that may conflict with their independence of judgement or integrity in relation to conformity assessment activities for which they are notified;
 - 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, his authorised representative, a supplier or a commercial competitor as regards the design, construction, marketing or maintenance of the products or processes under assessment.
 - **be linked to any organisation which itself provides consultancy services as referred to in the previous indent.** This does not preclude general training activities relating to medical device regulations or related standards that are not client specific.

- 1.2.3a. *Involvement in consultancy services in the field of in vitro diagnostic medical 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 according to criteria set out in this Annex. Personnel who were former employees or provided consultancy services in the field of in vitro diagnostic medical devices for a 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 3 years.***
- 1.2.4. The impartiality of the notified bodies, of their top level management and of the assessment personnel shall be guaranteed. The remuneration of the top level management and assessment personnel of a notified body shall not depend on the results of the assessments.
- 1.2.5. 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 national authority responsible for notified bodies and/or competent authority and, on the other hand, the notified body.
- 1.2.6. 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 objectivity of its conformity assessment activities.
- 1.2.7. 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 by [Commission Recommendation 2003/361/EC](#) ***in relation to fees***.
- 1.2.8. The requirements of this section in no way preclude exchanges of technical information and regulatory guidance between a notified body and a manufacturer seeking their conformity assessment.

1.3. Confidentiality

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

1.3.2. The personnel of a notified body shall observe professional secrecy with regard to all information obtained in carrying out their tasks under this Regulation ***or any provision of national law giving effect to it***, except in relation to the national authorities responsible for notified bodies, competent authorities ***for in vitro diagnostic medical devices in the Member States*** or the Commission. Proprietary rights shall be protected. To this end, the notified body shall have documented procedures in place.

1.4. Liability

1.4.1. The notified body shall take out appropriate liability insurance ~~that corresponds to the conformity assessment activities for which it is notified, including the possible suspension, restriction or withdrawal of certificates, and the geographic scope of its activities~~, unless liability is assumed by the State in accordance with national law, or the Member State itself is directly responsible for the 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 sustainable economic viability, taking in to account 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 the relevant standardisation activities and the activities of the notified body coordination group 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.

1.6.1a. The notified body shall take into consideration guidance and best practice documents.

~~1.6.2. The notified body shall adhere to a code of conduct, addressing among other things, ethical business practices for notified bodies in the field of *in vitro* diagnostic medical devices that is accepted by the national authorities responsible for notified bodies. The code of conduct shall provide for a mechanism of monitoring and verification of its implementation by notified bodies.~~

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 capable of supporting and demonstrating the consistent achievement of the requirements of this Regulation.

- 2.2. The quality management system of the notified body shall at least address the following:
- ***management system structure and documentation, including policies and objectives for its activities;***
 - policies for assignment of personnel to activities and their responsibilities,
 - ***assessment and*** decision-making process in accordance with the tasks, responsibilities and role of the top-level management and other notified body personnel;
 - ***planning, conducting, evaluating and, if necessary, adapting its conformity assessment procedures;***
 - control of documents;
 - control of records;
 - management review;
 - internal audits;
 - corrective and preventive actions;
 - complaints and appeals.

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

2.3. ***The notified body top management shall ensure that the quality management system is fully understood, implemented and maintained throughout the notified body organisation including subsidiaries and subcontractors being involved in conformity assessment activities according 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. The commitment shall consider 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 to confidentiality, independence and impartiality principles.***

3. RESOURCE REQUIREMENTS

3.1. General

3.1.1. A notified body shall be capable of carrying out all the tasks assigned to it by this Regulation with the highest degree of professional integrity and the requisite ~~technical~~ 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, it shall have the necessary personnel and ~~shall~~ possess or have access to all equipment, ~~and~~ facilities **and competence** needed to perform properly the technical, **scientific** and administrative tasks entailed in the conformity assessment activities in relation to which it has been ~~notified~~ **designated**.

~~This presupposes the availability within its organisation of sufficient scientific personnel who possess experience and knowledge sufficient to assess the medical functionality and performance of devices for which it has been notified, having regard to the requirements of this Regulation and, in particular, those set out in Annex I.~~

~~3.1.2.~~ **At This presupposes at** all times and for each conformity assessment procedure and each kind or category of products in relation to which it has been ~~notified~~ **designated, that the** a notified body **has** ~~shall have~~ **permanent availability of** ~~within its organisation the necessary~~ **sufficient** administrative, technical and scientific personnel **who possess with** technical knowledge and sufficient and appropriate experience **and knowledge** relating to **the relevant in vitro diagnostic medical devices and the corresponding technologies. These shall be sufficient to ensure that the notified body can** perform the conformity assessment tasks, including the assessment of ~~clinical data~~ **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 specific notified body's cumulative competence must enable it to assess the specific devices for which it is designated. The notified body must have sufficient internal competence to critically evaluate assessments conducted by external expertise. Specific tasks which a notified body cannot subcontract are outlined in Section 4.2 of this Annex.

Personnel involved in the management of the operation of the notified body's conformity assessment activities for devices shall have appropriate knowledge to set up and operate a system for the selection of the assessment and verification staff, verification of their competence, authorisation for and allocation of their tasks, their initial and ongoing training, their instruction and monitoring to ensure that personnel who administer 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 having overall responsibility for all conformity assessment activities in relation to in vitro diagnostic medical devices.

3.1.2a. *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 the limits of the duties, responsibilities and authorities in relation ~~of~~ *to* the personnel, ***including any subcontractors and external experts*** involved in conformity assessment activities and inform ~~the~~ ***these*** personnel ***accordingly*** ~~concerned about it.~~

3.2. Qualification criteria in relation to personnel

- 3.2.1. The **Notified Body** ~~notified body~~ shall establish and document qualification criteria and procedures for selection and authorisation of persons involved in conformity assessment activities (knowledge, experience and other competence required) and the required training (initial and ongoing training). The qualification criteria shall address the various functions within the conformity assessment process (e.g. auditing, product evaluation/testing, **technical documentation** ~~design dossier/file~~ review, decision-making, **batch release**) as well as the devices, technologies and areas (*e.g. biocompatibility, sterilisation, self and near patient-testing, companion diagnostics, performance evaluation*) covered by the scope of designation.
- 3.2.2. The qualification criteria 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 31, providing 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 ~~biocompatibility aspects~~ **biological safety**, ~~clinical~~ **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 ~~and the personnel with overall responsibility for the final review and decision-making on certification~~ shall be employed by the notified body itself and shall not be subcontracted. ~~This personnel altogether~~ **They** shall have proven knowledge and experience in the following:
- Union *in vitro* diagnostic medical devices legislation and relevant guidance documents;
 - the conformity assessment procedures in accordance with this Regulation;
 - a broad base of *in vitro* diagnostic medical device technologies, ~~the *in vitro* diagnostic medical device industry~~ and the design and manufacture of *in vitro* diagnostic medical devices;
 - the notified body's quality management system ~~and~~, related procedures **and the required qualification criteria;**
 - ~~the types of qualifications (knowledge, experience and other competence) required for carrying out conformity assessments in relation to *in vitro* diagnostic medical devices as well as the relevant qualification criteria;~~
 - training relevant to personnel involved in conformity assessment activities in relation to *in vitro* diagnostic medical devices;
 - ~~the ability to draw up certificates, records and reports demonstrating that the conformity assessments have been appropriately carried out.~~

3.2.4. ~~Notified bodies~~ **The notified body** shall have available personnel with **relevant** clinical expertise. ~~This~~ **These** personnel shall be integrated **throughout** in the notified body's **assessment and** decision-making process in ~~a steady way~~ in order to:

- identify when specialist input is required for the assessment of the ~~clinical~~ **performance** evaluation conducted by the manufacturer and identify appropriately qualified experts;
- appropriately train external clinical experts in the relevant requirements of **regulation** ~~this Regulation, CS, guidance delegated and/or implementing acts, harmonised standards, and CTS and guidance documents~~ and ensure that the external clinical experts are fully aware of the context and implication of their assessment and advice provided;
- be able to ~~discuss~~ **review and scientifically challenge** the clinical data contained within the manufacturer's ~~clinical~~ **performance** evaluation, **and with the manufacturer and with external clinical experts** and to appropriately guide external clinical experts in the assessment of the ~~clinical~~ **performance** evaluation **presented by the manufacturer**;
- be able to scientifically **evaluate and, if necessary, challenge** the ~~clinical~~ **performance evaluation** ~~data~~ presented, and the results of the external clinical experts' assessment of the manufacturer's ~~clinical~~ **performance** evaluation;
- be able to ascertain the comparability and consistency of the ~~clinical~~ assessments **of performance evaluation** conducted by clinical experts;
- be able to make an ~~objective clinical judgement about the~~ assessment of the manufacturer's ~~clinical~~ **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.

3.2.5. The personnel (**Product Reviewers**) responsible for carrying out product related review (e.g. ~~design dossier review~~, technical documentation review or type examination including aspects such as ~~clinical~~ **performance** evaluation, **biological safety**, sterilisation, software validation) shall have the following proven qualifications:

- successful completion of a university or a technical college degree or equivalent qualification in relevant studies, e.g. medicine, **pharmacy**, ~~natural science or engineering~~ **or other relevant sciences**;
- four years professional experience in the field of healthcare products or related sectors (e.g. industry, audit, healthcare, research experience) whilst two years of this experience shall be in the design, manufacture, testing or use of the device or technology to be assessed or related to the scientific aspects to be assessed;
- ~~appropriate~~ knowledge of **the in vitro diagnostic medical device legislation, including** the general safety and performance requirements laid down in Annex I as well as ~~related delegated and/or implementing acts~~;
- **appropriate knowledge and experience of relevant** harmonised standards, CTS and guidance documents;
- appropriate knowledge and experience of risk management and related *in vitro* diagnostic medical 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 VIII to X, in particular of those aspects for which they are authorised, and adequate authority to carry 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 (*Site Auditors*) responsible for carrying out audits of the manufacturer's quality management system shall have the following proven qualifications:

- successful completion of a university or a technical college degree or equivalent qualification in relevant studies, e.g. medicine, *pharmacy*, ~~natural sciences or~~ engineering *or other relevant sciences*;
- four years professional experience in the field of healthcare products or related sectors (e.g. industry, audit, healthcare, research experience) whilst two years of this experience shall be in the area of quality management;
- appropriate knowledge of the *in vitro* diagnostic medical devices legislation as well as related ~~delegated and/or implementing acts~~, harmonised standards, CTS and guidance documents;
- appropriate knowledge and experience of risk management and related *in vitro* diagnostic medical device standards and guidance documents;
- appropriate knowledge of quality management systems and related *in vitro diagnostic medical devices* standards and guidance documents;
- appropriate knowledge and experience of the conformity assessment procedures laid down in Annexes VIII to X, in particular of those aspects for which they are authorised, and adequate authority to carry out ~~the~~ *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 review and decision-making on certification shall be employee of the notified body and not be external expert or be subcontracted. These personnel, together, shall have proven knowledge and comprehensive experience of the following:*

- *the in vitro diagnostic medical devices legislation and relevant guidance documents;*
- *the in vitro diagnostic medical device conformity assessments relevant to this Regulation;*
- *the types of qualifications, experience and expertise relevant to medical device conformity assessment;*
- *a broad base of in vitro diagnostic medical device technologies, including sufficient experience of the conformity assessment of the devices being reviewed for final certification, the in vitro diagnostic medical device industry and the design and manufacture of devices;*
- *the notified body's quality system, related procedures and the required qualification criteria;*
- *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 process in place to fully document the qualification of each 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 ~~appropriately~~ justify **to the national authority responsible for notified bodies** the authorisation of ~~these~~ **this** personnel to carry out specific conformity assessment activities.

- 3.3.2. For **all of** its personnel referred to in Sections 3.2.3. to 3.2.67., the notified body shall establish and maintain up to date:
- a matrix detailing the **authorisations and** responsibilities of the personnel in respect of the conformity assessment activities;
 - records demonstrating 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. Without prejudice to the limitations emanating from Section 3.2., notified bodies may subcontract **certain** clearly defined **component** parts of ~~the a~~ conformity assessment ~~activities~~ **activity**.

The subcontracting of the auditing of quality management systems or of product related reviews as a whole is not allowed, **but nevertheless these activities can be conducted by subcontractors and external experts working on behalf of the notified body. The notified body retains the full responsibility for being able to produce appropriate evidence of the competence of subcontractors and experts to fulfil their specific tasks, retains responsibility for making a decision based on a subcontractor's assessment and full responsibility for the work conducted by subcontractors and experts on its behalf. The following activities may not be subcontracted by the notified body:**

- **review of the qualification and the monitoring of the performance of external experts;**
- **auditing and certification activities 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 this.***

Any subcontracting or consultation of external ***personnel*** ~~experts~~ shall be properly documented and ***shall*** be subject to a ***direct*** written agreement covering, among others, confidentiality and conflict of interests. ***The notified body shall take full responsibility for the tasks performed by subcontractors.***

3.4.3. Where subcontractors or external experts are used in the context of the conformity assessment, ***in particular regarding novel in vitro diagnostic medical devices or technologies***, the notified body shall have adequate own competence in each product area for which it is designated to lead the ***overall*** conformity assessment, to verify the appropriateness and validity of expert opinions and make the decision on the certification.

~~3.4.4. The notified body shall establish procedures for assessing and monitoring the competence of all subcontractors and external experts used.~~

3.5. Monitoring of competences ~~and~~, training and exchange of experience

3.5.1. The notified body shall ~~appropriately monitor the satisfactory~~ *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* the conformity assessment activities ~~by its personnel~~.

3.5.2. It shall review *at regular intervals*, the competence of its personnel, ~~and~~ identify training needs *and draw up a training plan* ~~in order~~ to maintain the required level of qualification and knowledge *of individual personnel. This review shall as a minimum, verify that personnel:*

- *are aware of the current in vitro diagnostic medical device Regulation, relevant harmonised standards, CS, guidance documents and the results of the coordination activities according to Section 1.6 of this Annex;*
- *take part in the internal exchange of experience and the continuous training and education programme according to Section 3.1.2a.*

4. PROCESS REQUIREMENTS

4.1. ~~The notified body's decision-making process shall be clearly documented, including the process for the issue, suspension, reinstatement, withdrawal or refusal of conformity assessment certificates, their modification or restriction and the issue of supplements.~~

4.2. *General*

The notified body shall have in place ~~a~~ documented processes *and sufficiently detailed procedures* for the conduct of ~~each~~ the conformity assessment *activity* ~~procedures~~ for which it is designated, *comprising the individual steps from pre-application activities until decision making and surveillance and* taking into account, *when necessary*, their respective specificities, ~~including legally required consultations, in respect of the different categories of the devices covered by the scope of notification, ensuring transparency and the ability of reproduction of those procedures.~~

The requirements outlined in Sections 4.4., 4.5., 4.8. and 4.9. shall be internal activities of the notified body and shall not be subcontracted.

4.3. *Notified body quotations and pre-application activities*

The notified body shall

- *publish a publicly available description of the application procedure by which manufacturers can obtain certification by the notified body. This description shall include which languages are acceptable for submission of documentation and for any related correspondence,*
- *have in place documented procedures relating to, and documented details about, covering at least: fees charged for specific conformity assessment activities and any other financial conditions relating to its assessment activities for devices,*
- *the application for conformity assessment by a manufacturer or by an authorised representative,*
- *the processing of the application, including the verification of the completeness of the documentation, the qualification of the product as *in vitro* diagnostic medical device and its classification,*
- *the language of the application, of the correspondence and of the documentation to be submitted,*
- *the terms of the agreement with the manufacturer or authorised representative,*
- *the fees to be charged for conformity assessment activities,*
- *the assessment of relevant changes to be submitted for prior approval,*
- *the planning of surveillance,*
- *the renewal of certificates.*
- *have documented procedures in relation to advertising of its conformity assessment services. These shall ensure that advertising or promotional activities in no way imply or could lead to inference that their conformity assessment will offer manufacturers earlier market access or be quicker, easier or less stringent than other notified bodies,*
- *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,*

- *ensure that all contracts relating to the conformity assessment activities covered by this Regulation are established directly between the manufacturer and the notified body and not with any other organisation.*

4.4. Application and contract review

The notified body shall require a formal application signed by the manufacturer or an authorised representative containing all of the information and manufacturer's declarations required by the relevant conformity assessment annexes VIII to X.

The contract between the notified body and the 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 by 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 to fulfil its information obligations.

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

- *the completeness with respect to the requirements provided in the respective Annex under which approval has been sought,*
- *the verification of the qualification of the products covered by the application as devices and their specific classification(s),*
- *the legal applicability of the conformity assessment route chosen by the applicant,*
- *the ability of the notified body to assess the application based on their designation,*
and
- *the availability of sufficient and appropriate resources.*

The outcome of this review shall be documented. Refusals or withdrawals of applications shall be notified to the European databank and shall be accessible to other notified bodies.

4.5. Allocation

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 resource needs and identify one individual responsible for ensuring that the assessment of each application is conducted in accordance with the relevant procedures and for ensuring that the appropriate resources/personnel are utilised for individual tasks of the assessment. The allocation of tasks required for the conformity assessment and any changes subsequently made to this allocation shall be documented.

4.6. Conformity assessment activities

4.6.1. 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 sufficient expertise, facilities and detailed documented procedures to effectively conduct the conformity assessment activities, taking account of the specific requirements set out in Annex VIII, IX and X of this Regulation for which it is designated, including the requirements:

- *to appropriately plan the conduct of each individual project; these shall ensure that the composition of the assessment teams assures experience with the technology concerned, continuous objectivity and independence, which shall include provision for rotation of the members of the assessment team at appropriate intervals,*
- *to detail 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 out in Annex I,*
- *to review the manufacturer's procedures and documentation relating to performance evaluation,*
- *to address the interface with the risk management process and the appraisal and analysis of the performance evaluation and its relevance to demonstrate conformity to the relevant requirements in Annex I,*
- *to carry out the "specific procedures" in the case of devices incorporating medicinal substances, human blood derivatives or in the case of devices manufactured utilising non-viable tissues or cells,*
- *to assess, in the case of devices falling into class B or C, on a representative basis the technical documentation,*
- *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 factory visits,*
- *relating to the sampling of devices to verify that the manufactured device is in conformity with the technical documentation, these shall define the relevant sampling criteria and testing procedure prior to sampling,*
- *to evaluate and verify a manufacturer's compliance with relevant Annexes.*

Specific requirements of a notified body in conducting conformity assessment activities, including quality system audits, technical documentation assessment and performance evaluation can be found in the relevant conformity assessment Annexes VIII to X.

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

4.6.2. *Quality management system audits*

- (a) *As part of the quality system assessment activity, the notified body shall prior to the audit and in accordance with its documented procedures:*
- *assess the documentation submitted according the relevant conformity assessment Annex and establish 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,*
 - *determine interfaces and responsibilities between different manufacturer sites, as well as the identification of relevant suppliers and/or subcontractors of the manufacturer, including consideration of the need to specifically audit any of these suppliers and/or subcontractors,*
 - *clearly define, for each audit identified in the audit programme, the objectives, criteria and scope of the audit and shall draw up an audit plan adequately addressing and taking account of the specific requirements for the devices, technologies and processes covered,*
 - *establish and maintain, for class B and C devices, a sampling plan for the assessment of technical documentation as referred to in Annex II covering the range of such devices comprised by the manufacturer's application. This 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) *According to the audit programme established, the notified body shall, in accordance with its documented procedures:*
- *audit the manufacturer's quality management system, which must ensure that the devices covered conform to the relevant provisions of this Regulation, which apply to devices at every stage, from design through final inspection to ongoing surveillance, and determine if the requirements of this Regulation are met,*

- *review and audit the manufacturer's processes/subsystems, based on relevant technical documentation – in particular for design and development, production and process controls, product documentation, purchasing controls including verification of purchased devices, corrective and preventive actions including post-market surveillance and post-market performance follow-up, requirements and provisions adopted by the manufacturer including those in relation to fulfilling the general safety and performance requirements to determine whether the manufacturer meets the requirements referred to in the relevant conformity assessment annex. Documentation shall be sampled to reflect the risks associated with the intended use for 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 documentations according to the established sampling plan and taking account of Section 4.6.4. of this Annex 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/best practice documents developed or adopted by the MDCG.*

4.6.3. Product verification

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

- *the allocation of appropriately qualified and authorised personnel for the examination of the individual aspects (use of the device, biocompatibility, performance evaluation, risk management, sterilisation, etc.),*
- *the assessment of the technical documentation taking account of Sections 4.6.4. and 4.6.5. of this Annex and the assessment of conformity of the design with the provisions of this Regulation. This examination shall include the assessment of the implementation and the results of incoming, in-process and final inspections. If further tests or other evidence is required to allow for the assessment of conformity with the requirements of the 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.*

Type-examinations

The notified body shall have detailed documented procedures, sufficient expertise and facilities for the type-examination of devices according to Annex IX including capacity to:

- *examine and assess the technical documentation taking account of Sections 4.6.4. and 4.6.5. of this Annex 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 of this Regulation. This shall include all necessary tests to verify that the manufacturer has applied the relevant standards.*
- *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 product

The notified body shall:

- *have detailed documented procedures, sufficient expertise and facilities for the verification by examination and testing of every batch of product according to Annex VIII and Annex X;*
- *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:*
 - = *for devices in class C, in accordance with Annex VIII and Annex IX, verify 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 them,*
 - = *for devices in class B, in accordance with Annex VIII, confirm the conformity with the technical documentation referred to in Annex II and with the requirements of this Regulation which apply to them,-*
and document its rationale for the selection of those parameters;

- *have documented procedures to carry out the appropriate assessments and tests in order to verify the conformity of the device with the requirements of the Regulation by examining and testing every batch of product as specified in Annex X, Section 5;*
- *have documented procedures providing for agreement 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 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.*

4.6.4. Performance evaluation assessment

The notified body assessment of procedures and documentation shall address the results of literature search and all validation, verification and testing performed and conclusions drawn and shall typically include considerations of alternative materials and substances to be used and of the packaging, stability/shelf life of the finished device. Where no new testing has been undertaken by the manufacturer or for deviations from procedures, the notified body shall appropriately challenge the justification presented by the manufacturer.

The notified body shall have documented procedures in place relating to the review 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:

- *the planning, conduct, assessment, reporting and updating of the performance evaluation according to Annex XII,*
- *post-market surveillance and post-market performance follow up,*
- *the interface with the risk management process,*
- *the appraisal and analysis of the available data and its relevance to demonstrate conformity to the relevant requirements in Annex I,*
- *the conclusions drawn with regard to the clinical evidence and elaboration of the performance evaluation report .*

These procedures shall take into consideration available CS, guidance and best practice documents.

The notified body assessment of performance evaluation according to Annex XII shall include:

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

In relation to data from performance studies included within the performance evaluation, the notified body shall ensure that the conclusions drawn by the manufacturer are valid in the light of the performance studies submitted to the competent authority.

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

4.6.5. “Specific Procedures”

The notified body shall have detailed documented procedures, sufficient expertise and facilities for the “-specific types of devices” according to Annex VIII, Section 6, for which it is designated.

In the case of companion diagnostics the notified body shall have documented procedures in place that relate to the requirements of this Regulation for consultation of the European Medicines Agency or a medicinal products competent authority during its assessment of such a device.

4.7. 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 provide objective evidence of this to personnel not directly involved in the assessment, for example in designating authorities,*
- *ensure that records for quality management system audits are available that are sufficient to provide a discernible audit trail,*
- *clearly document the conclusions of its assessment of the 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 content determined by the Medical Device Coordination Group.*

The notified body report shall:

- *clearly document the outcome of its assessments and draw clear conclusions on the verification of the manufacturer's conformity to the requirements of this Regulation,*
- *make a recommendation for review and final decision-making by the notified body; this recommendation shall be clearly signed off by the responsible notified body personnel,*
- *be provided to the manufacturer.*

4.8. Review

The notified body shall prior to making a final decision ensure:

- *that personnel assigned for review and decision making on specific projects are appropriately authorised and are different from those personnel who have conducted the assessments,*
- *that the report(s) and supporting documentation needed for decision making, including close out of nonconformities raised during assessment, are complete and sufficient with respect to the scope of the application,*
- *that no unresolved nonconformities exist that prevent issuance of an EU certificate.*

4.9. Decisions and certifications

The notified body shall have documented procedures for decision making including responsibilities for the issuance, suspension, restriction and withdrawal of certificates. These procedures shall include the notification requirements according to Chapter V of this Regulation. These procedures shall allow it to:

- *decide, based on the assessment documentation and additional information available whether the requirements of the Regulation are fulfilled, decide based on the results of their assessment of the performance evaluation and risk management if the PMS plan, including whether the PMPF is adequate and 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 outputs from the risk analysis of the device, on a period for certification not exceeding five years,*
- *clearly document decision making and approval steps including approval by signature of the responsible individuals,*
- *clearly document responsibilities and mechanisms for communication of decisions, in particular, if the final signatory of a certificate differs from the decision maker(s) or does not fulfil the requirements outlined in Section 3.2.7. of this Annex,*
- *issue a certificate(s) according to the minimum requirements defined in Annex XI for a period of validity not exceeding five years and shall indicate if there are specific conditions or limitations associated with the certification,*
- *issue a certificate(s) for the applicant alone and shall not issue certificates covering multiple entities,*
- *ensure that the outcome of the assessment and the resultant decision is notified to the manufacturer and entered into the European databank according to Article 43(4).*

4.10. Changes and modifications

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

- *the approved quality management system(s) or 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 “specific procedures” according to Section 4.6.5.*

These procedures and contractual arrangements shall include processes for checking the significance of changes.

In accordance with its documented procedures, the notified body shall:

- *ensure that manufacturers submit plans for such changes and relevant information relating to the change for prior approval,*
- *assess the changes proposed and verify whether after these changes the quality management system or the design/type of a device still meets the requirements of this Regulation,*
- *notify the manufacturer of its decision and provide a (supplement) report, which shall contain the justified conclusions of its assessment/audit.*

4.11. 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. These shall include provisions for unannounced visits to manufacturers and when applicable subcontractors and suppliers, carrying out product tests and the monitoring of compliance to any conditions on manufacturers associated with certification decisions, e.g. updates to clinical data at defined intervals,*
- *for screening relevant sources of scientific, clinical and post-market information relating to the scope of its designation. Such information shall be taken into account in the planning and conducting of surveillance activities,*
- *to review vigilance information accessible according to Article 60 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 shall, upon receipt of information about vigilance cases from the manufacturer or the competent authorities, decide about the following options:

- *that no action is required as the vigilance case is clearly not related to the certification granted,*
- *observation of the manufacturer's and competent authorities activities and the results of the manufacturer's investigation to allow a conclusion that the certification granted is not endangered or adequate corrective action has been performed,*
- *performance of extraordinary surveillance measures (document review, short-notice or unannounced audit, product testing, etc.) if it is likely that certification granted is endangered,*
- *increasing the frequency of surveillance audits,*
- *reviewing specific products or processes during the next audit of the manufacturer,*
or
- *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 4.6.,*
- *ensure that it adequately assesses the manufacturer's documentation on, and application of, the provisions on vigilance, the post-market surveillance plan (including post-market performance follow-up),*
- *sample and test devices and technical documentations, 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 that manufacturer complies with the documentation and information obligations laid down in the respective Annex(es) of this Regulation and that his procedures take into account best practices in 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,*
- *if non-conformities are detected ask the manufacturer for corrections, corrective actions, when applicable preventative actions, and*
- *when 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 up to date performance evaluation of the manufacturer based on post-market surveillance, post-market performance follow up and clinical literature relevant to the condition being treated or similar devices,*
- *clearly document the outcome of this review and address any specific concerns or conditions to the manufacturer,*
- *ensure that the updated performance evaluation is appropriately reflected in the Instructions For Use and Summary of Safety and Performance Data.*

4.12. *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 or EU type-examination certificates shall occur at least every 5 years.

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

- *all changes to the originally approved device, including changes not yet notified,*
- *experience gained from post -market surveillance,*
- *experience from risk-management,*
- *experience from updating the proof of compliance with the general safety and performance requirements,*
- *experience from reviews of the performance evaluation, including the results of any clinical investigations and post-market clinical follow up,*
- *changes of the requirements, of components of the device or of the scientific or regulatory environment,*
- *changes of applied or new (harmonised) standards, CS or equivalent documents,*
- *changes in medical, scientific and technical knowledge, such as:*
 - = *new treatments,*
 - = *changes in test methods,*
 - = *new scientific findings on materials, components, etc., also with respect to biocompatibility,*
 - = *experience from market research on comparable devices,*
 - = *data from registers/registries,*
 - = *experience from performance studies with comparable devices.*

The notified body shall have documented procedures to assess this information and shall pay particular attention to clinical data from post-market surveillance and PMPF activities undertaken since the previous (re-)certification, including appropriate updates to manufacturer's performance evaluation reports.

For the decision on the extension the notified body shall use the same methods and principles as for the initial decision. If necessary, separate forms shall be established taking into account the above mentioned steps, e.g. for application and application review.

CLASSIFICATION CRITERIA

1. IMPLEMENTING RULES FOR THE CLASSIFICATION RULES

- 1.1. Application of the classification rules shall be governed by the intended purpose of the devices.
- 1.2. If the device is intended to be used in combination with another device, the classification rules shall apply separately to each of the devices.
- 1.3. Accessories are classified in their own right separately from the device with which they are used.
- 1.4. **Software** ~~Standalone software~~, which drives a device or influences the use of a device, falls automatically in the same class as the device.
If ~~standalone~~ **the** software is independent of any other device, it is 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** ~~Standalone 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 the rules in order to establish the proper classification for the device.
- 1.8. Where a device has multiple intended purposes stated by the manufacturer, which place the device 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 rules applies to first line assays, confirmatory assays and supplemental assays.**

2. CLASSIFICATION RULES

2.1. Rule 1

Devices intended for the following purposes are classified as **class D**:

- Devices intended to be used to detect 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, ~~or~~ transplantation *or cell administration*.
- Devices intended to be used to detect the presence of, or exposure to, a transmissible agent that causes a life-threatening disease with a high or *suspected high* ~~currently undefined~~ risk of propagation.
- *Devices intended to be used to determine the infectious load of a life-threatening disease where its monitoring is critical in the process of patient management.*

~~This rule applies to first line assays, confirmatory assays and supplemental assays. All assays for the clinical diagnosis and monitoring of infection by HIV 1/2, Hepatitis C virus, Hepatitis B virus and HTLV I/II devices shall be classified as class D. Assays for the clinical diagnosis of Hepatitis B virus are taken to include the following infectious disease markers: Hepatitis B surface antigen (HBsAg), Hepatitis B core total antibodies (anti-HBc total) and Hepatitis B virus nucleic acid detection (HBV NAT).~~

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), *RHW_I*, 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 for:

- (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 ~~with~~ ***without a high or suspected high*** risk of ~~limited~~ 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 or foetus 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, if 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) ~~selection of patients, i.e.~~ (i) ~~Devices intended~~ to be used as companion diagnostics; ~~or~~
- (fa) (ii) ~~Devices intended~~ to be used for disease staging, ***if 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; or***
- (fb) (iii) ~~Devices intended~~ to be used in screening, ~~for or in the~~ diagnosis, ***or staging*** of cancer;
- (g) *for* human genetic testing;
- (h) *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 an ~~imminent~~ life-threatening situation for the patient or for the patient's offspring;
- (i) *for* management of patients suffering from a life-threatening ~~infectious~~ disease ***or condition***;
- (j) *for* screening for congenital disorders in the foetus;;
- (k) ***for screening for congenital disorders in new-born 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 those devices from which the result is not determining a medically critical status, or is preliminary and requires follow up with the appropriate laboratory test in which case they are Class B.~~
- (b) Devices intended for ~~blood gases and blood glucose determinations~~ for near-patient testing are ~~class C~~. Other devices that are intended for near-patient testing shall be 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, and washing solutions* ~~reagents or other articles which possess specific characteristics~~, intended by the manufacturer to make them suitable for *in vitro* diagnostic procedures related 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**.

**CONFORMITY ASSESSMENT BASED ON FULL A QUALITY
MANAGEMENT SYSTEM ASSURANCE AND DESIGN EXAMINATION ON
ASSESSMENT OF THE TECHNICAL DOCUMENTATION**

Chapter I: Full Quality Management System

1. The manufacturer shall ensure application of the *establish, document and implement a quality management system as described in Article 8(5) of this Regulation and maintain its effectiveness through the life cycle* approved for the design, manufacture and final inspection of the devices concerned. *The manufacturer shall ensure the application of the quality management system* as specified in Section 3, and is subject to audit as laid down in Sections 3.3. and 3.4. and to the surveillance as specified in Section 4.

2. The manufacturer who fulfils the obligations imposed by Section 1 shall draw up and keep an EU declaration of conformity in accordance with Article 15 and Annex III for the device model covered by the conformity assessment procedure. By issuing a declaration of conformity, the manufacturer ensures and declares that the devices concerned meet the provisions of this Regulation which apply to them.

3. **Quality management system assessment**
 - 3.1. The manufacturer shall lodge an application for assessment of his quality management system with a notified body. The application shall include:
 - the name and address *of the registered place of business* of the manufacturer and any additional manufacturing site covered by the quality management system, and, if the application is lodged by the authorised representative, his name and address *of his registered place of business* as well,
 - all the relevant information on the device or ~~device category~~ *group of devices* covered by the *quality management system* procedure,

- 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 ~~that has been refused by another notified body,~~
- ***a draft of an EU declaration of conformity in accordance with Article 15 and Annex III for the device model covered by the conformity assessment procedure,***
- the documentation on the quality management system,
- a ***documented*** description of the procedures in place to fulfil the obligations imposed by the quality management system ~~approved~~ ***and required by this Regulation*** and the undertaking by the manufacturer to apply these procedures,
- a description of the procedures in place to keep the ~~approved~~ quality management system adequate and efficacious and an undertaking by the manufacturer to apply these procedures,
- the documentation on the post-market surveillance ~~system plan~~, including, when applicable, a plan for the post-market ***performance*** follow-up, and the procedures put in place to ensure compliance with the obligations emanating from the provisions on vigilance set out in Articles 59 to 64a,
- a description of the procedures in place to keep up to date the post-market surveillance ~~plan-system~~, including, when applicable, a plan for the post-market ***performance*** follow-up, and the procedures ensuring compliance with the obligations emanating from the provisions on vigilance set out in Articles 59 to 64a, as well as the undertaking by the manufacturer to apply these procedures.
- ***documentation on the performance evaluation plan,***
- ***a description of the procedures in place to keep up to date the performance evaluation plan taking into account the state of the art.***

3.2. **Implementation** Application of the quality management system shall ensure that the **compliance** devices conform to **with** the provisions of this Regulation which apply to them at every stage, from design to final inspection. All the elements, requirements and provisions adopted by the manufacturer for his 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, ~~quality manuals~~ 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 clear assignment to critical procedures**, the responsibilities of the managerial staff and their organisational authority ~~where quality of design and manufacture of the products is concerned~~,
 - the methods of monitoring the efficient operation of the quality management system and in particular its ability to achieve the desired quality of design and of ~~product~~ **device**, including control of ~~products~~ **devices** which fail to conform,
 - where the design, manufacture, and/or final ~~inspection~~ **verification** and testing of the ~~products~~ **devices, or the performance evaluation**, or elements **of any of these** thereof, 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 of the authorised representative to accept the mandate;

- (c) the procedures and techniques for monitoring, verifying, validating and controlling the design **and performance evaluation** of the devices, **and including** the corresponding documentation as well as the data and records arising from those procedures and techniques, **where these procedures and techniques shall specifically address:**
- ***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 address these, under consideration of applicable CS and harmonized standards or equivalent solutions,***
 - ***the risk management according to Section 1a of Annex I,***
 - ***the performance evaluation, according to Article 47 and Annex XII, including post-market performance follow-up,***
 - ***the solutions to address the applicable specific requirements regarding design and construction, including appropriate preclinical evaluation, addressing specifically Chapter II of Annex I,***
 - ***the solutions to address the applicable specific requirements regarding the information to be supplied with the device, addressing specifically 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,***
 - ***management of design or quality management system changes;***
- (d) the ~~inspection~~ **verification** and quality assurance techniques at the manufacturing stage and in particular:
- ~~the processes and procedures which will be used, particularly as regards sterilisation, purchasing and the relevant documents,~~
 - ~~the product identification procedures drawn up and kept up to date from drawings, specifications or other relevant documents at every stage of manufacture;~~

- (e) the appropriate tests and trials which will be carried out before, during and after manufacture, the frequency with which they will take place, and the test equipment used; it shall be possible to trace back the calibration of the test equipment adequately.

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

3.3. Audit

- (a) The notified body shall audit the quality *management* system to determine whether it meets the requirements referred to in Section 3.2. ***Where the manufacturer uses a harmonised standard or a CS related to quality management system, it shall assess conformity with those standards.*** Unless duly substantiated, it shall presume that quality management systems which satisfy the relevant harmonised standards or CFS conform to the requirements covered by the standards or CFS.
- (b) The ~~assessment~~ *audit* team shall include at least one member with past experience of assessments of the technology concerned ***in accordance with Section 4.4. of Annex VI.*** ***In circumstances where this experience is not immediately obvious or applicable the notified body shall provide a documented rationale for the allocation of this auditor.*** 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 ~~inspect~~ *verify* the manufacturing and other relevant processes.

- (c) Moreover, in the case of devices classified as class C, the *quality management system assessment shall be accompanied by the assessment of the technical documentation in accordance with provisions in Sections 5.3a to 5.3e of Chapter II of this Annex, for the selected devices* ~~audit procedure shall include an assessment, on a representative basis, of the design documentation within the technical documentation as referred to in Annex II of the device(s) concerned.~~ In choosing representative sample(s) the notified body shall take into account the novelty of the technology, *the potential impact on the patient and practice of medicine*, similarities in design, technology, manufacturing and ~~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 shall document its rationale for the sample(s) taken.
- (d) If the quality management system conforms to the relevant provisions of this Regulation, the notified body shall issue an EU ~~full~~ quality assurance *management system* certificate. The decision shall be notified to the manufacturer. It shall contain the conclusions of the audit and a reasoned ~~assessment~~ *report*.

3.4. The manufacturer shall inform the notified body which approved the quality management system of any plan for substantial changes to the quality management system, or the ~~product~~ *device*-range covered. The notified body shall assess the changes proposed, *determine the need for additional audits* and verify whether after these changes the quality management system still meets the requirements referred to in Section 3.2. It shall notify the manufacturer of its decision which shall contain the conclusions of the *assessment, and where applicable, conclusions of additional* audits ~~and a reasoned assessment~~. The approval of any substantial change to the quality management system or the ~~product~~ *device*-range covered shall take the form of a supplement to the EU ~~full~~ quality assurance *management system* certificate.

4. Surveillance assessment applicable to devices classified as class C and D

- 4.1. The aim of surveillance is to ensure that the manufacturer duly fulfils the obligations imposed by the approved quality management system.
- 4.2. The manufacturer shall authorise the notified body to carry out all the necessary audits, including ~~inspections~~ **on-site audits**, and supply it with all relevant information, in particular:
- the documentation on the quality management system,
 - the documentation on **any findings and conclusions resulting from the application of** the post-market surveillance plan, including ~~a~~ **the** post-market **performance** follow-up **plan for a selection of devices**, ~~as well as, if applicable, any findings resulting from the application of the post-market surveillance plan, including the post-market follow-up,~~ and of the provisions on vigilance set out in Articles 59 to 64a,
 - 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 2 of Annex I,
 - the data stipulated in the part of the quality management system relating to manufacture, such as inspection reports and test data, calibration data, qualification reports of the personnel concerned, etc.
- 4.3. The notified body shall periodically, at least **once** every 12 months, carry out appropriate audits and assessments to make sure that the manufacturer applies the approved quality management system and the post-market surveillance plan, ~~and shall supply the manufacturer with an assessment report.~~ This shall include ~~inspections~~ **audits** on the premises of the manufacturer and, if appropriate, of the manufacturer's suppliers and/or subcontractors. At the time of such ~~inspections~~ **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 ~~an inspection~~ **a surveillance audit** report and, if a test has been carried out, with a test report.

- 4.4. The notified body shall randomly perform unannounced factory ~~inspections~~ ***on-site audits*** to the manufacturer and, if appropriate, of the manufacturer's suppliers and/or subcontractors, which may be combined with the periodic surveillance assessment referred to in Section 4.3. or be performed in addition to this surveillance assessment. The notified body shall establish a plan for the unannounced ~~inspections~~ ***on-site audits*** which shall not be disclosed to the manufacturer.

Within the context of such unannounced ~~inspections~~ ***on-site audits***, the notified body shall check an adequate sample from the production or the manufacturing process to verify that the manufactured device is in conformity with the technical documentation ~~and/or design dossier~~. Prior to the unannounced ~~inspection~~ ***on-site audits***, the notified body shall specify the relevant sampling criteria and testing procedure.

Instead of, or in addition to, the sampling from the production, the notified body shall take samples of devices from the market to verify that the manufactured device is in conformity with the technical documentation ~~and/or design dossier~~. Prior to the sampling, the notified body shall specify the relevant sampling criteria and testing procedure.

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

- 4.5. In the case of devices classified as class C, the surveillance assessment shall also include ~~the~~ assessment of ~~the design documentation within~~ the technical documentation ***in accordance with the provisions in Sections 5.3a to 5.3e of Chapter II of this Annex*** of the device(s) concerned on the basis of further representative sample(s) chosen in accordance with the rationale documented by the notified body in accordance with point (c) of Section 3.3.
- 4.6. The notified body shall ensure that the composition of the assessment team assures experience with the ***evaluation of the devices, systems and processes*** ~~technology~~ 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 not lead and attend an audit for more than three consecutive years in respect to the same manufacturer.

- 4.7. If the notified body establishes a divergence between the sample taken from the production 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: ~~Design dossier examination~~ *Assessment of the technical documentation*

5. **~~Examination of the design~~ *Assessment of the technical documentation of the device and batch verification applicable to devices in class D***
- 5.1. In addition to the obligation imposed by Section 3, the manufacturer of devices classified as class D shall lodge with the notified body referred to in Section 3.1 an application for the ~~examination~~ *assessment* of the ~~design dossier~~ *technical documentation* relating to the device which he plans to ~~manufacture~~ *place on the market or put into service* and ~~which falls into the device category~~ *is* covered by the quality management system referred to in Section 3.
- 5.2. The application shall describe the design, manufacture and performances of the device in question. It shall include the technical documentation as referred to in Annex II; ~~where the technical documentation is voluminous and/or held in different locations, the manufacturer shall submit a summary technical documentation (STED) and grant access to the full technical documentation upon request.~~

In the case of devices for self-testing or near-patient testing, the application shall also include the aspects referred to in Section 6.1, point b).

5.3. The notified body shall examine the application employing staff with proven knowledge and experience ~~regarding~~ ***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 further tests or other evidence 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.

5.3a. The notified body shall in particular review the clinical evidence presented by the manufacturer in the performance evaluation report according to Annex XII Section 1.4.2. The notified body shall employ device reviewers with sufficient clinical expertise, including the use of external clinical expertise with direct and current experience on the clinical application of the device in question for the purposes of this review.

5.3b. The notified body shall, in circumstances when the clinical evidence is based on data, in total or in part, from devices which are claimed to be similar or equivalent to the device under assessment, assess the suitability of this route, taking into account factors such as new indications and innovation. The notified body shall clearly document its conclusions on the claimed equivalency, the relevance and adequacy of the data to demonstrate conformity.

5.3c. The notified body shall ensure the adequacy of the clinical evidence and the clinical evaluation and verify the conclusions drawn by the manufacturer on the conformity with the relevant general safety and performance requirements. This review shall include consideration of the adequacy of the benefit-risk determination, the instructions for use, the user training, the manufacturer's post-market surveillance plan, and include a review of the need for, and adequacy of, the post-market performance follow up proposed, where applicable.

5.3d. The notified body shall consider based on its assessment of the clinical evidence, the performance evaluation, and the benefit-risk determination if specific milestones are required to be defined to allow for review by the notified body on updates to the clinical evidence based on post-market surveillance and post-market performance follow up data.

5.3e. The notified body shall clearly document the outcome of its assessment in the performance evaluation assessment report.

5.4. Before issuing an EU design-examination **technical documentation assessment** certificate, the notified body shall request a reference laboratory, where designated in accordance with Article 78, to verify **whether the performance of the device is in** compliance of the device with the **available** CTS, ~~when available,~~ **and with the state of the art** 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 reference laboratory according to Article 40(2).**

The reference laboratory shall provide a scientific opinion within ~~30~~ **60** days.

The scientific opinion of the reference laboratory 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 when making its decision. The notified body shall not deliver the certificate if the scientific opinion is unfavourable.

5.5. The notified body shall provide the manufacturer with an **report on the EU design-examination technical documentation assessment report, including a performance evaluation assessment report.**

If the device conforms to the relevant provisions of this Regulation, the notified body shall issue an EU ~~design-examination~~ **technical documentation assessment** certificate. The certificate shall contain the conclusions of the ~~examination~~ **assessment**, the conditions of validity, the data needed for identification of the approved ~~design~~ **device**, **and**, where appropriate, a description of the intended purpose of the device .

5.6. Changes to the approved ~~design~~ **device** shall receive further approval from the notified body which issued the EU ~~design-examination~~ **technical documentation assessment** certificate, wherever the changes could affect ~~conformity with the general~~ safety and performance requirements of this Regulation **the device** or with the conditions prescribed for use of the device. **Where the applicant plans to introduce any of the above mentioned changes he** shall inform the notified body which issued the EU ~~design-examination~~ **technical documentation assessment** certificate **thereof** of any planned changes to the approved design. The notified body shall examine the planned changes **and decide whether the planned changes require a new conformity assessment in accordance with Article 40 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 him with a supplement to the EU ~~design-examination~~ **technical documentation assessment report certificate.**

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

The reference laboratory shall provide a scientific opinion within ~~30~~ **60** days.

The approval of any change to the approved ~~design~~ **device** shall take the form of a supplement to the EU ~~design-examination~~ **technical documentation assessment** certificate.

- 5.7. To verify conformity of manufactured devices classified as class D, the manufacturer shall carry out tests on ~~the~~ **each** manufactured ~~devices or each~~ batch of devices. After the conclusion of the controls and tests he shall forward to the notified body without delay the relevant reports on these tests. Furthermore, the manufacturer shall make the samples of manufactured ~~devices or~~ batches of devices available to the notified body in accordance with pre-agreed conditions and modalities which shall include that the notified body or the manufacturer, ~~in regular intervals,~~ shall send samples of the manufactured ~~devices or~~ batches of devices to a reference laboratory, where designated in accordance with Article 78, to carry out appropriate tests. The reference laboratory shall inform the notified body about its findings.
- 5.8. The manufacturer may place the devices on the market, unless the notified body communicates to the manufacturer within the agreed time-frame, 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. ~~Examination of the design~~ **Assessment of the technical documentation of specific types of devices**

6.1. ~~Examination of the design~~ **Assessment of the technical documentation** of **Class C** devices for self-testing and **devices for** near-patient testing classified as class A, B or C

- (a) The manufacturer of **Class C self-test devices and devices for** near-patient testing classified as class A, B and C shall lodge with the notified body referred to in Section 3.1 an application for the ~~examination of the design~~ **assessment of the technical documentation**.
- (b) The application shall enable the design of the device to be understood and shall enable conformity with the design related requirements of this Regulation to be assessed. It shall include:
- test reports, including results of studies carried out with intended users;
 - where practicable, an example of the device; if required, the device shall be returned on completion of the ~~design examination~~ **technical documentation assessment**;
 - data showing the ~~handling~~ suitability of the device in view of 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.

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

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

- (c) The notified body shall ~~examine~~ **assess** the application employing staff with proven knowledge and experience regarding the technology concerned **and the intended purpose of the device** and provide the manufacturer with an ~~EU design examination~~ **technical documentation assessment** report.
- (d) If the device conforms to the relevant provisions of this Regulation, the notified body shall issue an EU ~~design examination~~ **technical documentation assessment** certificate. The certificate shall contain the conclusions of the ~~examination~~ **assessment**, the conditions of validity, the data needed for the identification of the approved ~~design~~ **devices** and, where appropriate, a description of the intended purpose of the device.

- (e) Changes to the approved ~~design~~ **device** shall receive further approval from the notified body which issued the EU ~~design-examination~~ **technical documentation assessment** certificate, wherever the changes could affect ~~conformity with the general~~ safety and performance requirements of this Regulation ~~the device~~ or with the conditions prescribed for use of the device. ~~The~~ **Where the applicant plans to introduce any of the above mentioned changes he** shall inform the notified body which issued the EU ~~design-examination~~ **technical documentation assessment** certificate of any planned changes to the approved design **thereof**. The notified body shall ~~examine~~ **assess** the planned changes **and decide whether the planned changes require a new conformity assessment in accordance with Article 40 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 him with a supplement to the EU ~~design-examination~~ report. The approval of any change to the approved design shall take the form of a supplement to the EU ~~design-examination~~ **technical documentation assessment** certificate.

6.2. ~~Examination of the design~~ **Assessment of the technical documentation** of companion diagnostics

- (a) The manufacturer of a companion diagnostic shall lodge with the notified body referred to in Section 3.1 an application for the ~~examination-assessment~~ of the ~~design~~ **technical documentation**.
- (b) The application shall enable the ~~design~~ **characteristics and performance(s)** 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) ~~For companion diagnostic intended to be used to assess the patient eligibility to a treatment with a specific medicinal product, the~~ **The** notified body shall, ~~consult~~ before issuing an EU ~~design examination~~ **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, **consult** one of the competent authorities designated by the Member States in accordance with Directive 2001/83/EC (hereinafter referred to as 'medicinal products competent authority') or the European Medicines Agency (hereinafter referred to as 'EMA') established by ~~the~~ Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, 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 of Regulation (EC) No 726/2004, the notified body shall consult the EMA. ***If the medicinal product is 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.***

- (d) The medicinal products competent authority or the EMA *consulted pursuant to point (c)* shall give its opinion, ~~if any,~~ within 60 days after receipt of valid documentation. This 60-day period may be extended ~~only~~ once for a further 60 days on *justified* scientifically valid grounds. The opinion ~~of the medicinal products authority or of the EMA~~ 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 opinion *referred to in point (d)*, ~~if any,~~ expressed by the medicinal products competent authority concerned or the EMA when making its decision. **The notified body** ~~it~~ shall convey its final decision to the medicinal products competent authority concerned or to the EMA *consulted pursuant to point (c)*. The ~~EU design examination~~ *technical documentation assessment* certificate shall be delivered in accordance with point (d) of Section 6.1.
- (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 40 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,** ~~which~~ shall consult the medicinal products competent authority *or the EMA* that was involved in the initial consultation ~~or the EMA~~. The medicinal products competent authority or the EMA *consulted pursuant to this point* shall give its opinion, ~~if any,~~ within 30 days after receipt of the valid documentation regarding the changes. A supplement to the ~~EU design examination~~ *technical documentation assessment* certificate shall be issued in accordance with point (e) of Section 6.1.

Chapter III: Administrative provisions

7. The manufacturer or *where the manufacturer does not have a registered place of business in a Member State* his authorised representative shall, for a period ending at least five years after the last device has been placed on the market, keep at the disposal of the competent authorities:
- the declaration of conformity,
 - the documentation referred to in the ~~fourth~~ *fifth* indent of Section 3.1. and in particular the data and records arising from the procedures referred to in point (c) of Section 3.2.,
 - the changes referred to in Section 3.4.,
 - the documentation referred to in Sections 5.2. and point (b) of Section 6.1., and
 - the decisions and reports from the notified body as referred to in Sections 3.3., 4.3., 4.4., 5.5., 5.6., 5.8., points (c), (d) and (e) of Section 6.1., point (e) of Section 6.2. and point (f) of Section 6.2.
8. Each Member State shall make provision that this documentation is kept at the disposal of the competent authorities for the period indicated in the first sentence of the preceding paragraph in case the manufacturer, or his authorised representative, established within its territory goes bankrupt or ceases its business activity prior to the end of this period.

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 production covered fulfils the relevant provisions of this Regulation *including those covering the performance evaluation and the PMS-planning*.

2. Application

The application shall include:

- the name and address *of the registered place of business* of the manufacturer and, if the application is lodged by the authorised representative, the name and address *of the registered place of business* of the authorised representative,
- the technical documentation referred to in Annex II ~~needed~~ *suitable* to assess the conformity of the representative sample of the production in question, hereinafter referred to as the ‘type’, with the requirements of this Regulation, *including those covering the performance evaluation and the PMS-planning* ~~where the technical documentation is voluminous and/or held in different locations, the manufacturer shall submit a summary technical documentation (STED) and grant access to the full technical documentation upon request.~~ The applicant shall make a *representative sample of the production in question, hereinafter referred to as ‘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 view of 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 view of 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,*
- 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 has been refused by another notified body *or withdrawn.*

3. Assessment

The notified body shall:

3.0. *examine the application employing 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 further tests or other evidence 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.*

3.1. *examine and assess the technical documentation for conformity with the requirements of this regulation 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 specifications of the standards referred to in Article 6 or CFS, as well as the items not designed on the basis of the relevant provisions of the abovementioned standards;*

3.1b. *in particular review the clinical evidence presented by the manufacturer in the performance evaluation report according to Annex XII Section 1.4.2. The notified body shall employ device reviewers with sufficient clinical expertise, including the use of external clinical expertise with direct and current experience on the clinical application of the device in question for the purposes of this review.*

3.1c. in circumstances when the clinical evidence is based on data, in total or in part, from devices which are claimed to be similar or equivalent to the device under assessment, assess the suitability of this route, taking into account factors such as new indications and innovation. The notified body shall clearly document its conclusions on the claimed equivalency, the relevance and adequacy of the data to demonstrate conformity.

3.1d. clearly document the outcome of its assessment in the performance evaluation report as defined in Annex XII.

3.2. 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 of this Regulation if the standards referred to in Article 6 or CFS have not been applied; if the device is to be connected to other equipment 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 equipment having the characteristics specified by the manufacturer;

3.3. carry out or arrange for the appropriate assessments and the physical or laboratory tests necessary to verify whether, if the manufacturer has chosen to apply the relevant standards, these have actually been applied;

3.4. agree with the applicant on the place where the necessary assessments and tests will be carried out; *and*

3.4a. draw up an EU type-examination report on the results of the assessments and tests carried out under Sections 3.0 to 3.3., including a performance evaluation report;

3.5. in the case of devices classified as class D, request a reference laboratory, where designated in accordance with Article 78, to verify compliance of the device with the CTS ~~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 reference laboratory according to Article 40(2).*** The reference laboratory shall provide a scientific opinion within ~~30~~ **60** days. The scientific opinion of the reference laboratory 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 views expressed in the scientific opinion when making its decision. The notified body shall not deliver the certificate if the scientific opinion is unfavourable;

- 3.6. For companion diagnostics ~~intended to be used to assess the patient eligibility to a treatment with a specific medicinal product~~, seek the opinion, on the basis of the draft summary of safety and performance and the draft instructions for use, of ~~a~~ one of the competent authorities designated by the Member States in accordance with Directive 2001/83/EC (hereinafter referred to as 'medicinal products competent authority') or the European Medicines Agency (hereinafter referred to as 'EMA') 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 is 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 or the ~~European Medicines Agency~~ EMA shall deliver its opinion, ~~if any~~, within 60 days upon receipt of the valid documentation. This 60-day period may be extended ~~only~~ once for a further 60 days on ***justified*** ~~scientifically valid~~ grounds. The opinion of the medicinal products authority or of the EMA 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, ~~if any~~, expressed by the medicinal products competent authority concerned or the EMA when making its decision. It shall convey its final decision to the medicinal products competent authority concerned or to the EMA ***consulted pursuant to this section, and***
- 3.7. ***draw up an EU type-examination report on the results of the assessments, tests and scientific opinions under Sections 3.0 to 3.6., including a performance evaluation report for devices classified as class C or D or covered by Section 2, third indent.***

4. **Certificate**

If the type conforms to the provisions of 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 assessment, the conditions of validity and the data needed for identification of the type approved. *The certificate shall be drawn up in accordance with Annex XI.* 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 its intended purpose and use.*

5.2. Changes to the approved product *including limitations of its intended purpose and use* shall receive further approval from the notified body which issued the EU type-examination certificate wherever the 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 initial EU type-examination certificate.

5.2a. Changes to the intended purpose and use of the approved device, with the exception of limitations of the intended purpose and use, require a new application for a conformity assessment.

5.3. Where the changes could affect *the claimed performance or* compliance with the CFS or with other solutions chosen by the manufacturer which were approved through the EU type-examination certificate, the notified body shall consult the reference laboratory that was involved in the initial consultation, in order to confirm that compliance with the CFS, 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 reference laboratory shall provide a scientific opinion within ~~30~~ **60** days.

5.4. Where the changes affect *the performance or the intended use of* a companion diagnostic approved through the EU type-examination certificate ~~with regard to~~ *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 competent authority or the EMA 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*, his authorised representative shall, for a period ending at least five 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,
- the changes referred to in Section 5,
- copies of EU type-examination certificates, *scientific opinions and reports* and their additions/*supplements*.

Section 8 of Annex VIII shall apply.

CONFORMITY ASSESSMENT BASED ON PRODUCTION QUALITY ASSURANCE

1. The manufacturer shall ensure application of the quality management system approved for the manufacture of the devices concerned *and for continuous life cycle processes including risk management, performance evaluation and PMS* and carry out the final inspection, as specified in Section 3, and is subject to the surveillance referred to in Section 4.

2. The manufacturer who fulfils the obligations imposed by Section 1 shall draw up and keep an EU declaration of conformity in accordance with Article 15 and Annex III for the device model covered by the conformity assessment procedure. By issuing an EU declaration of conformity, the manufacturer ensures and declares that the devices concerned ~~conform to the type described in the EU type-examination certificate~~ and meet the provisions of this Regulation which apply to them, *and in the case of Class C and Class D devices that undergo a type examination, conform 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 his quality management system with a notified body.

The application shall include:

- all elements listed in Section 3.1 of Annex VIII,
- the technical documentation as referred to in Annex II for the types approved; where the technical documentation is voluminous and/or held in different locations, the manufacturer shall submit a summary technical documentation (STED) and grant access to the full technical documentation upon request;
- a copy of the EU-type examination certificates referred to in Section 4 of Annex IX; 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 is ~~sufficient~~ *necessary*.

3.2. ~~Application~~ **Implementation** of the quality management system shall ensure ~~that the~~ **compliance with** ~~devices conform to~~ the type described in the EU type-examination certificate and ~~to~~ **with** the provisions of this Regulation which apply to them at every stage. All the elements, requirements and provisions adopted by the manufacturer for his quality management system shall be documented in a systematic and orderly manner in the form of written policies and **Standard Operating Procedures (SOPs)**, ~~procedures~~ such as quality programmes, quality plans, quality manuals and quality records.

It shall, in particular, include an adequate description of all elements listed in points (a), (b), (d) and (e) of Section 3.2. of Annex VIII.

3.3. The provisions of points (a) and (b) of Section 3.3. of Annex VIII, apply.

If the quality **management** system ensures that the devices conform to the type described ~~in~~ ~~the~~ in the EU type-examination certificate and conforms to the relevant provisions of this Regulation, the notified body shall issue an EU **production** quality assurance certificate. The decision shall be notified to the manufacturer **in an EU production quality assurance report**. It shall contain the conclusions of the inspection and a reasoned assessment.

3.4. The provisions of ~~the~~ Section 3.4. of Annex VIII apply.

4. **Surveillance**

The provisions of Section 4.1., the first, second and fourth indents of Section 4.2., Section 4.3., Section 4.4., Section 4.6. and Section 4.7. of Annex VIII apply.

5. Verification of manufactured devices classified as class D

- 5.1. In the case of devices classified as class D, the manufacturer shall carry out tests on *each* ~~the~~ manufactured ~~devices or each~~ batch of devices. After the conclusion of the controls and tests he shall forward to the notified body without delay the relevant reports on these tests. Furthermore, the manufacturer shall make ~~the~~ samples of manufactured devices or batches of devices available to the notified body in accordance with pre-agreed conditions and modalities which shall include that the notified body or the manufacturer, ~~in regular intervals,~~ shall send samples of the manufactured devices or batches of devices to a reference laboratory, where designated in accordance with Article 78, to carry out appropriate *laboratory* tests. The 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 time frame, 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 his authorised representative shall, for a period ending at least five 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 ~~fourth~~ *fifth* indent of Section 3.1 of Annex VIII,
- the documentation referred to in the ~~seventh~~ *eighth* indent of Section 3.1 of Annex VIII, including the EU type-examination certificate referred to in Annex IX,
- the changes referred to in Section 3.4 of Annex VIII and
- the decisions and reports from the notified body as referred to in Sections 3.3., 4.3. and 4.4. of Annex VIII.

Section 8 of Annex VIII shall apply.

**~~MINIMUM CONTENT OF CERTIFICATES ISSUED BY A NOTIFIED~~
BODY**

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 (natural or legal person). 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 23 of this Regulation.***
- 4. The scope of the certificates shall unambiguously describe the device(s) covered.***
 - (a) EU technical documentation assessment and EU type-examination certificates shall include a clear identification (name, model, type) of the device(s), the intended purpose (as indicated by the manufacturer in the instructions for use and that has been assessed by the conformity assessment procedure), risk classification and the Basic UDI-DI unit of use as referred to in Article 22(4b).***
 - (b) EU quality management system certificates shall include the identification of the devices or groups of devices, the risk classification and the intended purpose.***
- 5. Irrespective of the description used in/with the certificate, the Notified Body shall be able to demonstrate on request, which (individual) devices are covered by the certificate. The Notified Body shall set out 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(s) covered by this certificate, another certificate according to this Regulation is required.***

7. *EU quality management system certificates for class A sterile devices shall include a statement that the Notified Body has audited the quality system restricted to the aspects of manufacture concerned with securing and maintaining sterile conditions.*
8. *For tracking information, when the certificate replaces a previous one (i.e. supplemented, modified, re-issued), a note like “this certificate replaces certificate xyz from dd/mm/yyyy”, with the identification of the change to be included.*

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 ;
- 3a. *the single registration number of the manufacturer according to Article 23a(2);*
4. date of issue;
5. date of expiry;
6. data needed for the *unambiguous* identification of the device(s) ~~or, as specified in Section 4 of Chapter I of this Annex~~ *categories of devices covered by the certificate, including the intended purpose of the device(s) and the GMDN code(s) or internationally recognised nomenclature code(s);*
7. ~~if applicable, the manufacturing facilities covered by the certificate;~~
- 7a. *if applicable, reference to a previous certificate as specified in Section I.8 of this Annex;*
8. reference to this Regulation and the relevant Annex according to which the conformity assessment has been carried out;
9. examinations and tests performed, e.g. reference to relevant ~~CS, standards~~ / test reports / audit report(s);
10. if applicable, reference to the relevant parts of the technical documentation or other certificates required for the placing on the market of the device(s) covered;
11. if applicable, information about the surveillance by the notified body;
12. conclusions of the notified body’s *conformity* assessment, ~~examination or inspection~~ *with regard to the relevant Annex;*
13. conditions for or limitations to the validity of the certificate;
14. legally binding signature of the notified body according to the applicable national law.

CLINICAL EVIDENCE PERFORMANCE EVALUATION AND POST-MARKET FOLLOW-UP

Part A: *Performance Evaluation and Clinical evidence Performance Studies*

~~The demonstration of conformity with the general safety and performance requirements set out in Annex I, under the normal conditions of use of the device, shall be based on clinical evidence.~~

~~The clinical evidence includes all the information supporting the scientific validity of the analyte, the analytical performance and, where applicable, the clinical performance of the device for its intended purpose as stated by the manufacturer.~~

1. ~~SCIENTIFIC VALIDITY DETERMINATION AND 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.

1.1. ~~Scientific validity determination~~

~~1.1.1. The scientific validity refers to the association of the analyte to a clinical condition or a physiological state.~~

- ~~1.1.2. The determination of the scientific validity may not be necessary where the association of the analyte to a clinical condition or a physiological state is well known, based on available information, such as peer reviewed literature, historical data and experience.~~
- ~~1.1.3. For a new analyte and/or a new intended purpose, the scientific validity shall be demonstrated based on one or a combination of the following sources:~~
- ~~- information on devices measuring the same analyte with the same intended purpose that have marketing history;~~
 - ~~- literature;~~
 - ~~- expert opinions;~~
 - ~~- results from proof of concept studies;~~
 - ~~- results from clinical performance studies.~~
- ~~1.1.4. The information supporting the scientific validity of the analyte shall be summarised as part of the clinical evidence report.~~

1.2. Performance evaluation plan

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

- a specification of the intended purpose of the device according to Article 2 point 2;*
- a specification of the characteristics of the device as described in Section 6 of Chapter II of Annex I and in point (ii) of Section 17.3.1. in 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 groups with clear indications, limitations and contraindications;*
- an identification of the general safety and performance requirements as described in Annex I section I and Annex I section II.6 that require support from relevant scientific validity and analytical and clinical performance data;*

- *a specification of methods (2.3), 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 the acceptability of the benefit/risk ratio for the intended purpose(s) and for the analytical and clinical performance of the device according to the state of the art in medicine;*
- *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 post-market performance follow-up (PMPF) planning according to 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.

~~The performance evaluation of a device is the process by which generated data are assessed and analysed to demonstrate the analytical performance, and where applicable the clinical performance of that device for its intended purpose as stated by the manufacturer.~~

~~Interventional performance studies and other clinical performance studies involving risks for the subjects of the studies shall only be performed once the analytical performance of the device has been established and determined to be acceptable.~~

1.2.1. Analytical performance

1.2.1.1. The analytical performance characteristics are described in point (a) of Section 6(1) of Annex I.

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

1.2.1.3. For novel devices, it may not be possible to demonstrate trueness since suitable higher order reference materials or a suitable comparative method may not be available. If there are no comparative methods, different approaches may be used (e.g. comparison to some other well documented method, comparison to the composite reference method). In the absence of such approaches, a clinical performance study comparing test performance to the current clinical standard practice would be needed.

1.2.1.4. The analytical performance data shall be summarised as part of the clinical evidence report.

1.2.2. Clinical performance

1.2.2.1. The clinical performance characteristics are described in point (b) of Section 6(1) of Annex I.

1.2.2.2. Clinical performance data may not be required for established and standardised devices and for devices classified as class A according to the rules set out in Annex VII.

1.2.2.3. Clinical performance of a device shall be demonstrated based on one or a combination of the following sources

- clinical performance studies;
- literature;
- experience gained by routine diagnostic testing.

1.2.2.4. Clinical performance studies shall be performed unless it is duly justified to rely on other sources of clinical performance data.

~~1.2.2.5. Clinical performance data shall be summarised as part of the clinical evidence report.~~

~~1.2.2.6. When the clinical performance evaluation includes a clinical performance study, the level of detail of the clinical performance study report referred to in Section 2.3.3 of this Annex will vary based on the risk class of the device determined according to the rules set out in Annex VII:~~

- ~~- For devices classified as class B according to the rules set out in Annex VII, the clinical performance study report may be limited to a summary of the study protocol, results and conclusion;~~
- ~~- For devices classified as class C according to the rules set out in Annex VII, the clinical performance study report shall include the method of data analysis, the study conclusion and the relevant details of the study protocol;~~
- ~~- For devices classified as class D according to the rules set out in Annex VII, the clinical performance study report shall include the method of data analysis, the study conclusion, the relevant details of the study protocol and the individual data points.~~

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

As a general methodological principle the manufacturer shall:

- identify through 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 available data by evaluating their suitability for establishing the safety and performance of the device;*
- generate any new or additional data needed to address outstanding issues.*

1.3.1. 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.

1.3.2. Demonstration of the analytical performance

The manufacturer shall demonstrate the analytical performance of the device according to all the parameters described in point (a) of Section 6(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, it may not be possible to demonstrate trueness since certified reference materials or reference measurement procedures may not be available. If there are no comparative methods, different approaches may be used if demonstrated to be appropriate (e.g. comparison to some other well-documented methods, comparison to the composite reference method). 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.

1.3.3. Demonstration of the clinical performance

The manufacturer shall demonstrate the clinical performance of the device according to all the parameters described in point (b) of Section 6(1) of Annex I, unless any omission 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 it is duly justified to rely on other sources of clinical performance data.

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

1.4. Clinical evidence and performance evaluation report

1.4.1. *The manufacturer shall assess all relevant scientific validity, analytical and clinical performance data to verify the conformity of his device with the general safety and performance requirements 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(s) 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(s) and safety will be achieved according to the state of the art in medicine.*

1.4.2. 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 these 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 post-market performance follow-up reports according to Part B of this Annex.*

1.4.3. *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 post-market performance follow-up 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 8(6). The Performance Evaluation Report shall be part of 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

Every step in the clinical performance study, from first consideration of the need and justification of the study to the publication of the results, shall be carried out in accordance with recognised ethical principles, ~~as for example those laid down in the World Medical Association Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects adopted by the 18 World Medical Assembly in Helsinki, Finland, in 1964 and last amended by the 59 World Medical Association General Assembly in Seoul, Korea, in 2008.~~

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. ~~The design of the study shall provide the data necessary to address the clinical performance of the device.~~

2.3.2. Clinical performance study ~~protocol~~ *plan*

Clinical performance studies shall be performed on the basis of an appropriate *a* 'clinical performance study ~~protocol~~ *plan*'.

The clinical performance study *plan* (*CPSP*) ~~protocol~~ shall set out how the study is intended to be conducted. It shall contain information about the study design such as the purpose, objectives, study population, description of test method(s) and interpretation of results, site training and monitoring, specimen type, specimen collection, preparation, handling and storage, inclusion and exclusion criteria, limitations, warning and precautions, data collection/management, data analysis, required materials, number of study sites and if applicable, clinical endpoints/outcomes, and requirements for patient follow-up. *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 information as laid down below. If part of this information is submitted in a separate document, it shall be referenced in the CPSP.*

- (a) *Identification of the clinical performance study and the CPSP.*
- (b) *Identification of the sponsor— 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 his contact person/ legal representative pursuant to Article 48 paragraph 3 established in the Union.*
- (c) *Information on investigator(s) (i.e. principal, coordinating, other; qualifications; contact details) and investigation site(s) (number, qualification(s), 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(s) or marker(s), 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 (eg 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, 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 in- 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 (e.g. randomisation) and management of potential confounding factors.*
- (k) *The analytical performance according to point a) of Section 6(1) of Annex I with justification for any omission.*
- (l) *Parameters of clinical performance according to point b) of Section 6(1) of Annex I to be determined, with justification for any omission; 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 to target population and, if applicable, information on vulnerable subjects involved (e.g. children, immuno-compromised, elderly, pregnant women);*
- (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 (incl. those according to Article 53) 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. Procedures for communication of test results outside the study, including communication of test results to the performance study subjects.*
- (y) Policy as regards the establishment of the clinical performance study report and publication of results in accordance with the legal requirements and the ethical principles referred to in Section 1 of Chapter I.*
- (z) List of the technical and functional features of the device indicating those that are covered by the performance study.*
- (aa) Bibliography.*

Where any of the above-mentioned elements are not deemed appropriate for inclusion in the CPSP due to the specific study design chosen (e.g. use of left-over samples versus interventional clinical performance studies), a justification shall be provided.

~~In addition, the clinical performance study protocol shall identify the key factors which may impact the completeness and significance of results, such as intended participant follow-up procedures, decision algorithms, discrepancy resolution process, masking/blinding, approaches to statistical analyses, and methods for recording endpoints/outcomes and, where appropriate, communication of test results.~~

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. CLINICAL EVIDENCE REPORT

3.1 ~~The clinical evidence report shall contain the scientific validity data, the analytical performance data and, where applicable, the clinical performance data. If the analytical performance data is determined to be sufficient to declare conformity with the general safety and performance requirements set out to in Annex I without the need for clinical performance data, a rationale should be documented and included in the clinical evidence report.~~

- 3.2 The clinical evidence report shall in particular outline:
- the justification for the approach taken to gather the clinical evidence;
 - the technology on which the device is based, the intended purpose of the device and any claims made about the device's clinical performance or safety;
 - the nature and extent of the scientific validity and the performance data that has been evaluated;
 - how the referenced information demonstrate the clinical performance and safety of the device in question;
 - the literature search methodology, if a literature review is the approach taken to gathering clinical evidence.
- 3.3 The clinical evidence and its documentation shall be updated throughout the life cycle of the device concerned with data obtained from the implementation of the manufacturer's post-market surveillance plan referred to in Article 8(5) which shall include a plan for the device post market follow up in accordance with Part B of this Annex.

Part B: Post-market performance follow-up

1. *Post-market performance follow-up (PMPF) is a continuous process to update the performance evaluation referred to in Article 47 and Part A of this Annex and shall be part of the manufacturer's post-market surveillance plan. To this end, the manufacturer*
Manufacturers shall *proactively* put in place procedures to enable them to collect and evaluate information relating to the *performance and relevant* scientific validity, as well as the analytical and clinical performance of their devices on the basis of data obtained from post-market follow-up *the use of a device which bear the CE marking, 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, the continued acceptability of the benefit/risk ratio and to detect emerging risks on the basis of factual evidence.*
2. ~~Where such information becomes available to the manufacturer, an appropriate risk assessment shall be conducted and the clinical evidence report shall be amended accordingly.~~

2a. The PMPF shall be performed pursuant to a documented method laid down in a PMPF plan.

2a.1. The PMPF plan shall specify the methods and procedures to proactively collect and evaluate 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 contraindications,**
- (c) identifying and analysing emergent risks on the basis of factual evidence,**
- (d) assuring the continued acceptability of the clinical evidence and of the benefit/risk ratio referred to in Sections 1 and 5 of Annex I, and**
- (e) identifying possible systematic misuse or off-label use of the device with a view to verify the correctness of its intended purpose.**

2a.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 (e.g. ring trials and other quality assurance activities, epidemiological studies, evaluation of suitable patient or disease registers, genetic data banks 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 1.5 of Part A of this Annex and to the risk management referred to in Section 2 of Annex I;**
- (e) the specific objectives to be addressed by the PMPF;**
- (f) an evaluation of the performance data related to equivalent or similar devices, and the current state of the art;**
- (g) reference to relevant CS, standards and guidance on PMPF;**
- (h) a detailed and adequately justified time schedule for PMPF activities (e.g. analysis of PMPF data and reporting) to be undertaken by the manufacturer.**

3. ~~Where changes to devices are necessary, the conclusion of the post market follow-up shall be taken into account for the clinical evidence referred to in Part A of this Annex and for the risk assessment referred to in Section 2 of Annex I. If necessary, the clinical evidence or risk management shall be updated and/or corrective actions be implemented.~~
- 3a. ***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.***
4. ~~Any new intended purpose of a device shall be supported by an updated clinical evidence report.~~
- 4a. ***The conclusions of the PMPF evaluation report shall be taken into account for the performance evaluation referred to in Article 47 and Part A of this Annex and in the risk management referred to in Section 2 of Annex I. If through the PMPF the need for preventive and/or corrective measures has been identified, the manufacturer shall implement them.***
5. ***If PMPF is not deemed appropriate for a specific device then a justification shall be provided and documented within the performance evaluation report.***

INTERVENTIONAL CLINICAL PERFORMANCE STUDIES AND OTHER ~~CLINICAL~~ PERFORMANCE STUDIES INVOLVING RISKS FOR THE SUBJECTS OF THE STUDIES

I. Documentation regarding the application for interventional clinical performance studies and other ~~clinical~~ performance studies involving risks for the subjects of the studies

For devices ~~for performance evaluation~~ intended to be used in the context of interventional clinical performance studies or other ~~clinical~~ performance studies involving risks for the subjects of the studies the sponsor shall draw up and submit the application in accordance with Article 49 accompanied by the documentation as laid down below:

1. Application form

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

- 1.1. Name, address and contact details of the sponsor and, if applicable, name, address and contact details of his contact person *or legal representative according to Article 48(3)* established in the Union.
- 1.2. If different from the above, name, address and contact details of the manufacturer of the device intended for performance evaluation and, if applicable, of his authorised representative.
- 1.3. Title of the ~~clinical~~ performance study.
- 1.4. Single identification number in accordance with Article 49(1).
- 1.5. Status of the ~~clinical~~ performance study (*e.g. i.e.* first submission, resubmission, significant amendment);
 - 1.5a. *Details/reference to the performance study plan (e.g. including details of the design phase of the performance study).*

- 1.6. If resubmission with regard to same device, previous date(s) and reference number(s) of earlier submission(s) or in the case of significant amendment, reference to the original submission. *The sponsor shall identify all of the changes from the previous submission together with a rationale for those changes, in particular, whether any changes have been made to address outcomes of previous competent authority or ethics committee reviews.*
- 1.7. If parallel submission for a clinical trial on a medicinal product in accordance with Regulation (EU) No 536/2014 [~~Ref. of future Regulation on clinical trials~~], reference to the official registration number of the clinical trial.
- 1.8. Identification of the Member States, EFTA countries, Turkey and third countries in which the clinical performance study shall be conducted as part of a multicentre/multinational study at the time of application.
- 1.9. Brief description of the device for performance evaluation, *its classification and other information necessary for the identification of the device and device type* (~~e.g. name, GMDN code or internationally recognised nomenclature code, intended purpose, risk class and applicable classification rule according to Annex VII~~).
- 1.10. Summary of the clinical performance study *plan protocol*.
- 1.11. If applicable, information regarding a comparator *device, its classification and other information necessary for the identification of the comparator device*.
 - 1.11a. *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.*
 - 1.12. *Details of the anticipated start date and duration of the performance study.*
 - 1.13. *Details to identify the notified body, if the sponsor is using one at the time of application for the performance study.*
 - 1.13a. *Confirmation that the sponsor is aware that the competent authority may contact the ethics committee that is assessing or has assessed the application.*
 - 1.14. *The statement referred to in Section 4.1 of this Annex.*

2. Investigator's Brochure

The investigator's brochure (IB) shall contain the information on the device for performance evaluation that is relevant for the study and available at the time of application. ***Any updates to the brochure 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 according to Annex VII, 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 use, including storage and handling requirements, as well as the label and instructions for use to the extent that this information is available. ***In addition, information relating to any relevant training required.***
- 2.3. ***Analytical performance*** ~~Pre-clinical testing and experimental data.~~
- 2.4. Existing clinical data, in particular the following:
 - relevant ***peer reviewed*** scientific literature ***and consensus expert opinions/positions from relevant professional associations*** available 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 equivalent or similar devices ***including details of their similarities and differences*** ~~of the same manufacturer, including length of time on the market and a review of performance and safety related issues and any corrective actions taken.~~
- 2.5. Summary of the risk/benefit 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 the tissues, cells and substances.
- 2.7. Reference to harmonised or other internationally recognised standards complied with in full or in part. ***A list detailing how the relevant general safety and performance requirements set out in Annex I are fulfilled, including the standards and Common Specifications 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 these standards and CS have not or only been partly fulfilled or are lacking.***
- 2.7a. ***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.***
- 2.8. ~~A clause that any updates to the IB or any other relevant information that is newly available shall be brought to the attention of the investigators.~~

3. **Clinical performance study ~~protocol~~ plan** as referred to in Section 2.3.2. of Annex XII.

4. **Other information**

- 4.1. A signed statement by the natural or legal person responsible for the manufacture of the device for performance evaluation that the device in question conforms to the general safety and performance requirements apart from the aspects covered by the clinical performance study and that, with regard to these aspects, every precaution has been taken to protect the health and safety of the subject. ~~This statement may be supported by an attestation issued by a notified body.~~
- 4.2. Where applicable according to national law, a copy of the opinion(s) of the ethics committee(s) concerned ~~as soon as available~~. ***When according to national law the opinion(s) of the ethics committee(s) is not required at the time of the submission of the application, copy of the opinion(s) of ethics committee(s) shall be submitted as soon as available.***

- 4.3. Proof of insurance cover or indemnification of subjects in case of injury, according to ~~the Article 48c and the corresponding~~ national law *legislation*.
- 4.4. Documents ~~and procedures~~ 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 concerned in clinical performance studies;
 - a description of measures that will be implemented in case of 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.*

II. Other sponsor's obligations

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 evaluation, this obligation may be fulfilled by that person on behalf of the sponsor.
2. The *sponsor shall have an agreement in place to ensure that the serious adverse reportable events shall be provided are reported* by the investigator(s) *to the sponsor in a timely manner* ~~conditions~~.

3. The documentation mentioned in this Annex shall be kept for a period of time of at least five years after the clinical performance study with the device in question has ended, or, when the device is subsequently placed on the market, at least five years after the last device has been placed on the market.

Each Member State shall make provision that this documentation is kept at the disposal of the competent authorities for the period indicated in the preceding paragraph 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 from 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 establish follow-up measures for the investigation subjects.***

ANNEX XIV

CORRELATION TABLE⁴

| Directive 98/79/EC | This Regulation |
|-----------------------------|---|
| Article 1(1) | Article 1(1) |
| Article 1(2) | Article 2 |
| Article 1(3) | Number (36) of Article 2 |
| Article 1(4) | - |
| Article 1(5) | Article 4(4) and (5) |
| Article 1(6) | Article 1(6) |
| Article 1(7) | Article 1(4) |
| Article 2 | Article 4(1) |
| Article 3 | Article 4(2) |
| Article 4(1) | Article 20 |
| Article 4(2) | Article 17(1) |
| Article 4(3) | Article 17(3) |
| Article 4(4) | Article 8(7) |
| Article 4(5) | Article 16(6) |
| Article 5(1) | Article 6(1) |
| Article 5(2) | - |
| Article 5(3) | Article 7 |
| Article 6 | - |
| Article 7 | Article 84 |
| Article 8 | Articles 67 to 70 |
| Article 9(1) 1 subparagraph | Article 40(5) 1 subparagraph |
| Article 9(1) 2 subparagraph | Article 40(3) 2 subparagraph and (4) 2 subparagraph |

⁴ This annex has not been updated - it reflects the Cion proposal.

| | |
|------------------|---|
| Article 9(2) | Article 40(2) |
| Article 9(3) | Article 40(3) |
| Article 9(4) | Article 40(7) |
| Article 9(5) | - |
| Article 9(6) | Article 9(3) |
| Article 9(7) | Article 8(4) |
| Article 9(8) | Article 41(1) |
| Article 9(9) | Article 41(3) |
| Article 9(10) | Article 43(2) |
| Article 9(11) | Article 40(8) |
| Article 9(12) | Article 45(1) |
| Article 9(13) | Article 5(2) |
| Article 10 | Article 23 |
| Article 11(1) | Numbers (43) and (44) of Article 2, Article 59(1) and Article 61(1) |
| Article 11(2) | Article 59(3) and Article 61(1) 2 subparagraph |
| Article 11(3) | Article 61(2) and (3) |
| Article 11(4) | - |
| Article 11(5) | Article 61(3) and Article 64 |
| Article 12 | Article 25 |
| Article 13 | Article 72 |
| Article 14(1)(a) | Article 39(4) |
| Article 14(1)(b) | - |
| Article 14(2) | - |
| Article 14(3) | - |
| Article 15(1) | Article 31 and Article 32 |
| Article 15(2) | Article 27 |
| Article 15(3) | Article 33(1) and Article 34(2) |
| Article 15(4) | - |
| Article 15(5) | Article 43(4) |

| | |
|---------------|----------------------------------|
| Article 15(6) | Article 43 (3) |
| Article 15(7) | Articles 29(2) and Article 33(1) |
| Article 16 | Article 16 |
| Article 17 | Article 71 |
| Article 18 | Article 73 |
| Article 19 | Article 80 |
| Article 20 | Article 75 |
| Article 21 | - |
| Article 22 | - |
| Article 23 | Article 90 |
| Article 24 | - |
