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Drugs Controller General (India)
Directorate General of Health Services
FDA Bhawan, Kotla Road, New Delhi

Notice

Subject: Draft Guidance Documents on Essential Principles for safety and performance of medical devices as per Medical Devices Rules, 2017-Reg.

The Medical Devices Rules, 2017 has already been published which is to be implemented w.e.f. 01.01.2018. Under the provisions of Rule 6 of the Chapter II of the said rules, a Guidance documents on "*Essential Principles for Safety and performance of medical devices*" is to be issued by the MoH&FW, Government of India. In this regard, a draft has been prepared in consultation with the Medical Devices and IVD industry stakeholders.

In view of the above, all the stakeholders are hereby requested to give their comments/suggestions within a period of three weeks either through e-mail to ddcimd-cdsco@nic.in or by post to the DDCI (MD), CDSCO, HQ, FDA Bhawan, Kotla Road, New-Delhi-110002 for finalization of the said Guidance Document.

(Dr. G.N. Singh)
Drugs Controller General (I)

To,
1. **All State/UT Drugs Controllers.**
2. **Medical Devices and IVD industry Associations.**

Copy to:
1. **PS to JS(R).**
2. **CDSCO, Website.**

Enclosure:
Draft Guidance document on "*Essential Principles for safety and performance of medical devices*".

MINISTRY OF HEALTH AND FAMILY WELFARE
GOVERNMENT OF INDIA

DRAFT GUIDANCE DOCUMENT

ON

ESSENTIAL PRINCIPLES FOR SAFETY AND PERFORMANCE OF MEDICAL DEVICES

Preface

This document is prepared under the provisions of rule 6 of Medical Devices Rules, 2017 to provide binding guidance for use in the manufacturing of medical devices which are intended to be sold in India. This document provides an overview on meeting the essential principles for safety and performance of medical devices. This document does not dictate how a manufacturer should prove that their medical device has met the essential principles laid down in this document, hence providing flexibility to the manufacturers and catering to technological advances and changes in the development of new medical devices.

1. Introduction

This guidance document describes fundamental design and manufacturing requirements, referred to as 'Essential Principles for Safety and Performance' that, when met, indicate a medical device including *in vitro* diagnostic medical device (hereafter referred as IVD medical device) is safe and performs to its specification.

There are seven general requirements of safety and performance that apply to all medical devices including IVD medical devices as specified in section 4 of this document.

There are further design and manufacturing requirements of safety and performance, some of which are relevant to each medical device. The design and manufacturing requirements in this document are grouped in following categories.

- chemical, physical and biological properties;
- infection and microbial contamination;
- manufacturing and environmental properties;
- devices incorporating a substance considered to be a medicinal product or drug;
- devices incorporating materials of biological origin;
- devices with a diagnostic or measuring function;
- devices that incorporate software and standalone medical device software;
- active medical devices and devices connected to them;
- environmental properties;
- protection against radiation;
- protection against mechanical risks;
- protection against the risks posed to the patient by supplied energy or substances;
- protection against the risks posed to the patient for devices for self-testing or self-administration or intended by the manufacturer for use by lay persons;
- information supplied by the manufacturer i.e. Label and Instruction for Use;
- performance evaluation including analytical performance and where appropriate, clinical evaluation.

In addition to the general essential principles as specified in the section 4 of this document, above listed additional essential principles for safety and performance which need to be considered during the design and manufacturing process are further specified separately for,-

(i) medical devices other than IVD medical devices, and
(ii) IVD medical devices.

Note: ***The manufacturer will select which of the design and manufacturing requirements are relevant to a particular medical device, documenting the reasons for excluding the others.***

2. Applicable Standards used to meet essential principles for safety and performance

(A) A standard is a document, established by consensus and approved by a recognised body that provides, for common and repeated use, rules, guidelines or characteristics for activities or their results, aimed at the achievement of the optimum degree of order in a given context. Primarily, there are three types of standards:

(i) **Basic Standards or Horizontal Standards:** Standard indicating fundamental concepts, principles and requirements, with regard to general safety and performance aspects which are applicable to all kinds or a wide range of products and/or processes (e.g., standards concerning risk management, clinical investigation and the quality management system for the manufacture of medical devices).

(ii) **Group Standards or Semi-Horizontal Standards**: Standard indicating aspects applicable to families of similar products and/or processes making reference as far as possible to basic standards (e.g., standards concerning sterile medical devices, electrically-powered medical devices, stability of *in vitro* diagnostics reagents).

(iii) **Product Standard or Vertical Standard:** Standard indicating necessary safety and performance aspects of specific products and/or processes, making reference, as far as possible, to basic standards and group standards (e.g., standards for

infusion pumps, for anaesthetic machines or for blood glucose meters for self-testing).

(B) **Source of standards:**

Selection of Medical Devices Standards, as referred to in clause (A), which are used to establish conformity with the essential principles laid down in this document shall be as per the provisions of rule 7 of the Medical Devices Rules, 2017.

3. Definitions

(i) "Analytical performance" means the ability of an IVD medical device to detect or measure a particular analyte.

(ii) "Clinical data" means safety or performance information that is generated from the clinical use of a medical device.

(iii) "Clinical evaluation" means the assessment and analysis of clinical data pertaining to a medical device to verify the clinical safety and performance of the device when used as intended by the manufacturer.

(iv) "Clinical performance of an IVD medical device" means the ability of an IVD medical device to yield results that are correlated with a particular clinical condition or physiological state in accordance with target population and intended user.

(v) "Harm" means injury or damage to the health of people or damage to property or the environment.

(vi) "Hazard**"** potential source of harm.

(vii) "Lay person" means an individual that does not have formal training in a relevant field or discipline.

(viii)"Risk" means combination of the probability of occurrence of harm and the severity of that harm.

(ix) Words and expressions used but not defined in this document shall have the meanings respectively assigned to them in the Medical Devices Rules, 2017.

4. Essential Principles applicable to all medical devices including IVD medical devices - General Principles

4. 1 Medical devices should be designed and manufactured in such a way that, when used under the conditions and for the purposes intended and, where applicable, by virtue of the technical knowledge, experience, education or training, and the medical and physical conditions of intended users, they will perform as intended by the manufacturer and not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.

4. 2 The solutions adopted by the manufacturer for the design and manufacture of the devices should conform to safety principles, taking account of the generally acknowledged state of the art. When risk(s) reduction is required, the manufacturer should control the risk(s) so that the residual risk associated with each hazard is judged acceptable. The manufacturer should apply the following principles in the priority order listed:

- identify known or foreseeable hazards and estimate the associated risks arising from the intended use and foreseeable misuse;
- eliminate risks as far as reasonably practicable through inherently safe design and manufacture;
- reduce as far as reasonably practicable the remaining risks by taking adequate protection measures, including alarms; and
- inform users of any residual risks.

4. 3 Medical devices should achieve the performance intended by the manufacturer and be designed, manufactured and packaged in such a way that, during normal conditions of use, they are suitable for their intended purpose.

4. 4 The characteristics and performances referred to in clauses (4.1), (4.2) and (4.3) should 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.

4. 5 Medical devices should be designed, manufactured and packaged in such a way that their characteristics and performances during their intended use will not be adversely affected by transport and storage conditions (for example, fluctuations of temperature and humidity) taking account of the instructions and information provided by the manufacturer.

4. 6 All known and foreseeable risks, and any undesirable effects, should be minimised and be acceptable when weighed against the benefits of the intended performance of medical devices during normal conditions of use.

4. 7 Every medical device requires clinical evidence, appropriate for its intended use and classification of the medical device, demonstrating that the device complies with the applicable provisions of the essential principles.

5. Essential Principles applicable to medical devices other than IVD medical devices

The design and manufacturing principles listed in this Section are additional to the general principles of safety and performance listed in Section 4.

5. 1 Chemical, physical and biological properties:

5.1. 1 The devices should be designed and manufactured in such a way as to ensure the characteristics and performance. Particular attention should be paid to,-

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

(b) the compatibility between the materials used and biological tissues, cells, and body fluids taking account of the intended purpose of the device;

(c) the choice of materials used, reflecting, where appropriate, matters such as hardness, wear and fatigue strength.

5.1. 2 The devices should be designed, manufactured and packaged in such a way as to minimize the risk posed by contaminants and residues to the persons involved in the transport, storage and use of the devices and to patients, taking account of the intended purpose of the device. Particular attention should be paid to tissues exposed and to the duration and frequency of exposure.

5.1. 3 The devices should be designed and manufactured in such a way that they can be used safely with the materials, substances and gases with which they enter into contact during their normal use or during routine procedures; if the devices are intended to administer medicinal products they should be designed and manufactured in such a way as to be compatible with the medicinal products concerned according to the provisions and restrictions governing these products and that their performance is maintained in accordance with the intended use.

5.1. 4 The devices should be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate the risks posed by substances that may leach or leak from the device. Special attention shall be given to substances which are carcinogenic, mutagenic or toxic to reproduction.

5.1. 5 Devices should be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate 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.

5. 2 Infection and microbial contamination:

5.2.1 The devices and manufacturing processes should be designed in such a way as to eliminate or to reduce as far as reasonably practicable and appropriate the risk of infection to patients, users and, where applicable, other persons. The design should,-

(a) allow easy handling, and, where necessary;

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

(c) prevent microbial contamination of the device or specimen, where applicable, by the patient, user or other person.

5.2.2 Devices labelled as having a special microbiological state should be designed, manufactured and packaged to ensure they remain so when placed on the market and remain so under the transport and storage conditions specified by the manufacturer.

5.2.3 Devices delivered in a sterile state should be designed, manufactured and packaged in a non-reusable pack, and/or according to appropriate procedures, to ensure that they are sterile when placed on the market and remain sterile, under the transport and storage conditions indicated by the manufacturer, until the protective packaging is damaged or opened.

5.2.4 Devices labelled either as sterile or as having a special microbiological state should have been processed, manufactured and, if applicable, sterilized by appropriate, validated methods.

5.2.5 Devices intended to be sterilized should be manufactured in appropriately controlled (e.g. environmental) conditions.

5.2.6 Packaging systems for non-sterile devices should maintain the integrity and cleanliness of the product and, if the devices are to be sterilized prior to use, minimize the risk of microbial contamination; the packaging system should be suitable taking account of the method of sterilization indicated by the manufacturer.

5.2.7 The packaging or labelling of the device should distinguish between identical or similar products placed on the market in both sterile and non-sterile condition.

5. 3 Medical devices incorporating a substance considered to be a medicinal product or drug:

5.3.1 Where a medical device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product or drug as defined in the Drugs and Cosmetics Act, 1940 and which is liable to act upon the body with action ancillary to that of the device, the safety, quality and performance of the device as a whole should be verified, as well as the safety, quality and efficacy of the substance in the specific application.

5. 4 Medical devices incorporating materials of biological origin:

5.4.1 Where a medical device incorporates substances of biological origin, the risk of infection must be reduced as far as reasonably practicable and appropriate by selecting appropriate sources, donors and substances and by using, as appropriate, validated inactivation, conservation, test and control procedures.

5.4.2 For medical devices incorporating non-viable tissues, cells and substances of animal origin should originate from animals that have been subjected to veterinary controls and surveillance adapted to the intended use of the tissues. The manufacturer is required to retain information on the geographical origin of the animals. Processing, preservation, testing and handling of tissues, cells and substances of animal origin should be carried out so as to provide optimal safety. In particular, safety with regard to viruses and other transmissible agents should be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.

Explanation: For the purpose of this clause, veterinary controls shall also include that an animal source should be tested and to be free from Transmissible spongiform encephalopathies (TSEs) and Bovine spongiform encephalopathy (BSEs).

5.4.3 For medical devices incorporating cells, tissues and derivatives of microbial or recombinant origin, the selection of sources or donors, the processing, preservation, testing and handling of cells, tissues and derivatives of such origin should be carried out so as to provide optimal safety. In particular, safety with regard to viruses and other transmissible agents should be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.

5.4.4 For medical devices incorporating non-viable human tissues, cells and substances, the selection of sources, donors or substances of human origin, the

processing, preservation, testing and handling of tissues, cells and substances of such origin should be carried out so as to provide optimal safety. In particular, safety with regard to viruses and other transmissible agents should be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.

5. 5 Manufacturing and Environmental properties:

5.5. 1 If the device is intended for use in combination with other devices or equipment the whole combination, including the connection system should be safe and should not impair the specified performance of the devices. Any restrictions on use applying to such combinations should be indicated on the label and/or in the instructions for use. Connections which the user has to handle, such as fluid, gas transfer or mechanical coupling, should be designed and constructed in such a way as to minimize all possible risks from incorrect connection.

5.5. 2 Devices should be designed and manufactured in such a way as to remove or reduce as far as reasonably practicable and appropriate:

(i) the risk of injury to the patient, user or other persons in connection with their physical and ergonomic features;

(ii) the risk of use error due to the ergonomic features, human factors and the environment in which the device is intended to be used;

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

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

(v) the risk associated with the possible negative interaction between software and the environment within which it operates and interacts;

(vi) the risks of accidental penetration of substances into the device;

(vii) the risks of reciprocal interference with other devices normally used in the investigations or for the treatment given; risks arising where maintenance or calibration are not possible (as with implants), from ageing of materials used or loss of accuracy of any measuring or control mechanism.

5.5. 3 Devices should be designed and manufactured in such a way as to minimize the risks of fire or explosion during normal use and in single fault condition. Particular attention should be paid to devices whose intended use includes exposure to or use in association with flammable substances or substances which could cause combustion.

5.5. 4 Devices should 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.

5.5. 5 Devices should be designed and manufactured in such a way as to facilitate the safe disposal of any waste substances.

5. 6 Devices with a diagnostic or measuring function:

5.6.1 Diagnostic devices should be designed and manufactured in such a way as to provide sufficient accuracy, precision and stability for their intended use, based on appropriate scientific and technical methods. In particular the design should

address sensitivity, specificity, trueness, repeatability, and reproducibility, control of known relevant interference and limits of detection, as appropriate.

5.6.2 Where the performance of devices depends on the use of calibrators or control materials, the traceability of values assigned to such calibrators or control materials should be assured through a quality management system.

5.6.3 Any measurement, monitoring or display scale should be designed in line with ergonomic principles, taking account of the intended purpose of the device.

5.6.4 Wherever possible values expressed numerically should be in commonly accepted, standardized units, and understood by the users of the device.

5. 7 Protection against radiation:

5.7.1 General:

Devices should be designed and manufactured and packaged in such a way that exposure of patients, users and other persons to any emitted radiation should be reduced as far as reasonably practicable and appropriate, compatible with the intended purpose, whilst not restricting the application of appropriate specified levels for therapeutic and diagnostic purposes.

5.7.2 Intended radiation:

Where devices are designed to emit hazardous, or potentially hazardous, levels of visible or invisible radiation necessary for a specific medical purpose the benefit of which is considered to outweigh the risks inherent in the emission, it should be possible for the user to control the emissions. Such devices should be designed and manufactured to ensure reproducibility of relevant variable parameters within acceptable tolerance. Where devices are intended to emit potentially hazardous, visible or invisible radiation, they should be fitted, where reasonably practicable, with visual displays or audible warnings of such emissions.

5.7.3 Unintended radiation:

Devices should be designed and manufactured in such a way that exposure of patients, users and other persons to the emission of unintended, stray or scattered radiation is reduced as far as reasonably practicable and appropriate.

5.7.4 Ionizing radiation:

(a) Devices intended to emit ionizing radiation should be designed and manufactured in such a way as to ensure that, where reasonably practicable, the quantity, geometry and energy distribution (or quality) of radiation emitted can be varied and controlled taking into account the intended use.

(b) Devices emitting ionizing radiation intended for diagnostic radiology should be designed and manufactured in such a way as to achieve appropriate image and/or output quality for the intended medical purpose whilst minimizing radiation exposure of the patient and user.

(c) Devices emitting ionizing radiation, intended for therapeutic radiology should be designed and manufactured in such a way as to enable reliable monitoring and control of the delivered dose, the beam type and energy and where appropriate the energy distribution of the radiation beam.

5.7.5 The operating instructions for a medical device that emits radiation must include detailed information about the following matters:

(a) the nature of the radiation emitted;

(b) the means by which patients and users can be protected from the radiation;

(c) ways to avoid misusing the device; and

(d) ways to eliminate any risks inherent in the installation of the device.

5. 8 Medical devices that incorporate software and standalone medical device software:

5.8.1 Devices incorporating electronic programmable systems, including software, or standalone software that are devices in themselves, should be designed to ensure repeatability, reliability and performance according to the intended use. In the

event of a single fault condition, appropriate means should be adopted to eliminate or reduce as far as reasonably practicable and appropriate consequent risks.

5.8.2 For devices which incorporate software or for standalone software that are devices in themselves, the software must be validated according to the state of the art taking into account the principles of development lifecycle, risk management, verification and validation.

5. 9 Active medical devices and devices connected to them:

5.9.1 For active medical devices, in the event of a single fault condition, appropriate means should be adopted to eliminate or reduce as far as reasonably practicable and appropriate consequent risks.

5.9.2 Devices where the safety of the patients depends on an internal power supply should be equipped with a means of determining the state of the power supply.

5.9.3 Devices where the safety of the patients depends on an external power supply should include an alarm system to signal any power failure.

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

5.9.5 Devices should be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate the risks of creating electromagnetic interference which could impair the operation of this or other devices or equipment in the usual environment.

5.9.6 Devices should 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.

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

5. 10 Protection against mechanical risks:

5.10.1 Devices should be designed and manufactured in such a way as to protect the patient and user against mechanical risks connected with, for example, resistance to movement, instability and moving parts.

5.10.2 Devices should be designed and manufactured in such a way as to reduce to the lowest practicable 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.

5.10.3 Devices should be designed and manufactured in such a way as to reduce to the lowest practicable 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.

5.10.4 Terminals and connectors to the electricity, gas or hydraulic and pneumatic energy supplies which the user has to handle should be designed and constructed in such a way as to minimize all possible risks.

5.10.5 Devices should be designed and manufactured in such a way as to reduce to the lowest practicable level, the risk of error when certain parts within the device are intended to be connected or reconnected before or during use.

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

5. 11 Protection against the risks posed to the patient or user by supplied energy or substances:

5.11.1 Devices for supplying the patient with energy or substances should be designed and constructed in such a way that the delivered amount can be set and maintained accurately enough to guarantee the safety of the patient and of the user.

5.11.2 Devices should be fitted with the means of preventing and/or indicating any inadequacies in the delivered amount which could pose a danger. Devices should incorporate suitable means to prevent, as far as possible, the accidental release of dangerous levels of energy or substances from an energy and/or substance source.

5.11.3 The function of the controls and indicators should be clearly specified on the devices. Where a device bears instructions required for its operation or indicates operating or adjustment parameters by means of a visual system, such information should be understandable to the user and, as appropriate, the patient.

5. 12 Protection against the risks posed by medical devices intended by the manufacturer for use by lay persons:

5.12.1 Devices for use by lay persons should be designed and manufactured in such a way that they perform appropriately for their intended purpose taking into account the skills and the means available to lay persons and the influence resulting from variation that can reasonably be anticipated in the layperson's technique and environment. The information and instructions provided by the manufacturer should be easy for the lay person to understand and apply.

5.12.2 Devices for use by lay persons should be designed and manufactured in such a way as to reduce as far as reasonably practicable the risk of error during use by the lay person in the handling of the device and also in the interpretation of results.

5.12.3 Devices for use by lay persons should, where reasonably possible, include a procedure by which the lay person can verify that, at the time of use, the product will perform as intended by the manufacturer.

5. 13 Label, direction or Instructions For Use (IFU):

5.13.1 Users should be provided with the information needed to identify the manufacturer, to use the device safely and to ensure the intended performance, taking account of their training and knowledge.

5.13.2 This information should be easily understood and detailed information for labelling should be incorporated as provided in the Chapter VI: labelling of Medical device, of the Medical Device Rules, 2017.

5. 14 Clinical evaluation:

5.14.1 For all medical devices, the demonstration of conformity with essential principles includes a clinical evaluation. The clinical evaluation should review clinical data in the form of any,

(a) clinical investigation reports; or

(b) literature reports/reviews; or

(c) clinical experience,

to establish that a favorable benefit-risk ratio exists for the device.

5.14.2 Clinical investigations:

Clinical Investigations on human subjects should be carried out in accordance with the provisions of Medical Devices Rules, 2017. This includes every step in the clinical investigation from first consideration of the need and justification of the study to publication of the results.

6. Essential Principles applicable to IVD medical devices

The design and manufacturing principles listed in this Section are additional to the general principles of safety and performance listed in Section 4.

6.1 Chemical, physical and biological properties:

6.1.1 The IVD medical devices should be designed and manufactured in such a way as to ensure the characteristics and performance referred to in Section 4. Particular attention should be paid to the possibility of impairment of analytical performance due to incompatibility between the materials used and the specimens and/or analyte (measurand) to be detected (such as biological tissues, cells, body fluids and microorganisms), taking account of its intended purpose.

6.1.2 The IVD medical devices should be designed, manufactured and packaged in such a way as to minimize the risk posed by contaminants and residues to the persons involved in the transport, storage and use of the devices and to patients, taking account of the intended purpose of the device.

6.1.3 The IVD medical devices should be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate the risks posed by substances that may leach or leak from the IVD medical device. Special attention should be given to substances which are carcinogenic, mutagenic or toxic to reproduction.

6.1.4 IVD medical devices should be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate risks posed by the unintentional ingress or egress of substances into or from the IVD medical device taking into account the device and the nature of the environment in which it is intended to be used.

6.2 Infection and microbial contamination:

6.2.1 The IVD medical devices and manufacturing processes should be designed in such a way as to eliminate or to reduce as far as reasonably practicable and appropriate

the risk of infection to user, professional or lay, or, where applicable, other person. The design should:

(a) allow easy and safe handling;

and, where necessary:

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

(c) prevent microbial contamination of the IVD medical device or specimen where applicable, by the user, professional or lay, or other person.

6.2.2 IVD medical devices labelled either as sterile or as having a special microbiological state should be designed, manufactured and packaged to ensure 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.

6.2.3 IVD medical devices labelled either as sterile or as having a special microbiological state should have been processed, manufactured and, if applicable, sterilized by appropriate, validated methods.

6.2.4 IVD medical devices intended to be sterilized should be manufactured in appropriately controlled (e.g. environmental) conditions.

6.2.5 Packaging systems for non-sterile IVD medical devices should maintain the integrity and cleanliness of the device.

6.3 IVD medical devices incorporating materials of biological origin:

6.3.1 Where IVD medical devices include tissues, cells and substances originating from animals, the processing, preservation, testing and handling of tissues, cells and substances of animal origin should 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 should be addressed by implementation of

validated methods of elimination or inactivation in the course of the manufacturing process. This may not apply to certain IVD medical devices if the activity of the virus and other transmissible agent are integral to the intended purpose of the IVD medical device or when such elimination or inactivation process would compromise the performance of the IVD medical device.

6.3.2 Where IVD medical devices include human tissues, cells and 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 should 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 should be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process. This may not apply to certain IVD medical devices if the activity of the virus and other transmissible agent are integral to the intended purpose of the IVD medical device or when such elimination or inactivation process would compromise the performance of the IVD medical device.

6.3.3 Where IVD medical devices include cells and substances of microbial origin, the processing, preservation, testing and handling of cells and substances should 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 should be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process. This may not apply to certain IVD medical devices if the activity of the virus and other transmissible agent are integral to the intended purpose of the IVD medical device or when such elimination or inactivation process would compromise the performance of the IVD medical device.

6.4 Environmental properties:

6.4.1 If the IVD medical device is intended for use in combination with other devices or equipment, the whole combination, including the connection system should not impair the specified performance of the devices. Any restrictions on use applying

to such combinations should be indicated on the label and/or in the instructions for use.

6.4.2 IVD medical devices should be designed and manufactured in such a way as to remove or reduce as far as reasonably practicable and appropriate:

(i) the risk of injury to user, professional or lay, or other person in connection with their physical and ergonomic features;

(ii) the risk of use error due to the ergonomic features, human factors and the environment in which the IVD medical device is intended to be used;

(iii) risks connected with reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, pressure, humidity, temperature or variations thereof;

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

(v) the risk associated with the possible negative interaction between software and the environment within which it operates and interacts;

(vi) the risks of accidental penetration of substances into the IVD medical device;

(vii) the risk of incorrect identification of specimens or samples;

(viii) the risks of reasonably foreseeable interference with other devices such as carry over between IVD medical devices.

6.4.3 IVD medical devices should be designed and manufactured in such a way as to minimize the risks of fire or explosion during normal use and in single fault condition. Particular attention should be paid to IVD medical devices whose intended use includes exposure to or use in association with flammable substances or substances which could cause combustion.

6.4.4 IVD medical devices should 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.

6.4.5 IVD medical devices should be designed and manufactured in such a way as to facilitate the safe disposal of any waste substances.

6.5 Performance Evaluation:

6.5.1 IVD medical devices should be designed and manufactured in such a way that the performance evaluation supports the intended use, based on appropriate scientific and technical methods. In particular, where appropriate, the design should address sensitivity, specificity, accuracy which is trueness and precision (repeatability and reproducibility), control of known relevant interference and limits of detection.

These performance evaluation need to be maintained during the lifetime of the IVD medical device as indicated by the manufacturer.

6.5.2 Where the performance of devices depends on the use of calibrators and/or control materials, the traceability of values assigned to such calibrators and/or control materials should be assured through available reference measurement procedures and/or available reference materials of a higher order.

6.5.3 Wherever possible values expressed numerically should be in commonly accepted, standardized units, and understood by the users of the device.

6.6 Protection against radiation:

6.6.1 IVD medical devices should be designed, manufactured and packaged in such a way that exposure of user, professional or lay, or other person to the emitted radiation (intended, unintended, stray or scattered) is reduced as far as reasonably practicable and appropriate.

6.6.2 When IVD medical devices are intended to emit potentially hazardous, visible and/or invisible radiation, they should as far as reasonably practicable and appropriate 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.

6.7 IVD medical devices that incorporate software and standalone IVD medical device software:

6.7.1 For IVD medical devices which incorporate software or for standalone software that are IVD medical devices in themselves, the software must be validated according to the state of the art taking into account the principles of development lifecycle, risk management, verification and validation.

6.8 IVD medical devices connected to, or equipped with, an energy source:

6.8.1 IVD medical devices where the safety of the patient depends on an internal power supply in the IVD medical device, should be equipped with a means of determining the state of the power supply.

6.8.2 IVD medical devices should be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate the risks of creating electromagnetic interference which could impair the operation of this or other devices or equipment in the usual environment.

6.8.3 IVD medical devices should 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.

6.8.4 IVD medical devices should be designed and manufactured in such a way as to avoid, as far as reasonably practicable, 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 IVD medical device is installed and maintained as indicated by the manufacturer.

6.9 Protection against mechanical and thermal risks:

6.9.1 IVD medical devices should be designed and manufactured in such a way as to protect the user, professional or lay, or other person against mechanical risks connected with, for example, resistance to movement, instability and moving parts.

6.9.2 Where there are risks due to the presence of moving parts, risks due to break-up or detachment, or leakage of substances, then appropriate protection means must be incorporated.

6.9.3 IVD medical devices should be designed and manufactured in such a way as to reduce to the lowest practicable level the risks arising from vibration generated by the devices, taking account of technical progress and of the means available for limiting vibrations, particularly at source, unless the vibrations are part of the specified performance.

6.9.4 IVD medical devices should be designed and manufactured in such a way as to reduce to the lowest practicable level the risks arising from the noise emitted, taking account of technical progress and of the means available to reduce noise, particularly at source.

6.9.5 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 should be designed and constructed in such a way as to minimize all possible risks.

6.9.6 IVD medical devices should be designed and manufactured in such a way as to reduce to the lowest practicable level, the risk of error when certain parts within the device are intended to be connected or reconnected before or during use.

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

6.10 Protection against the risks posed by IVD medical devices for self-testing:

6.10.1 IVD medical devices for self-testing should be designed and manufactured in such a way that they perform appropriately for their intended purpose taking into account the skills and the means available to lay persons and the influence resulting from variation that can reasonably be anticipated in the layperson's technique and environment. The information and instructions provided by the manufacturer should be easy for the lay person to understand and apply.

6.10.2 IVD medical devices for self-testing should be designed and manufactured in such a way as to reduce as far as reasonably practicable the risk of error by the lay person in the handling of the device and, if applicable, the specimen, and also in the interpretation of results.

6.10.3 IVD medical devices for self-testing should, where reasonably possible, include a procedure by which the lay person can verify that, at the time of use, the product will perform as intended by the manufacturer.

6.11 Label and Instructions for Use:

6.11.1 Users should be provided with the information needed to identify the manufacturer, to use the device safely and to ensure the intended performance, taking account of their training and knowledge. This information should be easily understood.

6.12 Performance evaluation including analytical performance and, where appropriate, clinical performance:

6.12.1 For an IVD medical device a performance evaluation should be conducted in accordance with provisions of Medical Device Rules, 2017. The performance evaluation should be reviewed for, but not limited to, analytical performance data and, where appropriate, clinical performance data in the form of any:

(i) literature;

(ii) performance study reports; and

(iii) Experience gained by routine diagnostic testing to establish that the IVD medical device achieves its intended performance during normal conditions of use and that the known, and foreseeable risks, and any undesirable effects, are minimized and acceptable when weighed against the benefits of the intended performance.

6.12.2 For **new *in vitro* diagnostic medical devices**, Clinical Performance Evaluation studies using specimens from human subjects should be carried out in accordance with the provisions of the Medical Devices Rules, 2017.

7. Technical Documentation

The manufacturer shall retain or be able to provide documentation to demonstrate that the device conforms to the selected standard or alternative means of meeting the Essential Principles.

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