



Australian Government

Department of Health

Therapeutic Goods Administration

Consultation: Proposed changes to the medical device Essential Principles for safety and performance

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TGA Health Safety
Regulation

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Contents

Introduction	5
This consultation	5
Background	6
Regulation of medical devices	6
The Essential Principles - a brief timeline	7
The problem	8
Do the regulations need to change?	8
Proposed regulatory changes	9
Proposal 1 - Incorporation of IMDRF Essential Principles and EU GSPR details	9
Summary of new IMDRF and EU regulations as compared to Australia	9
Proposal 2 - Clarification of existing requirements	10
Proposal 3 - Restructure for improved clarity	10
Proposal 4 - ARTG number	10
Benefits of proposed changes	11
Regulatory impact of proposed changes	11
What will change for sponsors?	11
What will change for manufacturers?	11
Transitional arrangements	12
Fees and charges	12
Engagement	12
Feedback notes	12
What we invite you to do	13
Questions	13
How to submit	14
Enquiries	14
Appendices	15
Appendix 1—New requirements common to both the EU GSPR and the IMDRF Essential Principles and Labelling documents	15

Appendix 2—New requirements in the EU GSPR <i>not in</i> the IMDRF Essential Principles and Labelling documents	17
Appendix 3—New labelling requirements in the IMDRF Labelling document <i>not in</i> the EU GSPR	18
Appendix 4—IMDRF Essential Principles	19
5.0 Essential Principles applicable to all medical devices and ivd medical devices	19
6.0 Essential Principles applicable to medical devices other than IVD medical devices	28
7.0 Essential Principles applicable to IVD medical devices	29
Appendix 5—IMDRF Principles of labelling	31
4.0 Principles for medical device and IVD medical device identification	31
5.0 General labelling principles for medical devices and IVD medical devices	31
6.0 General Labelling Principles for medical devices other than IVD medical devices	38
7.0 General Labelling Principles for IVD medical devices	38
8.0 Labelling Principles for medical devices containing software or software as a medical device	40
9.0 Labelling Principles for medical devices and IVD medical devices intended for use by lay persons	40
10.0 Labelling Principles for information intended for the patient	41

Introduction

The Australian Government is undertaking a significant program of reform to further strengthen the regulation of medicines and medical devices in Australia. As part of the Australian Government Department of Health, the Therapeutic Goods Administration (TGA) regulates these products, and is responsible for implementing the Government's reforms.

In 2015, the Report of the Expert Panel Review of Medicines and Medical Devices Regulation (MMDR) made 58 recommendations for reform of the regulatory framework for medicines and medical devices in Australia. The Australian Government Response to the Review of Medicines and Medical Devices Regulation was released in September 2016. The Government accepted 56 MMDR recommendations including Recommendation Twenty which addressed matters within the remit of the TGA. This Recommendation provided that the regulation of medical devices, wherever possible and appropriate, align with the European Union (EU) framework.

This consultation

The TGA is seeking feedback on a proposal to align the Australian regulatory principles for medical devices with applicable international guidelines and regulations.

The purpose of this consultation paper is to obtain feedback on a proposal to revise Australia's *Essential Principles for medical devices* in line with international best practice.

[Consultation questions](#) and information on [How to submit your feedback to the TGA](#) are provided on pages 13 and 14.

Please ensure you familiarise yourself with the feedback notes, prior to providing feedback.

The scope of this paper includes both non-IVD and IVD¹ medical devices. It does not include proposed changes to the Essential Principles in relation to the following topics, as we have consulted separately on these topics:

- [requirements related to a proposal to implement a Unique Device Identification System in Australia](#); and
- [requirements relating to software including software as a medical device](#).



Please note

The scope of this paper covers all medical devices including IVD medical devices.

¹ *in vitro* diagnostic

Background

Regulation of medical devices

The [Therapeutic Goods Act 1989](#) (the Act) and the [Therapeutic Goods \(Medical Devices\) Regulations 2002](#) (the Regulations) specify requirements for the regulation of medical devices in Australia. The Essential Principles, detailed in the Act² and Regulations³, provide safety and performance requirements for manufacturers regarding design and production of their medical devices. Manufacturers of all medical devices supplied in Australia—amongst other requirements—must have evidence that demonstrates compliance of their medical devices with the relevant Essential Principles.

In addition to setting out general safety and performance requirements, the Essential Principles identify certain types of hazards and other considerations that must be addressed by manufacturers (e.g., around infection and microbial contamination), but they do not specify how compliance with the principles must be demonstrated. This principles-based approach provides flexibility for manufacturers of medical devices and supports different technologies and technological advances over time.

A common way to demonstrate compliance with the (non-clinical) Essential Principles is to comply with technical standards published by Australian or International Standards organisations or other technical reference materials (e.g., pharmacopoeias or regulatory guidance documents). In each case, where a manufacturer chooses to use a technical standard or other reference material, they must be able to provide evidence that the chosen approach satisfies the requirements of the Essential Principles. Compliance with (clinical) Essential Principles can be demonstrated by use of the [Clinical evidence guidelines: Medical devices](#)⁴, which are intended to provide guidance for manufacturers on the process of clinical data generation and clinical evaluation.

In Australia, there are eight⁵ Essential Principles that apply to all medical devices. These eight Essential Principles include requirements relating to health and safety; design and construction according to safety principles; suitability for intended purpose; long-term safety; transport and storage; ensuring that the benefits outweigh any undesirable effects; information to be provided with the medical device, and clinical evidence requirements. A further seven⁶ Essential Principles apply to the design and construction of devices. These latter principles apply on a case-by-case basis depending on the type of device and technology used.

It is important to periodically review regulatory requirements applicable to medical devices to ensure they continue to be appropriate. When undertaking such reviews, amongst other things, it is necessary to consider the international best regulatory practices as well as emerging regulatory considerations (such as new technologies and new methodologies relating to safety).

This will ensure sustainability of the Australian regulatory system for medical devices, appropriateness and robustness of the regulatory framework, and timeliness of access to medical devices.

² *Therapeutic Goods Act 1989*, s. 3, Part 4-1 (ss. 41BA, 41BH), and Part 4-2 (ss. 41C, 41CA)

³ Part 2 (Reg. 2.1), and Schedule 1

⁴ Clinical evidence guidelines: Medical devices (2017), <https://www.tga.gov.au/publication/clinical-evidence-guidelines-medical-devices>

⁵ Essential Principles 1–6, 13, and 14.

⁶ Essential Principles 7–12 and 15.

The Essential Principles - a brief timeline

This timeline demonstrates that the requirements for safety and performance of medical devices in Australia and Europe are similar and are based on the [Global Harmonization Task Force on Medical Devices](#) (GHTF) framework.

1990	EU legislates Essential Requirements as part of Council Directive 90/385/EEC for Active Implantable Medical Devices (AIMDD).
1992	Global Harmonization Task Force on Medical Devices (GHTF) established ⁷ .
1993	EU legislates Essential Requirements as part of Council Directive 93/42/EEC for Medical Devices (MDD).
1998	EU legislates Essential Requirements as part of Council Directive 98/79/EC for In Vitro Diagnostic Medical Devices (IVDD).
1999	GHTF Essential Principles of Safety and Performance of Medical Devices (SG1/N020)—based heavily on the European MDD Essential Requirements – published (excludes IVD medical devices).
2002	Australia adopts the GHTF framework, including the Essential Principles , in its 2002 Medical Devices Regulations ⁸ .
2010	Australia adds Essential Principle 15 for IVD medical devices.
2011	International Medical Device Regulators' Forum (IMDRF) formed ⁹ to replace the GHTF.
2012	GHTF final documents published including updated Essential Principles of Safety and Performance of Medical Devices ¹⁰ (includes IVD medical devices).
2017	The EU Regulations on medical devices (2017/745) ¹¹ (EU MDR) and IVD medical devices (2017/746) ¹² (EU IVDR) published to replace the three Directives. Both include General Safety and Performance Requirements (GSPR) in place of the Essential Requirements. The GSPR are heavily based on the 2012 GHTF Essential Principles.
2018	IMDRF publishes updated Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices ¹³ based heavily on the 2012 GHTF Essential Principles and the 2017 EU General Safety and Performance Requirements.
2019	IMDRF publishes Principles of Labelling for Medical Devices and IVD Medical Devices ¹⁴ based heavily on labelling requirements in the 2012 GHTF Essential Principles and the 2017 EU General Safety and Performance Requirements.

⁷ Australia and Europe, are founding members of the GHTF.

⁸ [Therapeutic Goods \(Medical Devices\) Regulations 2002](#)

⁹ Australia and Europe, are founding members of the IMDRF.

¹⁰ N68:2012 GHTF SG1—Essential Principles of Safety and Performance of Medical Devices—November 2012

¹¹ The Regulation 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC

¹² <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32017R0746>

¹³ [Essential Principles of Safety and Performance of Medical Devices](#), Final Document, IMDRF/GRRP WG/N47 FINAL:2018, 31 October 2018

¹⁴ [Principles of Labelling for Medical Devices and IVD Medical Devices](#), Final Document, IMDRF/GRRP/WG/N52 FINAL:2019, 21 March 2019

The problem

The principles-based regulatory framework allows coverage of the vast diversity of medical devices (form, function, intended purpose, composition, manufacturing method, etc.).

This approach provides flexibility and extensibility of the framework as new technologies emerge. Although such flexibility has significant advantages, it has been internationally recognised that—in some cases—additional clarity on certain requirements may improve conformance and adherence with the Essential Principles and, consequently, improve safety and performance of medical devices. In addition, the emergence of new technologies over time can introduce factors that are not accounted for in the existing language of the Essential Principles.

Do the regulations need to change?

The Essential Principles have not been amended since 2002 (other than adding an Essential Principle specifically for IVD medical devices). The international requirements and guidance for principles regarding safety and performance of medical devices have changed, and Australia's existing Essential Principles no longer align with international best practice, in particular, in areas where there have been changes and advancements in medical technology such as software and other complex systems, medical devices incorporating new materials, advanced manufacturing methods, cybersecurity, human factors (including useability, accessibility, and ergonomics), and information required for appropriate use of the device for the intended purpose by the user.

There is also insufficient clarity around expectations for some existing topics, e.g., on the safe cleaning, disinfection, re-sterilisation, disposal, adjustment, calibration, and maintenance of medical devices.

Proposed regulatory changes

There are four areas of proposed changes, as follows:

Proposal 1 - Incorporation of IMDRF Essential Principles and EU GSPR details

It is proposed to amend the Essential Principles set out in the [Therapeutic Goods \(Medical Devices\) Regulations 2002](#), Schedule 1, to:

- incorporate¹⁵ new requirements specified in the following IMDRF documents (refer to Appendices 1 and 3):
 - [Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices](#) (IMDRF/GRRP WG/N47 FINAL:2018),
 - [Principles of Labelling for Medical Devices and IVD Medical Devices](#) (IMDRF/GRRP WG/N52 FINAL:2019); and
- include relevant additional details¹⁶ captured by the General Safety and Performance Requirements specified in the EU regulations (refer to Appendices 1 and 2) :
 - Annex I of the [EU Regulation on medical devices \(2017/745\)](#); and
 - Annex I of the [EU Regulation on *in vitro* diagnostic medical devices \(2017/746\)](#)

Summary of new IMDRF and EU regulations as compared to Australia

- The IMDRF Essential Principles and Labelling documents and the GSPR in the EU regulations include new requirements as compared to the existing Australian Essential Principles in the following areas:
 - risk management
 - chemical, physical, biological, material, and electromagnetic properties of a device
 - human factors (ergonomics, useability)
 - software and security (Note that new software and security Essential Principles have already been consulted ¹⁷)
 - implantable devices
 - use of devices by lay persons
 - labelling and IFU
 - safe cleaning, disinfection, re-sterilisation, disposal, adjustment, calibration, maintenance
 - compatibility and interoperability
 - management of devices containing animal, plant, bacterial-origin materials and of devices containing medicinal substances
- The details about the differences are provided in Appendices 1-3.

¹⁵ Considering the Australian regulatory and legal context

¹⁶ As compared with the IMDRF guidance documents

¹⁷ <https://www.tga.gov.au/consultation/consultation-regulation-software-including-software-medical-device-samd>

Proposal 2 - Clarification of existing requirements

It is proposed to provide greater clarity for manufacturers for meeting existing expectations for compliance in the following areas:

1. Public health and safety (ensuring it is clear that current public health considerations for IVD devices should also be applied to non-IVD devices where relevant).
2. Infection and contamination control (e.g. – providing further clarity around expectations for EO residuals, endotoxins and bioburden, and that sterilisation processes are not to compromise other properties of the medical device).
3. Operation, (ensuring adequate consideration of factors associated with components of medical device systems that are operated by a manufacturer)
4. Decommissioning, and disposal (ensuring that factors related to these lifecycle stages are adequately considered)
5. Human and social factors (ensuring it is clear that these factors are to be considered where relevant, e.g. – physical and cognitive capabilities of intended user groups)
6. Ethics (ensuring adequate reference to ethical principles e.g. – for privacy, for devices used in a clinical trial, for devices with AI features)

Proposal 3 - Restructure for improved clarity

It is proposed to restructure the current presentation of the Essential Principles to improve clarity and readability. An example can be seen in the 2018 IMDRF version of the Essential Principles (refer to Appendix 4), which was restructured to ensure that all Essential Principles that apply to all medical devices are included in the same section, and to create separate sections for the Essential Principles that only apply to non-IVD medical devices and those that only apply to IVD medical devices

In addition, detailed requirements currently specified in Essential Principles 13 are proposed to be moved into another area of the regulations. This is to align with the IMDRF approach of specifying the essential principle of providing information with a medical device separately from the specific detailed requirements for the information, including labels and instructions for use (refer to Appendix 5).

Proposal 4 - ARTG number

It is proposed that certain medical devices should include the ARTG number in the information provided with the device, in particular, for medical devices that are software supplied without any physical packaging. Under reforms for software that are progressing separately (and in alignment with IMDRF), it has been proposed that such devices be allowed to present labels and instructions for use in electronic form. This means that these devices would display the ARTG number on the electronic label to make it clear under which ARTG entry the device will be supplied. Device labels in electronic form are limited to these devices only.

Benefits of proposed changes

The proposed regulatory changes will allow greater international alignment and offer benefits such as:

- improved health and safety of the Australian public;
- improved consumer and health professional confidence in medical device safety and performance;
- safer use of medical devices through improved information provided to users;
- more informed decision making regarding the use of devices through the provision of precautions and information about foreseeable adverse effects;
- improved clarity and transparency for industry regarding our expectations;
- alignment, as appropriate, with international best practice; and
- reduction in unnecessary regulatory burden (time and cost) for manufacturers and sponsors of medical devices.

The proposed changes are expected to provide benefits to regulated industry sector because the requirements will be clearer and will provide additional detail and precision, improving and enhancing product safety.

The consistency with the global approach of our requirements will increase consumer confidence, minimising patient health and safety risks.

Additionally, by moving Australia's regulation towards international harmonisation the proposed changes are expected to decrease the overall cost of regulatory compliance, promote global convergence, and improve timely access to medical devices.

Regulatory impact of proposed changes

What will change for sponsors?

Sponsors¹⁸ may be required to seek additional detail from manufacturers than is currently the case. However, as the Essential Principles will be more detailed, it may be easier for sponsors to obtain relevant information for applications, as there will be greater clarity around expectations for demonstrating regulatory compliance.

What will change for manufacturers?

Manufacturers will be required to reassess their compliance with the revised Essential Principles for safety and performance of medical devices. In some cases, additional technical and clinical documentation may be required to demonstrate compliance.

The manufacturers using European EC certificates as conformity assessment evidence to support current ARTG entries will be transitioning to the majority of the same requirements, therefore impact would be minimal. This is because most devices supplied in Australia that require certification, have European EC certification.

¹⁸ Sponsors are required to ensure they have access to information from the manufacturer to demonstrate compliance with the relevant Essential Principles in order to be able to submit any new applications for marketing approval (ARTG inclusion) for medical devices and to comply with the conditions of the ARTG inclusion.

Transitional arrangements

In the EU, under the transitional arrangements, medical devices and IVD medical devices lawfully placed on the market that have pre-market authorisation in the form of a valid European EC Certificate¹⁹ can remain on the market until the expiry date of that EC Certificate or until 26 May 2025 (one year after these certificates become void) for medical devices and 26 May 2027 for IVD medical devices, whichever is the earliest.

We propose that the revised Essential Principles for new medical devices in Australia—that is, a device to be included in the ARTG following successful completion of an application submitted to the TGA on or after the commencement date of the amended regulations—would start from November 2020 for medical devices and November 2022 for IVD medical devices.

If the application for ARTG inclusion for a medical device is submitted to the TGA before the date of the proposed amendment takes effect, the device will be subject to the transitional arrangements and will have four (4) years to transition.

Fees and charges

The changes proposed under this consultation will not affect fees or annual charges.

Engagement

Wherever practicable and possible, in addition to this consultation paper, TGA will also be:

- liaising with respective industry and health professional peak bodies, academic research organisations, and consumer groups in order to provide education, awareness, and feedback about this proposal; and
- providing relevant communication material on the TGA website.

Feedback notes

It is important to note that while it is intended to take the IMDRF documents and EU MD Regulations into account, the Australian legislative instruments are structured differently and there is variation in the legal terminology acceptable in each jurisdiction. It is acknowledged that legislation cannot always be successfully replicated across jurisdictions. When considering the proposed measures, you should assume that in-principle the proposals to align with the IMDRF documents and EU MD and IVD Regulations are in the context of the Australian MD Regulations.

¹⁹ EC certificates issued in accordance with EU Directive 93/42/EEC and that comply with the requirements in par. (2) of Article 120 of the EU MD Regulation.

What we invite you to do

In your submission, we ask you to consider the questions below and provide comments related to any other matter outlined in this consultation paper.

Questions

1. Do you agree with the proposal to update the Australian Essential Principles to:
 - a. align²⁰ with the IMDRF Essential Principles and Labelling documents?
 - b. include relevant additional details captured by the General Safety and Performance Requirements in the EU MD and IVD regulations²¹?

In your answer, please provide reasons for your position.

2. Do you agree with the proposal to provide additional clarity regarding expectations for compliance as specified under Proposal 2?

In your answer, please provide reasons for your position.

3. Do you agree with the proposal to restructure the Essential Principles and Labelling requirements for clarity and readability?

In your answer, please provide reasons for your position.

4. Do you agree with the proposal that software medical devices without any physical packaging should include the ARTG number on the electronic label?

Are there other devices where the ARTG number should be provided?

In your answer, please provide reasons for your position.

5. What financial or other effects—including any that are unintended—do you anticipate the changes to the Essential Principles may have for yourself, your business, and other stakeholders (such as consumers, healthcare professionals, health organisations, industry, etc.)?
6. Do you have any comments regarding the transitional arrangements proposed in this paper?
7. Are there any further issues, questions, or requirements we should consider when implementing this change (including areas that can/should be clarified in our guidance)?



²⁰ Considering the Australian regulatory and legal context.

²¹ As compared with the IMDRF documents.

How to submit

Complete the [online consultation submission form](#) to upload your submission in either PDF or MS Word format.

You can also submit your feedback directly to the TGA by email at: devicereforms@tga.gov.au. If you do so, **please ensure your submission is accompanied by a cover sheet.**

This consultation closes on 17 October 2019.

Enquiries

If you have any questions relating to submissions please direct them to: devicereforms@tga.gov.au.

Appendices

Appendix 1—New requirements common to both the EU GSPR and the IMDRF Essential Principles and Labelling documents²²

- a. Inclusion of aspects related to risk management processes, risk-control procedures along with usability risks.
- b. In regards to chemical physical and biological properties of the device consideration around risks posed by leachable substances, degradation products, and process residues to be reduced with special attention to substances that are carcinogenic, mutagenic, or toxic to reproduction.
- c. For non-IVD medical devices, consideration for reduction of risks linked to size of particles released into patient's body, particularly nanomaterials.
- d. Device to be designed to facilitate safe cleaning, disinfection, and/or re-sterilisation.
- e. Devices labelled as having a specific microbial state to retain their state when subjected to appropriate storage and transport conditions, specified by the manufacturer.
- f. Devices incorporating medicinal substance to require verification of identify and efficacy of medicinal substance contained in the device along with safety and quality currently covered in the Australian Essential Principles.
- g. Requirements for processing, handling, and preservation for devices containing tissues, cells or substances of animal, plant, or bacterial origin or their derivatives, which are non-viable or rendered non-viable.
- h. Medical devices that are intended to be operated together to be designed and manufactured in such a way that the interoperability and compatibility are reliable and safe.
- i. Devices to be designed in such a way that adjustment, calibration, and maintenance can be done safely and effectively.
- j. Devices to be designed to facilitate their safe disposal and safe disposal of related waste substances; instructions for use should identify safe disposal procedures and measures.
- k. Devices to be designed in such a way so as to reduce risks associated with the users or other persons in connection with their physical and ergonomic/usability features.
- l. Devices to be designed in such a way so as to reduce risks associated with possible negative interaction between software and IT environments within which they operate and interact.
- m. Devices to be designed in such a way so as to reduce risk of incorrect identification of specimen/data, and risk of erroneous results.
- n. Devices to be designed in such a way so as to reduce the risk of unauthorised access that could hamper devices from functioning as intended.

²² In comparison with the Essential principles in the Australian MD Regulations 2002

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- o. Devices to be designed and manufactured to provide a level of intrinsic immunity to electromagnetic interference to enable them to operate as intended.
 - p. Particular requirements for implantable devices to minimise risks connected with medical treatment, in particular those resulting from the use of defibrillators or high-frequency surgical equipment.
 - q. Specific requirements around protection of risks posed by medical devices intended by the manufacturer for use by lay persons.
 - r. Essential Principles applicable to IVD medical devices to include consideration of possibility of impairment of analytical performance due to physical and/or chemical incompatibility between the materials used and the specimens, analyte or marker to be detected and measured.
 - s. Labelling includes requirements around:
 - i. Provision of IFU in electronic format and the relevant considerations
 - ii. Labels can be provided in a human readable format, but may be supplemented by machine readable forms.
 - iii. Relevant considerations for availability of electronic labelling and IFU.
 - iv. Label to state if device contains medicinal substance, tissues, or cells or their derivatives of animal origin.
 - v. Labels to include information on residual risks to be communicated to user and/or other persons.
 - vi. Labels to include information on net quantity of contents expressed in terms of weight or volume or any other combination of these which accurately reflects the contents of the package
 - vii. UDI—Unique Device Identifier requirements
 - t. Instructions for use to contain information on:
 - i. Clinical benefits to be expected.
 - ii. Summary of safety and clinical performance.
 - iii. The performance characteristics of the device.
 - iv. Precautions related to materials that are potentially carcinogenic, mutagenic, or toxic to reproduction.
 - v. Recommendations for quality control procedures.
 - vi. Warnings, precautions and/or measures to be taken in regards to the risks of interference posed by the reasonably foreseeable presence of the medical device during specific diagnostic investigations, evaluations, therapeutic treatment, or use.
 - u. For IVD medical devices, the instructions for use should include the traceability of values assigned to calibrators and control materials, including identification of applicable reference materials and/or reference measurement procedures of higher order.

Appendix 2—New requirements in the EU GSPR *not in the IMDRF Essential Principles and Labelling documents*

- a. With regards to chemical and physical properties of a medical device consideration must be given to the compatibility between different parts of the device which consists of more than one implantable part.
- b. Devices to be designed in such a way so as to reduce risks posed by substances or particles including wear debris, degradation products, processing residues with special attention to substances with endocrine-disrupting properties.
- c. Medical devices composed of substances or combination of substances that are intended to be introduced into the human body and that are absorbed by or locally dispersed in the human body shall be evaluated for ADME²³, local tolerance, interaction with other devices, and potential for adverse reactions, as required.
- d. Particular requirement for implantable medical devices to minimise as far as possible risks which may arise where maintenance and calibration are impossible, including:
 - i. excessive increase of leakage currents,
 - ii. ageing of the materials used,
 - iii. excess heat generated by the device, and
 - iv. decreased accuracy of any measuring or control mechanism.
- e. Active implantable medical devices to be designed and manufactured so as to ensure compatibility of the devices with the substances they are intended to administer and the reliability of the source of energy.
- f. Specific labelling requirement for:
 - i. Devices composed of substances or combination of substances that are intended to be introduced into the human body and that are absorbed by or locally dispersed in the human body.
 - ii. For implantable devices, the overall qualitative and quantitative information on the materials and substances to which patients can be exposed.
 - iii. Sterile packaging.
 - iv. Devices containing substances or mixture that may be considered to be as dangerous, taking into account, nature, quantity, and the form under which they are present.
 - v. Safety warning related to substances that are carcinogenic, mutagenic, or toxic to reproduction; endocrine disruptors.
 - vi. For active implantable devices, the serial number, and for other implantable devices, the serial number or lot number.

²³ ADME – Absorption, Distribution, Metabolism and Excretion

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- g. Instruction for use to include information on:
 - i. Device can be reused only if it is reconditioned under the responsibility of the manufacturer to comply with general safety and performance requirements.
 - ii. A notice to the user and/or patient 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 in which the user and/or patient is established.
 - iii. For devices intended for self-testing, information shall be provided with advice to the user on action to be taken (in case of positive, negative, or indeterminate result), on the test limitations and on the possibility of false positive or false negative result and information shall also be provided as to any factors that can affect the test result such as age, gender, menstruation, infection, exercise, fasting, diet, or medication.
 - iv. For an IVD medical device, the mathematical approach upon which the calculation of the analytical result is made.
 - v. For companion diagnostics, the corresponding medicine or biological therapeutic good for which it is an IVD companion diagnostic test.

Appendix 3—New labelling requirements in the IMDRF Labelling document *not in the EU GSPR*

- a. The labelling should not contain any language regarding the manufacturer's liability in the case of damage or injury resulting from any use or malfunction of the medical device that contradicts the laws or regulations in the jurisdiction of use.
- b. The labelling should not contain any disclaimers related to the safety and performance of the medical device for its intended purpose that are incompatible with the laws or regulations in the jurisdiction of use, or the obligations of the manufacturer to design and manufacture a product that is safe and performs as intended throughout its expected lifetime.
- c. The instructions for use should include any instructions to be followed in the event of the packaging being damaged or unintentionally opened before use, or if the packaging is exposed to environmental conditions outside of those specified.
- d. The instructions for use, where relevant, should include a bibliography or references section.
- e. Specific Labelling Principles for Information Intended for the Patient
- f. Specific Labelling Principles for Medical Devices Containing Software or Software as a Medical Device (Note: these are already being proposed under a separate reform package for software).
- g. Specific Labelling Principles for Medical Devices Intended for Use by Lay Persons
- h. Specific Labelling principles for IVD medical devices

Appendix 4—IMDRF Essential Principles

[Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices](#)

(IMDRF/GRRP WG/N47 FINAL: 2018)

5.0 Essential Principles applicable to all medical devices and ivd medical devices

The essential design and manufacturing principles listed in this Section are applicable to medical devices and IVD medical devices.

5.1 General

5.1.1 Medical devices and IVD medical devices should achieve the performance intended by their manufacturer and should be designed and manufactured in such a way that, during intended conditions of use, they are suitable for their intended purpose. They should be safe and perform as intended, should have risks that are acceptable when weighed against the benefits to the patient, and should not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons.

5.1.2 Manufacturers should establish, implement, document and maintain a risk management system to ensure the ongoing quality, safety and performance of the medical device and IVD medical device. Risk management should be understood as a continuous iterative process throughout the entire lifecycle of a medical device and IVD medical device, requiring regular systematic updating. In carrying out risk management manufacturers should:

- a. establish and document a risk management plan covering each medical device and IVD medical device;
- b. identify and analyze the known and foreseeable hazards associated with each medical device and IVD medical device;
- c. estimate and evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse;
- d. eliminate or control the risks referred to in point (c) in accordance with the requirements of points 5.1.3 and 5.1.4 below;
- e. evaluate the impact of information from the production and postproduction phases, on the overall risk, benefit-risk determination and risk acceptability. This evaluation should include the impact of the presence of previously unrecognized hazards or hazardous situations, the acceptability of the estimated risk(s) arising from a hazardous situation, and changes to the generally acknowledged state of the art.
- f. based on the evaluation of the impact of the information referred to in point (e), if necessary amend control measures in line with the requirements of points 5.1.3 and 5.1.4 below.

5.1.3 Risk control measures adopted by manufacturers for the design and manufacture of the medical device and IVD medical device should conform to safety principles, taking account of the generally acknowledged state of the art. When risk reduction is required, manufacturers should control risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable. In selecting the most appropriate solutions, manufacturers should, in the following order of priority:

- a. eliminate or appropriately reduce risks through safe design and manufacture;

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- b. where appropriate, take adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated; and
 - c. provide information for safety (warnings/precautions/contra-indications) and, where appropriate, training to users.
- 5.1.4 The manufacturer should inform users of any relevant residual risks.
- 5.1.5 In eliminating or reducing risks related to use, the manufacturer should:
- a. appropriately reduce the risks related to the features of the medical device and IVD medical device and the environment in which the medical device and IVD medical device are intended to be used (e.g. ergonomic/usability features, tolerance to dust and humidity) and
 - b. give consideration to the technical knowledge, experience, education, training and use environment and, where applicable, the medical and physical conditions of intended users.
- 5.1.6 The characteristics and performance of a medical device and IVD medical device should not be adversely affected to such a degree that the health or safety of the patient and the user and, where applicable, of other persons are compromised during the expected life of the device, as specified by the manufacturer, when the medical device and IVD medical device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained and calibrated (if applicable) in accordance with the manufacturer's instructions.
- 5.1.7 Medical devices and IVD medical devices should be designed, manufactured and packaged in such a way that their characteristics and performance, including the integrity and cleanliness of the product and when used in accordance with the intended use, are not adversely affected by transport and storage (for example, through shock, vibrations, and fluctuations of temperature and humidity), taking account of the instructions and information provided by the manufacturer. The performance, safety, and sterility of the medical device and IVD medical device should be sufficiently maintained throughout any shelf-life specified by the manufacturer.
- 5.1.8 Medical devices and IVD medical devices should have acceptable stability during their shelf-life, during the time of use after being opened (for IVDs, including after being installed in the instrument), and during transportation or dispatch (for IVDs, including samples).
- 5.1.9 All known and foreseeable risks, and any undesirable side-effects, should be minimized and be acceptable when weighed against the evaluated benefits arising from the achieved performance of the device during intended conditions of use taking into account the generally acknowledged state of the art.

5.2 Clinical evaluation

5.2.1 Where appropriate and depending on jurisdictional requirements, a clinical evaluation may be required. A clinical evaluation should assess clinical data to establish that a favorable benefit-risk determination exists for the medical device and IVD medical device in the form of one or more of the following:

- clinical investigation reports (for IVDs, clinical performance evaluation reports)
- published scientific literature/reviews
- clinical experience

5.2.2 Clinical investigations should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. These principles protect the rights, safety and well-being of human subjects, which are the most important considerations and shall prevail over interests of science and society. These principles shall be understood, observed, and applied at every step in the clinical investigation. In addition, some countries may have specific regulatory requirements for pre-study protocol review, informed consent, and for IVD medical devices, use of leftover specimens.

5.3 Chemical, physical, and biological properties

5.3.1 Regarding chemical, physical, and biological properties of a medical device and IVD medical device, particular attention should be paid to the following:

- a. the choice of materials and substances used, particularly with respect to:
 - toxicity;
 - biocompatibility; and
 - flammability;
- b. the impact of processes on material properties;
- c. where appropriate, the results of biophysical or modelling research whose validity of which has been demonstrated beforehand;
- d. the mechanical properties of the materials used, reflecting, where appropriate, matters such as strength, ductility, fracture resistance, wear resistance and fatigue resistance;
- e. surface properties; and
- f. the confirmation that the device meets any defined chemical and/or physical specifications.

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

5.3.3 The medical device and IVD medical device should be designed and manufactured in such a way as to appropriately reduce the risks posed by substance egress (including leaching and/or evaporation), degradation products, processing residues, etc. Special attention should be given to leaking or leaching of substances, which are carcinogenic, mutagenic or toxic to reproduction.

5.3.4 The medical device and IVD medical device should be designed and manufactured in such a way as to appropriately reduce the risks posed by the unintentional ingress of substances into the device, taking into account the medical device and IVD medical device and the nature of the environment in which it is intended to be used.

5.3.5 Medical devices and IVD medical devices and their manufacturing processes should be designed in such a way as to eliminate or to appropriately reduce the risk of infection to users and all other persons who may come in contact with the medical device and IVD medical device. The design should:

- a. allow for easy and safe handling;

- b. appropriately reduce any microbial leakage from the medical device and IVD medical device and/or microbial exposure during use;
- c. prevent microbial contamination of the medical device and IVD medical device or its content (e.g., specimens); and/or
- d. appropriately reduce the risks from unintended exposure (e.g., cuts and pricks (such as needle stick injuries), eye splashes, etc.).

5.4 Sterilization and microbial contamination

5.4.1 Where necessary, medical devices and IVD medical devices should be designed to facilitate their safe cleaning, disinfection, sterilization, and re-sterilization by the user, as appropriate.

5.4.2 Medical devices and IVD medical devices labeled as having a specific microbial state should be designed, manufactured and packaged to ensure that they remain in that state when placed on the market and remain so under the transport and storage conditions specified by the manufacturer.

5.4.3 Medical devices and IVD medical devices, delivered in a sterile state should be designed, manufactured and packaged in accordance with appropriate procedures, to ensure that they are sterile when placed on the market and that, unless the packaging which is intended to maintain their sterile condition is damaged, they remain sterile, under the transport and storage conditions specified by the manufacturer, until that packaging is opened at the point of use. It should be ensured that the integrity of that packaging is clearly evident to the final user (for example, through the use of tamper-proof packaging).

5.4.4 Medical devices and IVD medical devices labelled as sterile should be processed, manufactured, packaged, and sterilized by means of appropriate, validated methods. The shelf-life of these medical devices and IVD medical devices should be determined by validated methods.

5.4.5 Medical devices and IVD medical devices intended to be sterilized, either by the manufacturer or user, should be manufactured and packaged in appropriate and controlled conditions and facilities.

5.4.6 Where the medical devices and IVD medical devices are provided non-sterile and are intended to be sterilized prior to use:

- a. the packaging system should minimize the risk of microbial contamination and should be suitable taking account of the method of sterilization indicated by the manufacturer; and
- b. the method of sterilization indicated by the manufacturer should be validated.

5.4.7 For medical devices and IVD medical devices placed on the market in both sterile and non-sterile conditions, the label should clearly distinguish between these versions.

5.5 Considerations of environment and conditions of use

5.5.1 If the medical device or IVD medical device is intended to be used in combination with other medical devices or IVD medical devices and/or equipment, the whole combination, including the connection system should be safe and should not impair the specified performance of the medical device or IVD medical device. Any known restrictions on use applying to such combinations should be indicated on the label and/or in the instructions for use. Any connections which the user has to handle, such as fluid, gas transfer, electrical or mechanical

coupling, should be designed and manufactured in such a way as to remove or appropriately reduce all possible risks, including incorrect connections or safety hazards.

5.5.2 Medical devices and IVD medical devices should be designed and manufactured in consideration of the intended environment and conditions of use, and in such a way as to remove or appropriately reduce the:

- a. risks of injury to the users or other persons in connection with its physical and ergonomic/usability features;
- b. risks of user error due to the design of the medical device or IVD medical device user interface, ergonomic/usability features, and the environment in which the medical device or IVD medical device is intended to be used;
- c. 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, and/or variations in pressure and acceleration;
- d. risks associated with the use of the medical device or IVD medical device when it comes into contact with materials, liquids, and substances, including gases, to which it is exposed during intended conditions of use;
- e. risks associated with the possible negative interaction between software and the information technology (IT) environment within which it operates and interacts;
- f. environmental risks from unexpected egress of substances from the medical device or IVD medical device during use, taking into account the medical device or IVD medical device and the nature of the environment in which it is intended to be used;
- g. the risk of incorrect identification of specimens/samples/data and the risk of erroneous results due to, for example, confusing color and/or numeric coding on specimen receptacles, removable parts and/or accessories used to perform the analysis, test, or assay as intended; and
- h. the risks of interference with other medical devices or IVD medical devices normally used in diagnosis, monitoring or treatment.

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

5.5.4 Medical devices and IVD medical devices should be designed and manufactured in such a way that adjustment, calibration, and maintenance can be done safely and effectively. Specifically,

- a. When maintenance is not possible, for example, with implants, the risks from ageing of materials, etc. should be appropriately reduced.
- b. When adjustment and calibration are not possible, for example, with certain kinds of thermometers, the risks from loss of accuracy of any measuring or control mechanism are appropriately reduced.

5.5.5 Medical devices and IVD medical devices that are intended to be operated together with other medical devices or IVD medical devices or products should be designed and manufactured in such a way that the interoperability and compatibility are reliable and safe.

5.5.6 Medical devices and IVD medical devices should be designed and manufactured in such a way as to appropriately reduce the risk of unauthorized access that could hamper the device from functioning as intended or impose a safety concern.

5.5.7 Any measurement, monitoring or display scale functions of medical devices and IVD medical devices should be designed and manufactured in line with ergonomic/usability principles, taking account of the intended purpose, users and the environmental conditions in which the medical devices and IVD medical devices are intended to be used.

5.5.8 Medical devices and IVD medical devices should be designed and manufactured in such a way as to facilitate their safe disposal or recycling and the safe disposal or recycling of related waste substances by the user, patient or other person. The instructions for use should identify safe disposal or recycling procedures and measures.

5.6 Protection against electrical, mechanical, and thermal risks

5.6.1 Medical devices and IVD medical devices should be designed and manufactured in such a way as to protect users against mechanical risks connected with, for example, resistance to movement, instability, and moving parts.

5.6.2 Medical devices and IVD medical devices should be designed and manufactured in such a way as to appropriately reduce the risks arising from vibration generated by the medical devices or IVD medical 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.

5.6.3 Medical devices and IVD medical devices should be designed and manufactured in such a way as to appropriately reduce 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.

5.6.4 Medical devices and IVD medical devices should be designed and manufactured in such a way as to appropriately reduce the risk related to the failure of any parts within the device that are intended to be connected or reconnected before or during use.

5.6.5 Accessible parts of medical devices and 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.

5.7 Active medical devices and IVD medical devices and medical devices connected to them

5.7.1 For active medical devices and IVD medical devices, in the event of a single fault condition, appropriate means should be adopted to eliminate or appropriately reduce consequent risks.

5.7.2 Medical devices and IVD medical devices where the safety of the patient depends on an internal power supply should be equipped with a means of determining the state of the power supply and an appropriate warning or indication for when the capacity of the power supply becomes critical.

5.7.3 Medical devices and IVD medical devices where the safety of the patient depends on an external power supply should include an alarm system to signal any power failure.

5.7.4 Medical devices and IVD medical 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.

5.7.5 Medical devices and IVD medical devices should be designed and manufactured in such a way as to appropriately reduce the risks of creating electromagnetic interference which could impair the operation of any devices or equipment in the intended environment.

5.7.6 Medical devices and IVD medical devices should be designed and manufactured in such a way as to provide a level of intrinsic immunity to electromagnetic interference such that is adequate to enable them to operate as intended.

5.7.7 Medical devices and IVD medical devices should be designed and manufactured in such a way as to appropriately reduce the risk of accidental electric shocks to the user or any other person, both during normal use of the medical device or IVD medical device and in the event of a single fault condition in the medical device or IVD medical device, provided the medical device or IVD medical device is installed and maintained as indicated by the manufacturer.

5.8 Medical devices and IVD medical devices that incorporate software or are software as a medical device

5.8.1 Medical devices and IVD medical devices that incorporate electronic programmable systems, including software, or are software as a medical device, should be designed to ensure accuracy, reliability, precision, safety, and performance in line with their intended use. In the event of a single fault condition, appropriate means should be adopted to eliminate or appropriately reduce consequent risks or impairment of performance.

5.8.2 For medical devices and IVD medical devices that incorporate software or are software as a medical device, the software should be developed, manufactured and maintained in accordance with the state of the art taking into account the principles of development life cycle (e.g., rapid development cycles, frequent changes, the cumulative effect of changes), risk management (e.g., changes to system, environment, and data), including information security (e.g., safely implement updates), verification and validation (e.g., change management process).

5.8.3 Software that is intended to be used in combination with mobile computing platforms should be designed and developed taking into account the platform itself (e.g. size and contrast ratio of the screen, connectivity, memory, etc.) and the external factors related to their use (varying environment as regards level of light or noise).

5.8.4 Manufacturers should set out minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorized access, necessary to run the software as intended.

5.8.5 The medical device and IVD medical device should be designed, manufactured and maintained in such a way as to provide an adequate level of cybersecurity against attempts to gain unauthorized access.

5.9 Medical devices and IVD medical devices with a diagnostic or measuring function

5.9.1 Medical devices and IVD medical devices with a diagnostic or measuring (including monitoring) function should be designed and manufactured in such a way as to provide, among other performance characteristics, sufficient accuracy, precision and stability for their intended purpose, based on appropriate scientific and technical methods.

- a. Where applicable, the limits of accuracy should be indicated by the manufacturer.
- b. Whenever possible, values expressed numerically should be in commonly accepted, standardized units, and understood by users of the medical device or IVD medical device. While generally supporting the convergence on the global use of internationally

standardized measurement units, considerations of safety, user familiarity and established clinical practice may justify the use of other recognized measurement units.

- c. The function of the controls and indicators should be clearly specified on the medical device and IVD medical device. Where a medical device or IVD medical 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.

5.10 Labeling

The following principle is a general recommendation for labeling. For additional guidance on the contents of the labeling, please refer to IMDRF/GRRP WG/N52.

5.10.1 Medical devices and IVD medical devices should be accompanied by the information needed to distinctively identify the medical device or IVD medical device and its manufacturer. Each medical device and IVD medical device should also be accompanied by, or direct the user to any safety and performance information relevant to the user, or any other person, as appropriate. Such information may appear on the medical device or IVD medical device itself, on the packaging or in the instructions for use, or be readily accessible through electronic means (such as a website), and should be easily understood by the intended user.

5.11 Protection against radiation

5.11.1 Medical devices and IVD medical devices should be designed, manufactured and packaged in such a way that exposure of users, other persons, or where appropriate, patients, to radiation is appropriately reduced in a manner that is compatible with the intended purpose, whilst not restricting the application of appropriate specified levels for diagnostic and therapeutic purposes.

5.11.2 The operating instructions for medical devices and IVD medical devices emitting hazardous or potentially hazardous radiation should contain detailed information as to the nature of the emitted radiation, the means of protecting the users, other persons, or where appropriate, patients, and ways of avoiding misuse and of appropriately reducing the risks inherent to transport, storage and installation.

5.11.3 Where medical devices and IVD medical devices are intended to emit hazardous, or potentially hazardous, radiation, they should be fitted, where possible, with visual displays and/or audible warnings of such emissions.

5.11.4 Medical devices and IVD medical devices should be designed and manufactured in such a way that that the exposure of users, other persons, or where appropriate, patients, to the emission of unintended, stray or scattered radiation is appropriately reduced. Where possible and appropriate, methods should be selected which reduce the exposure to radiation of users, other persons, or where appropriate, patients, who may be affected.

5.11.5 For medical devices and IVD medical devices emitting hazardous or potentially hazardous radiation and that require installation, information regarding the acceptance and performance testing, the acceptance criteria, and the maintenance procedure should be specified in the operating instructions.

5.11.6 Where medical devices and IVD medical devices are intended to emit hazardous, or potentially hazardous, radiation, accessible to user, they should be designed and manufactured in such a way as to ensure that the quantity, geometry, energy distribution (or quality), and other key characteristics of the radiation emitted can be appropriately controlled and adjusted and, where appropriate, monitored during use. Such medical devices and IVD medical devices

should be designed and manufactured to ensure reproducibility of relevant variable parameters within an acceptable tolerance.

5.12 Protection against the risks posed by medical devices and IVD medical devices intended by the manufacturer for use by lay users

5.12.1 Medical devices and IVD medical devices for use by lay users (such as self-testing or near-patient testing intended for use by lay users) should be designed and manufactured in such a way that they perform appropriately for their intended use/purpose taking into account the skills and the means available to lay users and the influence resulting from variation that can be reasonably anticipated in the lay user's technique and environment. The information and instructions provided by the manufacturer should be easy for the lay user to understand and apply when using the medical device or IVD medical device and interpreting the results.

5.12.2 Medical devices and IVD medical devices for use by lay users (such as self-testing or near-patient testing intended for use by lay users) should be designed and manufactured in such a way as to:

- a. ensure that the medical device and IVD medical device can be used safely and accurately by the intended user per instructions for use. When the risks associated with the instructions for use cannot be mitigated to appropriate levels, these risks may be mitigated through training.
- b. appropriately reduce the risk of error by the intended user in the handling of the medical device or IVD medical device and, if applicable, in the interpretation of the results.

5.12.3 Medical devices and IVD medical devices for use by lay users (such as self-testing or near-patient testing intended for use by lay users) should, where appropriate, include means by which the lay user:

- a. can verify that, at the time of use, the medical device or IVD medical device will perform as intended by the manufacturer, and
- b. is warned if the medical device or IVD medical device has failed to operate as intended or to provide a valid result.

5.13 Medical devices and IVD medical devices incorporating materials of biological origin

5.13.1 For medical devices and IVD medical devices that include tissues, cells, or substances of animal, plant, or bacterial origin or their derivatives, which are non-viable or rendered non-viable the following should apply:

- a. where appropriate, taking into account the animal species, tissues and cells of animal origin, or their derivatives, should originate from animals that have been subjected to veterinary controls that are adapted to the intended use of the tissues.

Information on the geographical origin of the animals may need to be retained by manufacturers depending on jurisdictional requirements.

- b. sourcing, processing, preservation, testing and handling of tissues, cells and substances of animal origin, or their derivatives, should be carried out so as to provide safety for patients, users and, where applicable, other persons. In particular, safety with regards to viruses and other transmissible agents should be addressed by implementation of validated state of the art methods of elimination or inactivation in the course of the

manufacturing process, except when the use of such methods would lead to unacceptable degradation compromising the medical device or IVD medical device.

5.13.2 For Regulatory Authorities, which regulate products manufactured utilizing tissues, cells, or substances of human origin or their derivatives as medical devices or IVD medical devices, the following should apply:

- a. donation, procurement and testing of the tissues and cells should be done in accordance with jurisdictional requirements; and
- b. processing, preservation and any other handling of those tissues and cells or their derivatives should be carried out so as to provide safety for patients, users and, where applicable, other persons. In particular, safety with regard to viruses and other transmissible agents should be addressed by appropriate methods of sourcing and by implementation of validated state of the art methods of elimination or inactivation in the course of the manufacturing process.

5.13.3 For medical devices and IVD medical devices manufactured utilizing biological substances other than those referred to in Sections 5.13.1 and 5.13.2 (for example, materials of plant or bacterial origin), the processing, preservation, testing and handling of those substances should be carried out so as to provide safety for patients, users and, where applicable, other persons, including in the waste disposal chain. In particular, safety with regards to viruses and other transmissible agents should be addressed by appropriate methods of sourcing and by implementation of validated state of the art methods of elimination or inactivation in the course of the manufacturing process. Other requirements can apply in specific regulatory jurisdictions.

6.0 Essential Principles applicable to medical devices other than IVD medical devices

The essential design and manufacturing principles listed in this Section of the document are additional to the Essential Principles listed in Section 5. These Essential Principles are applicable to medical devices other than IVD medical devices.

6.1 Chemical, physical and biological properties

6.1.1 With regards to chemical, physical, and biological properties of a medical device, particular attention should be paid to the compatibility between the materials and substances used and biological tissues, cells and body fluids, taking account of the intended purpose of the device and, where relevant (for example, for some absorbable products), absorption, distribution, metabolism and excretion.

6.1.2 Medical 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 intended use; 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 in accordance with the provisions and restrictions governing those medicinal products and that the performance of both the medicinal products and of the devices is maintained in accordance with their respective indications and intended use.

6.1.3 Medical devices should be designed and manufactured in such a way as to appropriately reduce the risks linked to the size and the properties of particles which are or can be released into the patient's or user's body, unless they come into contact with intact skin only. Special attention should be given to nanomaterials.

6.2 Protection against radiation

6.2.1 Medical devices emitting ionizing radiation intended for medical imaging should be designed and manufactured in such a way as to achieve an image and/or output quality that are appropriate to the intended medical purpose whilst minimizing radiation exposure of the patient, user, and other persons.

6.2.2 Medical devices emitting ionizing radiation should be designed to allow the accurate estimation (or monitoring), display, reporting, and recording of the dose from a treatment.

6.3 Particular requirements for implantable medical devices

6.3.1 Implantable medical devices should be designed and manufactured in such a way as to remove or appropriately reduce the risks associated with medical treatment, e.g. the use of defibrillators, high-frequency surgical equipment.

6.3.2 Active programmable implantable medical devices should be designed and manufactured in a manner that allows the unequivocal identification of the device without the need for a surgical operation.

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

6.4.1 Medical devices for supplying the patient with energy or substances should be designed and manufactured in such a way that the amount to be delivered can be set and maintained accurately enough to ensure the safety of the patient, user, and others.

6.4.2 Medical devices should be fitted with the means of preventing and/or indicating any inadequacies in the amount of energy delivered or substances delivered which could pose a danger. Devices should incorporate suitable means to appropriately reduce the risk of accidental release of dangerous levels of energy or substances from an energy and/or substance source.

6.5 Medical devices incorporating a substance considered to be a medicinal product/drug

6.5.1 Where a medical device incorporates, as an integral part, a substance which, if used separately may be considered to be a medicinal product/drug as defined in the relevant legislation that applies in that Regulatory Authority and which is liable to act upon the body with action ancillary to that of the medical device, the safety and performance of the medical device as a whole should be verified, as well as the identity, safety, quality and efficacy of the substance in the specific combination product.

7.0 Essential Principles applicable to IVD medical devices

The essential design and manufacturing principles listed in this Section of the document are additional to the Essential Principles of safety and performance listed in Section 5. These Essential Principles are applicable to only IVD medical devices.

7.1 Chemical, physical and biological properties

7.1.1 With regards to chemical, physical, and biological properties for IVD medical devices, attention should be paid to the possibility of impairment of analytical performance due to physical and/or chemical incompatibility between the materials used and the specimens, analyte or marker to be detected and measured (such as biological tissues, cells, body fluids and micro-organisms), taking account of the intended purpose of the device.

7.2 Performance characteristics

7.2.1 IVD medical devices should achieve the analytical and clinical performances, as stated by the manufacturer that are applicable to the intended use/purpose, taking into account the intended patient population, the intended user, and the setting of intended use. These performance characteristics should be established using suitable, validated, state of the art methods. For example:

- a. The analytical performance can include, but is not limited to,
 - i. Traceability of calibrators and controls
 - ii. Accuracy of measurement (trueness and precision)
 - iii. Analytical sensitivity/Limit of detection
 - iv. Analytical specificity
 - v. Measuring interval/range
 - vi. Specimen stability
- b. The clinical performance, for example diagnostic/clinical sensitivity, diagnostic/clinical specificity, positive predictive value, negative predictive value, likelihood ratios, and expected values in normal and affected populations.
- c. Validated control procedures to assure the user that the IVD medical device is performing as intended, and therefore the results are suitable for the intended use.

7.2.2 Where the performance of an IVD medical device depends on the use of calibrators or control materials, the traceability of values assigned to such calibrators or control materials should be ensured through available reference measurement procedures or available reference materials of a higher order.

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

7.2.4 The performance characteristics of the IVD medical device should be evaluated according to the intended use statement which may include the following:

- a. intended user, for example, lay user, laboratory professional;
- b. intended use environment, for example, patient home, emergency units, ambulances, healthcare centers, laboratory;
- c. relevant populations, for example, pediatric, adult, pregnant women, individuals with signs and symptoms of a specific disease, patients undergoing differential diagnosis, blood donors, etc. Populations evaluated should represent, where appropriate, ethnically, gender, and genetically diverse populations so as to be representative of the population(s) where the device is intended to be marketed. For infectious diseases, it is recommended that the populations selected have similar prevalence rates.

Appendix 5—IMDRF Principles of labelling

[Principles of Labelling for Medical Devices and IVD Medical Devices](#) (IMDRF/GRRP WG/N52 FINAL: 2019)

4.0 Principles for medical device and IVD medical device identification

Medical devices and IVD medical devices may be identifiable in multiple ways, as described below. The ways in which identifier information should be included in the labelling are discussed in subsequent sections of this document.

4.1 The medical device or IVD medical device should be identified through the use of a brand or trade name that allows differentiation from other products of the same or similar type.

4.2 A medical device or IVD medical device, or a combination of medical devices or IVD medical devices or accessories, should be distinguishable from other devices via use of a catalog number, or another method that allows identification of the device model and its distinguishing characteristics. Each catalog number should only involve one defined product specification.

4.3 If required by the RA having jurisdiction, a medical device or IVD medical device should be identified with a Unique Device Identifier (UDI) in human- and machine-readable form. For implantable devices, the UDI should be identifiable and able to be scanned prior to implantation. For further guidance on the information to be incorporated within the label for UDI purposes, the content of the information to be captured in the UDI, the inclusion of UDI information in the UDI database, and the linkage of UDI with clinical, industry, and government databases, refer to the IMDRF guidance document on this subject.

5.0 General labelling principles for medical devices and IVD medical devices

This section describes the general principles that apply equally to all medical devices and IVD medical devices. The primary purpose of labelling is to identify the medical device or IVD medical device and its manufacturer, and provide essential information about its safety, performance, and appropriate use to the user or other relevant persons. Such information may appear on the device itself, on packaging, or as instructions for use. These documents should be developed and evaluated using risk management principles and usability engineering processes. Certain jurisdictions may require the inclusion of additional information or the use of specific formatting.

The following principles are recommended.

5.1 Labelling

5.1.1 The medium, format, content, legibility, and location of the labelling should be appropriate to the particular medical device or IVD medical device, its intended purpose, and intended users to ensure safe and appropriate use, taking into consideration the following:

- user knowledge;
- user training;
- any special needs of the persons for whom the device is intended; and
- the location and environment in which the device can be used.

5.1.2 Labelling should be subject to document (version) control principles.

5.1.3 Depending on the requirements of the RA having jurisdiction, labelling may be provided in one or more language(s). Languages may be identified using the plain text name of the language or a language code.

5.1.4 The use of internationally recognized symbols in labelling is encouraged, provided that device safety is not compromised by a lack of understanding on the part of the user. Where the meaning of the symbol is not obvious to the user, e.g. for a newly introduced symbol, an explanation should be provided within the labelling.

5.1.5 Residual risks that are to be communicated to the user and/or other persons should be included in the labelling and are considered to be information for safety.

5.1.6 If required by the RA having jurisdiction, the labelling should include a summary of the performance studies and clinical investigations used to demonstrate conformance with regulatory review principles and that demonstrate the safety and clinical performance of the medical device or IVD medical device for its intended use. This summary should include but may not be limited to a summary of the investigation, clinical performance and outcome data, clinical safety information, and a summary of the clinical benefit, and should be presented in such a way as to accurately reflect the safety and performance of the medical device or IVD medical device. If not contained in the instructions for use, a reference should be included as to where such information may be accessed.

5.1.7 The labelling should not contain any language regarding the manufacturer's liability in the case of damage or injury resulting from any use or malfunction of the medical device or IVD medical device that contradicts the laws or regulations in the jurisdiction of use.

5.1.8 The labelling should not contain any disclaimers related to the safety and performance of the medical device or IVD medical device for its intended purpose that are incompatible with the laws or regulations in the jurisdiction of use, or the obligations of the manufacturer to design and manufacture a product that is safe and performs as intended throughout its expected lifetime.

5.2 Label

The label should contain the following information, which may appear on the medical device or IVD medical device itself, on the packaging of each unit, or on the packaging of multiple medical devices or IVD medical devices. It is important to note that medical device and IVD medical device kits may include individual reagents, articles, or medical devices that may be made available as separate medical devices or IVD medical devices. In this situation, those individual medical devices and IVD medical devices contained in the kit should comply with the label content principles in this section.

5.2.1 The information required on the label should be provided in a label on the device itself. If this is not practicable or appropriate (for example, for small-size devices, contact lenses, bone cement, software, etc.), some or all the information may appear on the packaging for each unit, and/or on the packaging of multiple devices. If UDI is required by the RA having jurisdiction, it should follow the requirements of the appropriate UDI-issuing agency/entity. The UDI should be on the label and on all device packages, and, for reprocessed devices intended to be used more than once, it should be provided on the device itself.

5.2.2 The label on the outside packaging should include any special handling measures or permissible environmental conditions (e.g., upper and lower temperature limits, light, humidity) for storage and transport of the medical device or IVD medical device. Where premature unpacking of a medical device or IVD medical device or its parts could result in an unacceptable risk, the label should be marked appropriately. The use of non-specific temperature or humidity indications that are open to interpretation, or which may vary according to geographic location

is to be avoided unless further qualification is included (e.g., “store at room temperature, i.e.15-25°C” or “store in a cool place below 15°C, do not freeze”).

5.2.3 Where relevant, the label on the packaging should include an indication of the net quantity of contents, expressed in terms of weight or volume (including volume after reconstitution), numerical count, or any combination of these or other terms which accurately reflects the contents of the package.

5.2.4 The label should contain the brand or trade name of the medical device or IVD medical device.

5.2.5 The label should contain the details necessary for a user to identify the device and its use, e.g. ‘cardiac ablation catheter 10 French / 20 cm’ or ‘pediatric thermometer’ or ‘blood glucose meter’ or ‘HIV-1/HIV-2 antibody test’.

5.2.6 The label should be provided in a human-readable format but may be supplemented by machine-readable forms, such as radio-frequency identification (RFID) or bar codes.

5.2.7 There should be only one machine-readable format on the label. If there are multiple, there should be a clear indication to anyone relying on capture/use of this format throughout distribution and use, including the provider of care, which machine-readable format to scan when and for what purpose.

5.2.8 If a catalog number is used to identify the medical device or IVD medical device, the label should include this catalog number.

5.2.9 The label should contain the name and address of the manufacturer in a format that is recognizable and allows the location of the manufacturer to be established. The address should contain information related to the physical location such as street/road, number/floor/house, city, state/region, postal code, country, etc. An abbreviated version of the address may be sufficient on the label if providing the full address on the label is not practical, and if the device includes instructions for use that provide a full address. If permitted by the RA having jurisdiction, this principle may be fulfilled with a URL on the label that when accessed contains the full address of the manufacturer in a format that is recognizable and allows the location of the manufacturer to be established.

5.2.10 If an authorized representative is acting on behalf of the manufacturer in the country/jurisdiction, the label should also contain the address of the authorized representative, if such information is required by the RA having jurisdiction. This information may be added by the authorized representative within the country of import rather than be provided by the manufacturer, in which case the additional information should not obscure any of the manufacturer's labels. If permitted by the RA having jurisdiction, this principle may be fulfilled with a URL on the label that when accessed contains the full address of the authorized representative in a format that is recognizable and allows the location of the authorized representative to be established.

5.2.11 For imported medical devices or IVD medical devices, the label should contain the name and physical address of the importer or distributor within the importing country/jurisdiction, if such information is required by the RA having jurisdiction. This information may be added by the importer or distributor within the country of import rather than be provided by the manufacturer, in which case the additional information should not obscure any of the manufacturer's labels.

5.2.12 If the label includes symbols and safety-related identification colors, the marking should be explained, where necessary.

5.2.13 The label should include the batch code, batch number, lot code, lot number, serial number, control number, or version number of the medical device or IVD medical device, as appropriate.

5.2.14 The label should include an unambiguous indication of the date, such as the expiry date, after which the medical device or IVD medical device cannot be used safely, where this is relevant (e.g. on devices supplied sterile or single-use disposable devices). Ideally, this date should be expressed as the full year, month, and day because this format provides the least ambiguity. The label should also include the date of manufacture, if required by the RA having jurisdiction. In this case, the date of manufacture may be included as part of the batch or serial number, provided the date is clearly identifiable.

5.2.15 If the medical device or IVD medical device is supplied sterile, the label should include an indication that the device is provided in a sterile state and, where applicable, the sterilization method.

5.2.16 Where appropriate, the label should state that the medical device or IVD medical device contains or incorporates a medicinal or biological substance, e.g. heparin-coated catheter or drug-coated stent. If required by the RA having jurisdiction, the label should also include the quantity, proportion or strength of that substance (e.g. contains 10mg/ml sodium hyaluronate; gentamicin (2%)) if the substance will be in direct contact with the patient.

5.2.17 The label should include any warnings or precautions to be taken that need to be brought to the immediate attention of the user of the medical device or IVD medical device as relevant, and to any other person where appropriate (e.g. 'CAUTION – HOT SURFACE' or 'THIS PRODUCT CONTAINS LATEX' or 'CONTAINS POTENTIALLY INFECTIOUS MATERIAL'). This information may be kept to a minimum, such as through the use of symbols, in which case more detailed information should appear in the instructions for use.

5.2.18 The label should indicate if the medical device or IVD medical device is intended by the manufacturer for single-use only or reuse on a single patient. The label may indicate reuse in more than one patient if warranted. If the medical device or IVD medical device is reusable and its reusability is limited, the label should indicate these limitations (e.g., maximum number of allowable reuses).

5.2.19 The label should indicate if the medical device or IVD medical device is intended only for premarket clinical investigation, premarket performance evaluation, non-clinical research, or presentation or demonstration purposes. In these situations, some of the principles listed in this document may not apply.

Labels should be durable and legible for at least the lifetime of the medical device or IVD medical device.

5.3 Instructions for use

5.3.1 Instructions for use should be written in terms readily understood by the intended user and, where appropriate, supplemented with drawings and diagrams near the corresponding text. Some medical devices or IVD medical devices may include separate information for the professional user and the lay person.

5.3.2 Where the manufacturer supplies multiple medical devices or IVD medical devices to a single user and/or location, it may be sufficient to provide only a single copy of the instructions for use. In these circumstances, the manufacturer should provide further copies upon request or make the instructions for use available in an electronic format.

5.3.3 Instructions for use may not be needed or may be abbreviated for certain medical devices or IVD medical devices if they can be used safely and as intended by the manufacturer

without any such instructions for use. Justification for any omission should be described in the manufacturer's risk analysis for the medical device or IVD medical device.

5.3.4 Instructions for use may be provided to the user in paper or electronic format or both, as permitted by the RA having jurisdiction. They may be supplied by various means either with the medical device or IVD medical device or separate from it. Examples of other means are: information displayed on a screen incorporated into the medical device or IVD medical device, information downloaded from the manufacturer's website, and machine-readable sources. The means chosen should be appropriate for the use environment and accessible to the anticipated user population. Any updates to the instructions for use need to be consistent across paper and electronic formats whether they are retrospective or batch specific.

5.3.5 If the manufacturer has a website, the instructions for use may also be made available on that website. In this situation, the medical device or IVD medical device packaging should include a means for the user to easily access the appropriate electronic instructions for use via inclusion of a web address or other information.

5.3.6 Where instructions for use are provided on a medium other than paper, the manufacturer should ensure the user has information on how to:

- view the instructions for use;
- access the correct version of the instructions for use; and
- obtain a paper version of the instructions for use.

NOTE: The RA having jurisdiction may set the conditions for when the electronic instructions for use should be provided to guarantee a high level of safety. These conditions may specify the types of medical devices or IVD medical devices that can use electronic instructions for use and the requirements the manufacturer needs to follow. For example, the RA may specify that the manufacturer should upon request provide a paper version free of charge.

5.3.7 The instructions for use should contain the name or trade name of the medical device or IVD medical device.

5.3.8 The instructions for use should include a description of the medical device or IVD medical device and how it is intended to be used.

5.3.9 The instructions for use should contain the name and address of the manufacturer in a format that is recognizable and allows the location of the manufacturer to be established, together with contact information (e.g., telephone number, fax number, website or email address) to obtain technical assistance, if such information is required by the RA having jurisdiction.

5.3.10 The instructions for use should state the medical device's or IVD medical device's intended use/purpose, including the indications for use, intended user (e.g. professional or lay person), and intended use environment, as appropriate.

5.3.11 The instructions for use should state the performance of the medical device or IVD medical device claimed by the manufacturer.

5.3.12 The instructions for use should include any specifications the user requires to use, process, and maintain the device appropriately. For example, if the medical device or IVD medical device performs any measurements, the instructions for use should include the claimed limits of accuracy.

5.3.13 The instructions for use should include information that allows the user and/or patient to be sufficiently informed of any warnings, precautions, measures to be taken and limitations of

use regarding the medical device or IVD medical device. This information should cover, where appropriate:

- a. warnings, precautions and/or measures to be taken in the event of malfunction of the medical device or IVD medical device or changes in its functionality that may affect safety or performance;
- b. warnings, precautions and/or measures to be taken in regard 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;
- c. warnings, precautions and/or measures to be taken in regard to the risks of interference posed by the reasonably foreseeable presence of the medical device or IVD medical device during specific diagnostic investigations, evaluations, therapeutic treatment or use (e.g. electromagnetic interference emitted by the device affecting other equipment);
- d. precautions related to materials incorporated into the device that are potentially carcinogenic, mutagenic or toxic, or could result in sensitization or allergic reaction for the patient or user; and
- e. precautions related to potentially infectious material that is included in a medical device or IVD medical device.

5.3.14 The instructions for use should include any recommended quality control procedures to be taken to verify that the medical device or IVD medical device performs as intended, including the following if applicable:

- a. the procedures for using any available controls;
- b. instructions recommending the frequency of use;
- c. the limitations of the quality control procedure;
- d. how the user should interpret the quality control procedure results, including a description of whether test results can or cannot be accepted; and
- e. the actions to be taken if there is a failure of any of the controls.

5.3.15 If the medical device or IVD medical device incorporates or includes a medicinal or biological substance, the instructions for use should identify that substance or material, and list any warnings, precautions and/or limitations related to this substance. If required by the RA having jurisdiction, the instructions for use should also include the quantity, proportion or strength of that substance if the substance will be in direct contact with the patient.

5.3.16 The instructions for use should include information describing the purpose and interpretation of any indicators (e.g., humidity, temperature) provided within the packaging, and what steps to take based on the indicator results.

5.3.17 The instructions for use should identify information for safety including any relevant residual risks, contraindications, and any expected and foreseeable adverse events, including information to be conveyed to the patient in this regard.

5.3.18 The instructions for use should include the details of any preparatory treatment or handling of the medical device or IVD medical device before it is ready for use (e.g., sterilization,

identification of other necessary equipment not provided with the medical device or IVD medical device, final assembly, reconstitution, calibration).

5.3.19 The instructions for use should include any requirements for special facilities (e.g. sterile field or clean room environment), or special training, or particular qualifications of the user and/or third parties.

5.3.20 The instructions for use should contain any information needed to verify that the medical device or IVD medical device is properly installed and ready to perform safely and as intended by the manufacturer, including when applicable:

- a. details and frequency of preventive and regular maintenance;
- b. cleaning and disinfection information
- c. identification of consumable components and how to replace them;
- d. necessary calibration information; and
- e. methods for mitigating risks encountered during cleaning, installation, calibration or servicing.

5.3.21 The instructions for use should include any special handling measures or permissible environmental conditions (e.g., upper and lower temperature limits, light, humidity) for storage and transport of the medical device or IVD medical device. The use of non-specific temperature or humidity indications that are open to interpretation, or which may vary according to geographic location is to be avoided unless further qualification is included.

5.3.22 The instructions for use should include any warnings or precautions to be taken related to the disposal of the medical device or IVD medical device and its accessories. This also includes any consumables that require special disposal as a result of being used with the medical device or IVD medical device. This information should cover, where appropriate:

- a. infection or microbial hazards (e.g. explants, needles or surgical equipment contaminated with potentially infectious substances of human origin);
- b. environmental hazards (e.g. batteries or materials that emit potentially hazardous levels of radiation); and
- c. physical hazards (e.g. from sharps).

5.3.23 If the medical device or IVD medical device is supplied sterile, the instructions for use should include instructions to be followed in the event of the sterile packaging being damaged or unintentionally opened before use.

5.3.24 The instructions for use should include any instructions to be followed in the event of the packaging being damaged or unintentionally opened before use, or if the packaging is exposed to environmental conditions outside of those specified.

5.3.25 If the medical device or IVD medical device is supplied non-sterile with the intention that it is sterilized before use, the instructions for use should include appropriate instructions for sterilization and should also include any instructions for cleaning the device prior to sterilization.

5.3.26 If the medical device or IVD medical device is reusable, the instructions for use should include information on the appropriate processes to allow reuse, including cleaning, disinfection, packaging and, where appropriate, the method of re-sterilization. Information

should 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).

5.3.27 For medical devices or IVD medical devices intended for use together with other medical devices, IVD medical devices, and/or general purpose equipment, the instructions for use should include sufficient information identify such devices or equipment, in order to obtain a safe combination, and/or information on any known restrictions to combinations of medical devices or IVD medical devices and equipment.

5.3.28 If the medical device or IVD medical device emits hazardous, or potentially hazardous levels of radiation for medical purposes, the instructions for use should include detailed information as to the nature, type and where appropriate, the intensity, distribution, and recommended dose of the emitted radiation; and/or the means of protecting the patient, user, or third party from unintended radiation during use of the device.

5.3.29 The instructions for use should state the date of issue or latest revision of the instructions for use and, where appropriate, an identification number.

6.0 General Labelling Principles for medical devices other than IVD medical devices

In addition to the principles outlined in Section 5.0, medical devices should also meet the following labelling principles.

6.1 Label

6.1.1 The label should indicate if the medical device is for use by a single individual and has been manufactured according to a written prescription or pattern (e.g., it is a personalized medical device).

6.2 Instructions for use

6.2.1 If the medical device administers medicinal or biological products, the instructions for use should indicate any limitations or incompatibilities in the choice of substances to be delivered.

7.0 General Labelling Principles for IVD medical devices

In addition to the principles outlined in Section 5.0, IVD medical devices should also meet the following labelling principles.

7.1 Label

7.1.1 The label should state that the IVD medical device is for in vitro diagnostic use.

7.2 Instructions for Use

7.2.1 The description of the intended use should include the following, where applicable:

- a. what the IVD medical device measures or detects;
- b. its function (e.g. screening, monitoring, diagnosis or aid to diagnosis, prognosis, prediction, companion diagnostic);
- c. the specific disorder, condition or risk factor of interest that it is intended to detect, define or differentiate;

- d. whether or not it includes automated components or is intended to be used with automated instruments;
- e. what the IVD medical device reports (e.g., qualitative test, semi-quantitative, quantitative test);
- f. the type of specimen(s) (e.g. serum, plasma, whole blood, tissue biopsy, urine) required including the specimen source(s) (e.g. capillary whole blood from arm), matrix (e.g. EDTA tube), time (e.g. 8 hours after injury) and collection method (e.g. self-collected urine); and
- g. target population (on whom the IVD medical device is used).

7.2.2 The instructions for use should include a statement of the test principle(s), such as the general biological, chemical, microbiological, immunochemical and other principles on which the IVD medical device is based. Proprietary information need not be disclosed, but should provide enough detail to allow the user to understand how the IVD medical device is able to carry out its function.

7.2.3 The instructions for use should include a description and the amount of the reagent, calibrators and controls and any limitation upon their use (e.g. suitable for a dedicated instrument only).

NOTE: IVD medical device kits include individual reagents and articles that may be made available as separate IVD medical devices. In this situation, where appropriate, these IVD medical devices should comply with the instructions for use content in this section.

7.2.4 The instructions for use should include a list of materials provided and a list of any materials required but not provided.

7.2.5 The instructions for use should include a description of in-use stability. This may include the storage conditions prior to opening 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.

7.2.6 The instructions for use should list the included and excluded conditions for collection, shipping, handling, and preparation of the specimen.

7.2.7 Where relevant, the instructions for use should include the traceability of values assigned to calibrators and trueness-control materials, including identification of applicable reference materials and/or reference measurement procedures of higher order.

7.2.8 The instructions for use should describe the assay procedure including calculations and interpretation of results, any additional software or reference database required, and where relevant, if any confirmatory testing should be considered.

7.2.9 The instructions for use should list the analytical performance characteristics, such as precision, accuracy, sensitivity, and specificity.

7.2.10 Where relevant, the instructions for use should list the clinical performance characteristics (e.g. diagnostic sensitivity, diagnostic specificity, positive predictive value, negative predictive value, likelihood ratio, expected values in normal and affected populations).

7.2.11 Where relevant, the instructions for use should include the reference intervals in normal and affected populations.

7.2.12 The instructions for use should include information on any interfering substances or limitations (e.g. visual evidence of hyperlipidemia or hemolysis, age of specimen/sample) that may affect the performance of the assay.

7.2.13 Where relevant, the instructions for use should include a bibliography or references section.

8.0 Labelling Principles for medical devices containing software or software as a medical device

8.1 Software that is incorporated into a medical device or IVD medical device or that is intended for use as software as a medical device (SaMD) should be identified with an identifier, such as version, revision level or date of build release/issue. The unique identifier should be accessible to the intended user, unless the medical device does not have a wired or wireless electronic interface.

8.2 For software incorporated into a medical device or IVD medical device, the identifier does not need to be on the outside of the medical device or IVD medical device.

8.3 For SaMD without a physical form or packaging, the label may be available electronically. In this situation, the medical device should incorporate a means for the user to easily access the electronic label via the software itself or via inclusion of a web address or other means.

9.0 Labelling Principles for medical devices and IVD medical devices intended for use by lay persons

9.1 The information and instructions provided by the manufacturer should allow the intended lay user to understand and apply, in order to correctly interpret the result provided by the device or to confirm that the device is operating or has operated as intended.

9.2 Instructions for use intended to be used principally by lay users should be available in a format appropriate and accessible to the lay user.

9.3 Some devices may include separate information for the professional user and the lay person, e.g. a simplified job aid for lay persons. This information should agree with the instructions for use and should state clearly the version it relates to. It should be written at a level consistent with the education, training and any special needs of its intended readers.

9.4 The language of the intended use statement may be simplified in instructions for use used by lay persons (including self-testing), provided key messages remain. In addition, instructions for use for home use medical devices or self-testing IVD medical devices may omit some of the recommended elements, provided this does not affect safety or performance. Justification for any omission should be described in the manufacturer's risk analysis for the product.

9.5 Interpretation of results should include pictorial representations of all possible test results (including when a device has failed to provide a valid result) for medical devices or IVD medical devices that give a visual readout, where applicable.

9.6 For medical devices or IVD medical devices intended for use by lay persons, the instructions for use should clearly and concisely describe the circumstances when the user should consult with a healthcare professional.

9.7 Instructions for use should clearly state if an IVD medical device is intended for self-testing. Self-testing may include the involvement of a third-party caregiver.

10.0 Labelling Principles for information intended for the patient

The following principles are not related to the use of a medical device or IVD medical device by a lay person, but instead describe general considerations for information intended to be provided to the patient before or after use of the medical device or IVD medical device by a professional.

Not all medical devices or IVD medical devices include information to be provided to the patient. The need for such information and the applicability of the principles below depend on the RA having jurisdiction and the type of medical device, including implantable devices in certain regulatory jurisdictions.

10.1 Information that is specifically intended for the patient should be provided with the medical device or IVD medical device. Depending on the device, the user population and the RA jurisdiction, it may be appropriate for this information to be available electronically. In this situation, the medical device or IVD medical device should include a means for the patient to easily access the electronic information via inclusion of a web address or other information.

10.2 Information identifying the device should be provided in a human-readable format but may be supplemented by machine-readable forms, such as bar codes. If UDI is required by the RA having jurisdiction, UDI should be included.

10.3 If the information intended for the patient includes an implant card, the card should be in a durable format and should include the following:

- a. identification of the medical device, including the brand or trade name and the device type or use, e.g. 'transcatheter heart valve' or 'synthetic hernia mesh';
- b. identification of the device model;
- c. the catalog number;
- d. the number used to uniquely identify the medical device, such as the lot number, serial number, or UDI; and
- e. the name and address of the manufacturer and any authorized representative or importer in a format that is recognizable and allows their location to be established. A full address should contain information related to the physical location such as street/road, number/floor/house, city, state/region, postal code, country, etc.

10.4 If the information intended for the patient includes an informational brochure, the information in the brochure should be written in a way that is readily understood by patients. In addition, the brochure should include the following information, as well as any other information relevant to the device or recommended in specific standards, as applicable:

- a. the name of the medical device;
- b. the model of the medical device;
- c. the intended use, including the intended purpose and patient population;
- d. any special operating instructions for the use of the medical device;
- e. a description of the medical device, its mechanism of action, and its expected performance;
- f. any adverse event the patient may potentially experience due to the medical device;
- g. warnings about any relevant residual risks;

- h. warnings about risks that could arise from the interaction of the medical device with other equipment, and precautions and other measures that should be taken by the patient or a health professional because of these risks;

Example 1: The risk of electrical interference from electro surgical medical devices.

Example 2: The risk of magnetic field interference from magnetic resonance imaging medical devices.

- i. the nature and frequency of regular or preventive examination, monitoring, or maintenance of the medical device that should be undertaken;
- j. the nature and frequency of any follow-up with healthcare professionals to be performed by the patient;
- k. signs that could indicate that the medical device is malfunctioning;
- l. precautions and other measures that should be taken by the patient if the performance of the medical device changes or the patient experiences any of the signs mentioned in item (k);
- m. the expected lifetime of the medical device, and any factors that could affect it;
- n. precautions and other measures that should be taken at, or near, the end of the expected lifetime;
- o. information about the materials and substances, including manufacturing residuals, in the medical device that could pose a risk to the patient;
- p. contact information for the manufacturer;
- q. circumstances in which the patient should contact a health professional; and
- r. guidance regarding whom the patient should contact in the case of any symptoms of an adverse event or a problem with the device

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