HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Guide for
Health Institutions that Manufacture and Use In-house *in vitro* Diagnostic Medical Devices (IVD) in Ireland

Guide for health institutions that manufacture and use in-house in vitro diagnostic medical devices (IVD) in Ireland

This guide does not purport to be an interpretation of law and/or regulations and is for guidance purposes only.

CONTENTS

1 GLOSSARY

1.1.1 *in vitro* diagnostic medical device (IVD)[1]

'in vitro diagnostic medical device' means any medical device which is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, piece of equipment, software or system, whether used alone or in combination, intended by the manufacturer to be used in vitro for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information on one or more of the following:

(a) concerning a physiological or pathological process or state.
(b) concerning congenital physical or mental impairments.
(c) concerning the predisposition to a medical condition or a disease.
(d) to determine the safety and compatibility with potential recipients.
(e) to predict treatment response or reactions.
(f) to define or monitoring therapeutic measures.

Specimen receptacles shall also be deemed to be *in vitro* diagnostic medical devices.

Note: For the purposes of this guide, the term 'device' refers to an IVD'

1.1.2 Health institution[2]

'health institution' means an organisation the primary purpose of which is the care or treatment of patients or the promotion of public health;

Note: Organisations primarily claiming to pursue health interests or healthy lifestyles, such as gyms, spas, wellness and fitness centres are not considered health institutions.
Note: Organisations primarily supporting clinical research or that are providing laboratory services in the context of clinical research do not meet the definition of a health institution.

1.1.3 In-house IVD[3]

In the context of this guidance an in-house IVD is an IVD which is manufactured and used only within a health institution, and which meets all the conditions of IVDR Article 5(5).

1.1.4 General Safety & Performance Requirements

The General Safety & Performance Requirements are outlined in IVDR Annex I and are a set of requirements that are applicable to all IVDs claiming compliance with the IVDR, including in-house IVDs.

[1] IVDR Article 2(2)
[2] IVDR Article 2(29)
[3] MDCG 2023-1,

1.1.5 Incident [4]

'incident' means any malfunction or deterioration in the characteristics or performance of a device made available on the market, including use-error due to ergonomic features, as well as any inadequacy in the information supplied by the manufacturer and any harm as a consequence of a medical decision, action taken or not taken on the basis of information or result(s) provided by the device.

1.1.6 Serious incident [5]

'serious incident' means any incident that directly or indirectly led, might have led or might lead to any of the following:

(a) the death of a patient, user or other person,

(b) the temporary or permanent serious deterioration of a patient's, user's or other person's state of health,

(c) a serious public health threat

Note Serious incidents involving in-house IVDs must be reported to the HPRA. See Section 5.4 of this guide.

2 SCOPE

The purpose of this guide is to provide an overview of legislation and key concepts relevant to in-house *in vitro* diagnostic medical devices (IVDs). This guide is targeted at health institutions within Ireland that manufacture and use in-house IVD's. The requirements of Regulation (EU) 2017/746 on *in vitro* diagnostic medical devices are described here including details on when they apply. In addition, this guide provides practical considerations for health institutions and outlines information that must be notified or submitted to the Health Products Regulatory Authority (HPRA). This guide does not cover in-house medical devices under Regulation (EU) 2017/745.

[4] IVDR Article 2(67)

[5] IVDR Article 2(68)

3 INTRODUCTION

The IVDR, which came into force on 26 May 2022, outlines that in-house IVDs can be manufactured and used by health institutions to address an unmet clinical need where CE marked alternatives are not available or suitable for the patient population. Under the IVDR, only health institutions within the EU may be permitted to manufacture in-house IVDs provided they are compliant with the relevant requirements. By including in-house IVDs within its scope, the IVDR aims to ensure a minimum level of safety and performance by requiring compliance to these specific requirements. Article 5(5) of the IVDR outlines which requirements apply to health institutions manufacturing in-house IVDs, these are discussed further in Section 5 of this guide. An amendment to the IVDR was published in January 2022[1] which, for in-house IVD manufacturers, staggered the applicable timelines for elements of Article 5(5). Further details on the timelines for application of these requirements can be found in Section 5.5 of this guide.

This guide aims to assist health institutions that manufacture and use in-house IVDs to understand and implement the requirements of the IVDR and takes into account national legislation for IVDs[6]. Information provided in this guide must be read in conjunction with the European guidance on in-house IVDs (MDCG-2023-1)[7]. The European guidance provides additional context and information on the requirements for in-house IVDs. This guide is intended as a supplement to MDCG 2023-1 to provide additional clarity for health institutions within Ireland.

4 WHAT IS AN IN-HOUSE IVD?

For a product to qualify as an in-house IVD it must first qualify as an IVD. IVDR Article 2(2) provides a useful definition of an IVD to assist in this determination (see glossary). Where a product is being used by a health institution for a medical purpose that meets the definition of an IVD, but is not a CE marked IVD, it could qualify as an in-house IVD. Similarly, where a health institution alters or changes the intended purpose of a CE marked IVD, it could also qualify as an in-house IVD. As discussed previously in house IVDs must comply with all applicable requirements as outlined in IVDR Article 5(5) see section 5 for further details.

The following is a non-exhaustive list of examples of the ways in which in-house IVDs may be manufactured.

- Manufacturing an IVD from raw materials parts or components,
- Use of 'research use only' products for a medical purpose,
- Use of software which is not CE marked to process data derived from IVDs for a specific medical purpose,

[6] S.I. No. 256 of 2022 & S.I. No 365 of 2022.
[7] MDCG 2023-1: Guidance on the health institution exemption under Article 5(5) of Regulation (EU) 2017/745 and Regulation (EU) 2017/746.

- Using a CE marked IVD for a purpose different to that intended by the manufacturer,
- Modifying a CE marked IVD to create a new IVD,
- Combining IVD's or products for a medical purpose, which may include: -
  - Products which do not bear CE marking,
  - Products which are labelled as 'research use only' (RUO),
  - CE marked IVD's,

  where either the products are not CE marked or where the combination of CE marked IVD's, and other IVD's/ products is not in line with their original intended purpose.

Figure 1 provides a flow chart to assist health institutions in determining whether products qualify as in-house IVDs under the IVDR. Health institutions in Ireland can contact the HPRA at devices@hpra.ie if they have queries on the qualification of in-house IVDs.

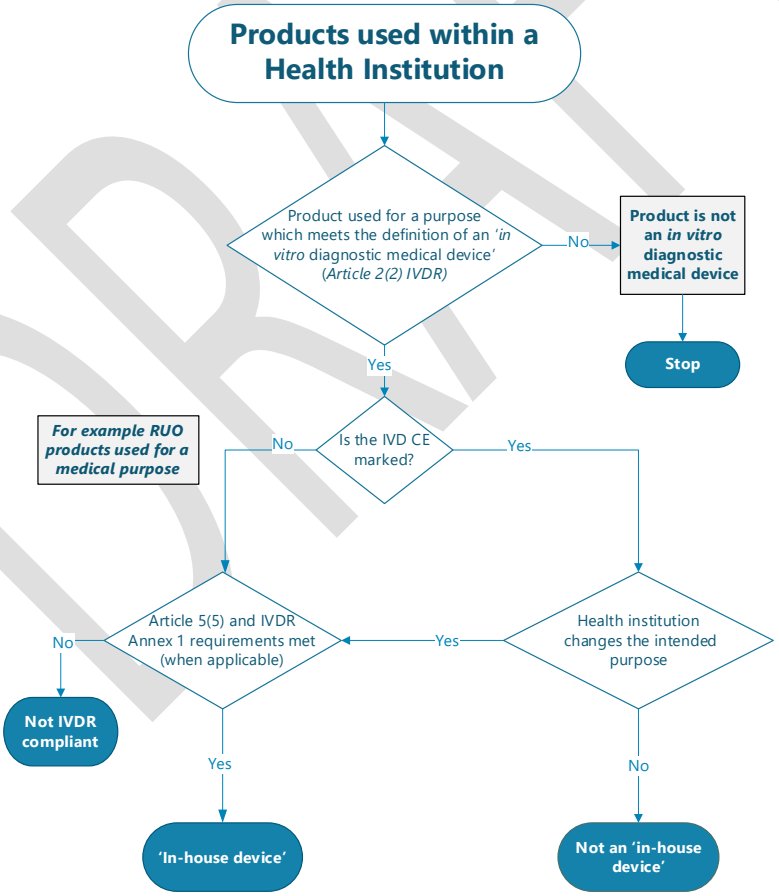

Figure 1: Flowchart highlighting scenarios, which can result in a health institution manufacturing an in-house IVD.

5 REQUIREMENTS FOR IN-HOUSE IVDS: IVDR ARTICLE 5(5)

This section examines the requirements for health institutions that manufacture and use in-house IVDs which are outlined in IVDR Article 5(5). For the purposes of this guide, the term 'device' refers to an 'IVD'.

5.1 General Safety & Performance Requirements

All in-house IVDs must meet the relevant General Safety & Performance Requirements as outlined in Annex I of the IVDR. The General Safety & Performance Requirements are divided into three chapters.

5.1.1 Chapter I (Section 1-8): General Requirements.

Chapter I outlines requirements which apply to all IVDs including in-house IVDs. These general requirements include requirements for the risk management system, risk control and risk minimisation.

5.1.2 Chapter II (Section 9-19): Requirements regarding Performance, Design and Manufacture.

Chapter II outlines requirements which depend on the nature of the IVD, and technology used. Notably this chapter describes information on the performance of the IVD and where applicable, specific design requirements.

Not all the requirements set out in Chapter II of Annex I may apply to every in-house IVD. For example, the requirements relating to self-testing or near-patient tests would only apply to self-tests and near-patient tests. Where a requirement does not apply to the in-house IVD this should be clearly documented in a General Safety & Performance Requirements checklist or similar document alongside a justification as to why that requirement does not apply. A sample checklist is provided in Annex 1 of this guide.

5.1.3 Chapter III (Section 20): Requirements regarding Information Supplied with the IVD.

Chapter III describes the requirements for information which should be included on the labelling, packing and the instructions for use.

Similar to Chapter II not all the requirements set out in Chapter III may apply to every in-house IVD. For example, the requirements relating to self-testing or near-patient tests would only apply to self-test and near-patient test. Where a requirement does not apply to the IVD in question, this should be clearly documented in the General Safety & Performance Requirements checklist alongside a justification as to why that requirement does not apply. A sample checklist is provided in Annex 1 of this guide.

Labelling & Packaging (Annex 1 Section 20.2-20.3): In-house IVDs should be accompanied by sufficient information to allow identification of the IVD and other relevant information such as batch number etc. This may be achieved through a combination of appropriate labelling and packaging. It is recommended that for in-

house IVDs, Annex 1 Sections 20.2 and 20.3 are reviewed together to determine how best to include such accompanying information.

Instructions for use (Annex 1 Section 20.4): In the case of in-house IVDs, the instructions for use may be in the form of a protocol or standard operating procedure. These should be sufficiently detailed to cover all relevant aspects of Section 20.4.1. In the case of IVDs for self-testing, Section 20.4.2 also applies and the end use should be considered when designing the instructions, form, format and usability.

5.2 Article 5(5) a-i

Article 5(5) describes nine core requirements for in-house IVDs. The European guidance on in-house devices (MDCG-2023-1) provides explanatory text on these points. This section explores each point providing a reference to the relevant section in MDCG 2023-1 for each requirement.

5.2.1 Article 5(5)a: the devices are not transferred to another legal entity.[8]

It is the responsibility of the health institution to understand the scope of its facilities as a legal entity. Some health institutions may have satellite sites, which remain part of the one legal entity. In other cases, there may be strong affiliations with other health institutions or organisations which remain as separate legal entities even if located at the same physical site. In-house IVDs manufactured within a health institution should not be transferred outside the legal remit of that health institution. It should remain within and be used by the health institution that is manufacturing it.

This requirement does not impose a restriction on specimens being referred or transferred to a health institution for testing using an in-house IVD or the issuance of results. For example, specimens referred from GP's or other health institutions for specialist testing. As such, whilst the in-house IVDs may not be transferred outside of the legal entity in which it is manufactured and used, specimens may be transferred.

5.2.2 Article 5(5)b: manufacture and use of the devices occur under appropriate quality management systems.[9]

The health institution must have in place an appropriate quality management system, which enables it to meet the requirements of IVDR Article 5(5) and IVDR Annex 1. This quality management system should govern the manufacture and use of the IVDs within the health institution.

[8] See also MDCG 2023-1 Section 3.4

[9] See also MDCG 2023-1 Section 3.5.2 & 3.5.3

5.2.3 Article 5(5)c: the laboratory of the health institution is compliant with standard EN ISO 15189 or where applicable national provisions, including national provisions regarding accreditation. [10]

The laboratories within health institutions must be compliant with EN ISO 15189. This can be demonstrated either by obtaining accreditation to EN ISO 15189 or by other means.

Accreditation to EN ISO 15189 is the preferred means of demonstrating compliance to the standard; however, this may not always be feasible. In the absence of EN ISO 15189 accreditation, it is the responsibility of the health institution to demonstrate that they are compliant with the standard and be in a position to provide a justification for the same. This includes maintaining up to date documentation to support this position and conducting internal audits to verify that the laboratory remains compliant.

Whilst compliance to EN ISO 15189 for the purposes of the IVDR may be demonstrated by other means, this does not replace any existing legal requirement for accreditation present from other legal frameworks. For example, hospital blood banks are required to be EN ISO 15189 accredited under national law.[11]

5.2.4 Article 5(5)d: the health institution justifies in its documentation that the target patient group's specific needs cannot be met or cannot be met at the appropriate level of performance by an equivalent device available on the market.[12]

It is important to note that the term device here refers to a CE marked IVD. The justification for the use of the in-house IVD can be for one of two reasons, either

- The target patient group's specific needs cannot be met by an equivalent CE marked IVD available on the market, or
- Such needs cannot be met at an appropriate level of performance by an equivalent CE marked IVD available on the market.

In the first instance, one may consider whether an equivalent IVD is available to address the target patient groups specific needs. In the second case, one may assess the performance of equivalent IVD(s). There are several ways to assess the performance of equivalent IVDs on the market for the purpose of making this justification, which could include, but is not limited to:

- A comparison of the performance of the in-house IVD with the performance data of an equivalent IVD provided in the instructions for use,
- An assessment of published literature comparing the equivalent IVDs, and/or

[10] See also MDCG 2023-1 Section 3.5.2
[11] S.I 360 of 2005.
[12] See also MDCG 2023-1 Section 3.6

- A concordance study conducted between the in-house IVD and the equivalent IVD.

Any assessment conducted to support this justification should be documented. The justification should be reviewed periodically, and the periodicity of the review should be defined in the health institution's processes. The emergence of an available IVD on the market does not invalidate the initial justification; however, if on review the performance of the available IVD is equivalent, a transition process towards usage of the CE marked IVDs should commence.

5.2.5 Article 5(5)e: the health institution provides information upon request on the use of such devices to its competent authority, which shall include a justification of their manufacturing, modification, and use.[13]

The competent authority for IVD's in Ireland is the HPRA. All health institutions, that manufacture and use in-house IVDs in Ireland are requested to notify the HPRA of their in-house activities (see Section 5.3 of this guide). In addition, health institutions must notify the HPRA of any serious incidents, which involve in-house manufactured IVDs (see Section 5.4 of this guide).

In our role as competent authority for IVD's, the HPRA may request additional information on the manufacturing and use of the IVDs.

5.2.6 Article 5(5)f: the health institution draws up a declaration which it shall make publicly available, including:[14]

(i) the name and address of the manufacturing health institution,
(ii) the details necessary to identify the devices,
(iii) a declaration that the devices meet the general safety and performance requirements set out in Annex I of the IVDR and, where applicable, information on which requirements are not fully met with a reasoned justification therefor.

The declaration must be available publicly and easily accessible. This requirement may be met by including a copy of the declaration on the website of the health institution or laboratory. The declaration must be updated where new in-house IVDs are manufactured and used, or where in-house IVDs are withdrawn from service. It is the health institution's responsibility to keep this public declaration current and accurate.

When making this declaration the health institution must assess and confirm that their in-house IVDs meet the General Safety & Performance Requirements. It is recommended that a checklist is used to confirm that the requirements are met and is retained as part of the documentation for the in-house IVD. An example of such a checklist can be found in Annex 1 of this guide.

[13] See also MDCG 2023-1 Section 3.7
[14] See also MDCG 2023-1 Annex A

5.2.7 Article 5(5)g: as regards Class D devices in accordance with the rules set out in IVDR Annex VIII, the health institution draws up documentation that makes it possible to have an understanding of the manufacturing facility, the manufacturing process, the design and performance data of the devices, including the intended purpose, and that is sufficiently detailed to enable the competent authority to ascertain that the general safety and performance requirements set out in IVDR Annex I. Member States may apply this provision also to class A, B or C devices in accordance with the rules set out in Annex VIII.[15]

This requirement applies for health institutions, which manufacture and use in-house Class D IVDs. IVDR Annex VIII Rules 1 and 2[16] define which IVDs are classified as Class D. If a health institution is not manufacturing and using Class D IVDs, this point (g), and the following point (h) do not apply.

Where a health institution is manufacturing and using a Class D in-house IVD they must provide a detailed account of the:

- Manufacturing facility
- Manufacturing process
- Intended purpose.
- Design of the IVD
- Performance of the IVD

This documentation may be requested by the HPRA to ascertain that the general safety and performance requirements outlined in IVDR Annex 1 have been met.

5.2.8 Article 5(5)h: the health institution takes all necessary measures to ensure that all devices are manufactured in accordance with the documentation referred to in point (g).[17]

This requirement applies to Class D in-house IVDs only. The IVDs should be manufactured within the manufacturing facility described, following the design and manufacturing process outlined. Documentation demonstrating the manufacturing took place as planned should be maintained.

5.2.9 Article 5(5)i: the health institution reviews experience gained from clinical use of the devices and takes all necessary corrective actions.[18]

The health institution should have a process in place to review the experience gained from use of the IVD including a review of the performance of the IVD. This process should describe how frequently such reviews should occur. The outcome of these reviews should be documented and retained. Where serious incidents occur, these

[15] See also MDCG 2023-1 Section 3.9
[16] IVDR Annex VIII Section 2.1 and 2.2.
[17] See also MDCG 2023-1 Section 3.10
[18] See also MDCG 2023-1 Section 3.10

should be reported to the HPRA (see Section 5.4 of this guide). Where corrective actions are identified, these should be implemented without any undue delay. Health institutions should ensure there have sufficient traceability to enable implementation of corrective actions including where results need to be reviewed or samples re-tested.

5.3 Health institution notification

All health institutions in Ireland that manufacture and use in-house IVDs must notify the HPRA of their activities. Further details of this notification will be provided in due course.

5.4 Incident Reporting

All 'incidents'[19] must be recorded, and records maintained. 'Serious incidents'[20] must be reported to the HPRA through our online incident report form in line with the following timelines:

- Immediately after they have established a causal relationship between the serious incident and their IVD or that such causal relationship is reasonably possible, and no later than 15 days after the health institution becomes aware of the serious incident.
- In the event of a serious public health threat, the report shall be provided immediately, and no later than two days after the health institution becomes aware of that threat.
- In the event of death or an unanticipated serious deterioration in a person's state of health, the report shall be provided immediately after the health institution has established or as soon as it suspects a causal relationship between the IVD and the serious incident and no later than 10 days after the date on which the health institution becomes aware of the serious incident.

[19] See Glossary for a definition of incident.
[20] See Glossary for a definition of a serious incident.

5.5 When do these requirements apply?

Not all the requirements of Article 5(5) apply at the same time.

- From 26 May 2022 all provisions of IVDR Article 5(5) apply except points b-i.
- From 26 May 2024 all provisions of IVDR Article 5(5) apply except point d.
- From 26 May 2028 all provisions of IVDR Article 5(5) apply.

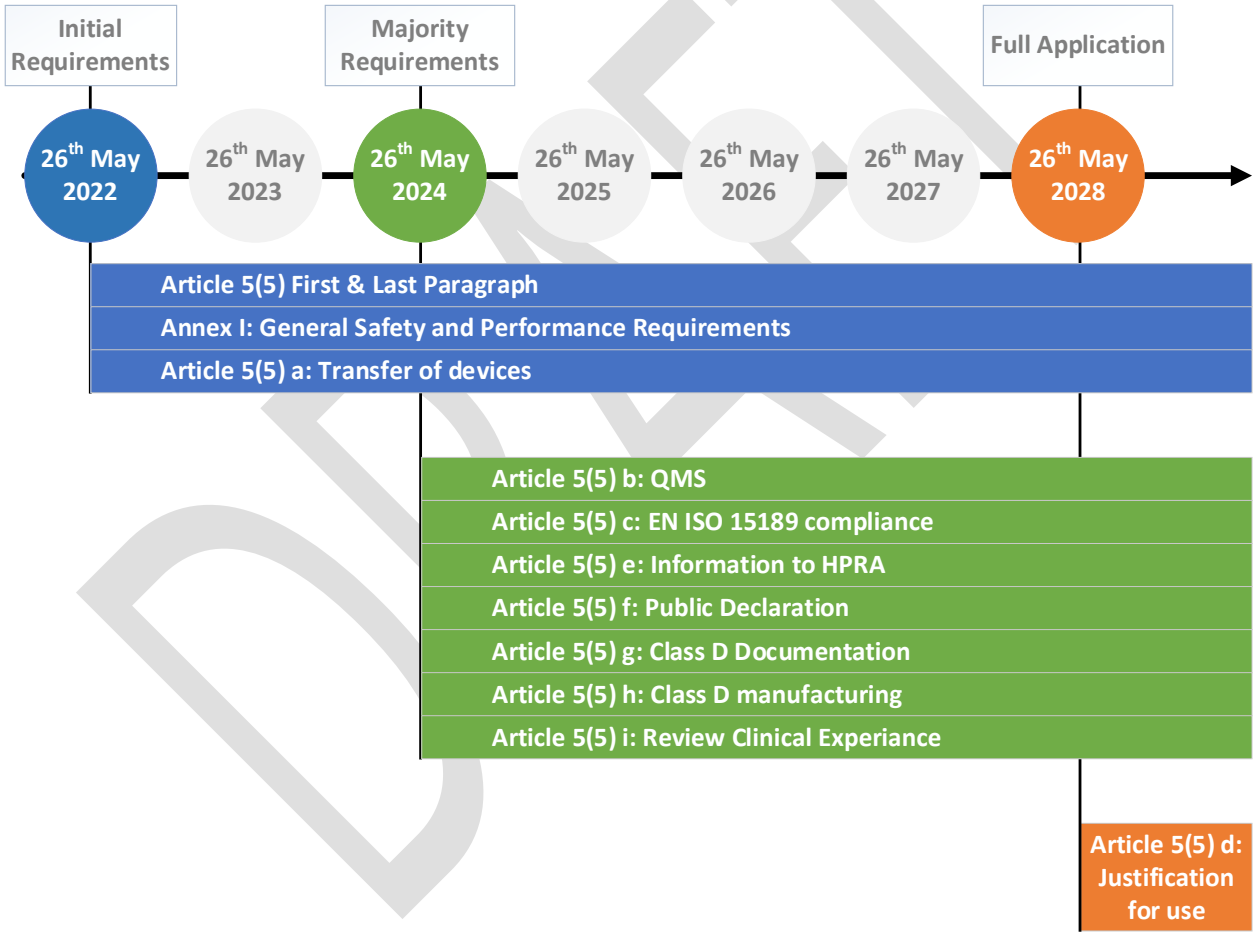

Figure 2: Timeline showing when each of the requirements of Article 5(5) apply.

5.6 Differentiating between organisational and IVD specific requirements

It is important to consider some of the requirements discussed in Article 5(5) and this section are organisational in nature whilst others are required to be completed on an IVD-by-IVD basis. Table 1 provides an overview as to which requirements may be addressed as part of organisational or laboratory processes and which require additional IVD-specific documentation. In principle, once the organisational requirements are met and processes are established, introducing an additional in-house IVD would require a health institution to draw up or update documentation to meet the IVD specific requirements.

Table 1: Overview of the in-house IVD requirements applicable at an organisational level, and those required on an IVD-by-IVD basis.

Requirement	Organisational	IVD specific	Comments
Article 5(5) Annex 1: General Safety and Performance requirements		X	Required for each IVD- checklist recommended.
Article 5(5) a: Transfer of devices	X		Procedures and Policies should be put in place at an organisation level to comply with this requirement.
Article 5(5) b: QMS	X		The QMS should be reviewed and assessed to meet the requirements of the IVDR.
Article 5(5) c: EN ISO 15189 compliance	X		The laboratories of the health institution should demonstrate compliance with EN ISO 15189.
Article 5(5) d: Justification for use		X	The justification will need to be made on an IVD-by-IVD basis.
Article 5(5) e: Information to HPRA - Notification	X		The HPRA should be notified of health institutions that are manufacturing and using in-house IVDs.
Article 5(5) e: Information to HPRA - Serious Incident Reporting		X	Each serious incident which occurs should be reported to the HPRA.
Article 5(5) f: Public Declaration	X	X	A process for making the public declaration should be established. Each in-house IVD should be listed on the public declaration.
Article 5(5) g: Class D documentation		X	Required for Class D in-house IVDs
Article 5(5) h: Class D manufacturing		X	Required for Class D in-house IVDs
Article 5(5) i: Review Clinical experience		X	Required for each in-house IVD.

6 IN-HOUSE IVD FRAMEWORKS

In-house IVDs are often manufactured and used in isolation to address a specific patient need. Other times modifications to a workflow or replacement of reagents using existing methods can create an in-house IVD. Reflecting the complexity and potential interdependence of in-house IVDs, in general, when meeting the requirements of the IVDR, two frameworks may be considered.

6.1 Framework 1: Standalone in-house IVD.

This framework will suit the majority of in-house IVDs which are created to address a specific need. Following this framework health institutions assess, document and meet the requirements for in-house IVDs, on an IVD-by-IVD basis. They must ensure the organisational requirements are met as outlined in Sections 5.2 & 5.6 of this guide, which include:

Organisational Records

- A policy on the non-transfer of in-house IVDs
- Appropriate QMS
- EN ISO 15189 compliance
- Health institution notifications to the HPRA (Sections 5.3 & 5.4 of this guide)
- Process for creating and updating the public declaration.

In addition to the organisational/infrastructure requirements outlined in Table 1, a general safety and performance requirement checklist should be completed for each in-house IVD. Supporting information should be collated and retained alongside the checklist to support the assessment of the general safety and performance requirements. Under this framework it is recommended that an IVD file or folder is created to collate and retain this information.

IVD Files:
This file should include the following: -

- A general safety and performance requirements checklist.
- Supporting documentation such as the intended purpose, risk assessments, instructions for use / standard operating procedures / protocols, etc. These may also be referenced in the general safety and performance requirements checklist.
- Data on IVD performance which may come from verification or validation activities or evidence from routine clinical use. In the case of in-house IVDs resulting from combining multiple IVDs and/or products, an assessment of the compatibility should be considered, e.g. cross reactivity testing, interference, etc.
- For Class D IVDs, the additional documentation as outlined in Sections 5.2.7 & 5.2.8 of this guide.
- The justification for the use of the IVD, when applicable.

- A record of any serious incidents, which occurred with the IVD and any corrective actions implemented.
- A copy of the review of experience gained from clinical use of the IVD.

Finally, the public declaration should be updated to ensure the in-house IVD is listed.

Framework 1: Standalone in house IVD

Organisational Records	IVD File
- Identify scope of health institution as a legal entity. Policy on non-transfer of in house IVDs - Appropriate QMS - EN ISO 15189 compliance - Health institution notifies the HPRA that they are manufacturing and using in house IVDs. - Process for creating and updating the public declaration	- General Safety and Performance Requirement Checklist. - Supporting documentation such as the intended purpose risk assessments, instructions for use, standard operating procedures, protocols, etc. - Data on IVD performance i.e. from verification or validation activities or evidence from routine clinical use. - For Class D IVDs the additional documentation as outlined in Section 5.2.7 & 5.2.8 - The justification for the use of the IVD, - Record of any serious incidents involving the IVD and any corrective actions implemented. - A copy of the review of experience gained from clinical use of the IVD.

Figure 3: Framework 1 showing the division of the requirements into two separate files. The organisational records document the overarching policies, procedures and documents required to comply with some of the requirements of Article 5(5). The IVD file shows the documentation needed to comply with the remaining requirements.

6.2 Framework 2: Combining or multiplexing in-house IVDs.

This framework is designed to accommodate the scenario where a health institution manufactures and uses a number of similar in-house IVDs, which share a common workflow or design. In this framework, some of the requirements can be met and documented on the process or workflow with the remaining IVD specific aspects covered in a separate file. This framework reduces the administrative burden on health institutions by allowing them to leverage common information for these similar tests. Examples include but are not limited to: -

- Multiplexing panels of antibodies, where either the antibody is not CE marked or the combination is not indicated by the manufacturer.
- Combining histological stains where either the stain is not CE marked or the combination is not indicated by the manufacturer.
- Use of a common workflow and equipment for genetic testing using custom primers.

While in these cases a common workflow can be leveraged to support part of the requirements, certain in-house IVD specific elements will still be required.

Under this framework the organisational requirements need to be met similar to framework 1.

Organisational Records

- A policy on the non-transfer of in-house IVDs
- Appropriate QMS
- EN ISO 15189 compliance
- Health institution notifications to the HPRA (Sections 5.3 & 5.4 of this guide)
- Process for creating and updating the public declaration.

It is recommended to create both a framework file and an IVD specific file. The framework file can document the common elements and processes for the overarching workflow with a separate IVD specific file for each in-house IVD. These files should include the following:

Framework File-

- A general safety and performance requirements checklist for the overarching framework including processes for risk identification mitigation and management, information on the workflow and information to be available to the IVD user and general IVD characteristics.
  Not all the general safety and performance requirements may be covered by the framework e.g., IVDR Chapter 2 Section 9 on performance characteristics. Requirements not covered by the framework checklist should be included in the IVD file.

- Supporting documentation such as risk assessments, instructions for use / standard operating procedures / protocols, intended purpose etc. These should be referenced in the general safety and performance requirements checklist.
- For Class D IVDs, the additional documentation for the framework as outlined in Sections 5.2.7 & 5.2.8 of this guide, i.e. information on the manufacturing facility, manufacturing process and IVD design.

IVD File-

- A general safety and performance requirements checklist. Any remaining sections which are IVD specific
- Data on IVD performance, i.e. from verification or validation activities. In particular, data supporting that the combination and or interchangeability of IVDs is suitable, e.g. cross reactivity testing, interference etc.
- For Class D IVDs the remaining additional documentation outlined in Sections 5.2.7 & 5.2.8 of this guide including information on the intended purpose and IVD performance.
- The justification for the use of the IVD, when applicable.
- A record of any serious incidents which occurred with the IVD, and any corrective actions implemented.
- A copy of the review of experience gained from clinical use of the IVD.

The public declaration should list all in-house IVDs manufactured and used under the framework.

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Framework 2: Combinations or multiplexing

Organisational Records	Framework File	IVD File
- Identify scope of health institution as a legal entity. Policy on non-transfer of in house IVDs - Appropriate QMS - EN ISO 15189 compliance - Health institution notifies the HPRA that they are manufacturing and using in house IVDs. - Process for creating and updating the public declaration	- GSPR Checklist for the overarching framework. - Supporting documentation such as risk assessments, instructions for use/ standard operating procedures/ protocols, intended purpose etc. These should be referenced in the GSPR Checklist. - For Class D IVDs the information on the manufacturing facility, manufacturing process and IVD design.	- GSPR Checklist for the remaining IVD specific aspects - Data on IVD performance i.e. from verification or validation activities. In particular data supporting that the combination of IVDs is suitable e.g. cross reactivity testing, interference etc. - For Class D IVDs the information on the intended purpose and IVD performance The justification for the use of the IVD, when applicable. - A record of any serious incidents which occurred with the IVD and any corrective actions implemented. - A copy of the review of experience gained from clinical use of the IVD.

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484 *Figure 4 Framework 2 showing the division of the requirements into three separate files. The organisational records document the overarching policies, procedures and*
485 *documents required to comply with some of the requirements of Article 5(5). The Framework file documents the common features of a given workflow or technique. The IVD*
486 *file in this instance covers the documentation needed to comply with the remaining requirements.*

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7 ANNEX 1: GENERAL SAFETY & PERFORMANCE CHECKLIST

Organisation:	**Product:**
Reference:	**Date:**

IVD description:

Notes:

This checklist is intended to assist health institutions that manufacture and use in-house IVD's to achieve compliance with the General Safety and Performance Requirements (Annex I) of the *in vitro* diagnostic medical device (EU) Regulation 2017/746 as amended by (EU) Regulation 2022/112. Space is provided in the comments/references box to cite any relevant internal documents/procedures or to provide comments/justifications. This checklist does not purport to be an interpretation of law and/or regulations and is for information only. The text below is taken from IVDR Annex I. In this Annex the term device refers to an IVD.

	GENERAL SAFETY & PERFORMANCE REQUIREMENT	COMMENTS / REFERENCES
1.	Devices shall achieve the performance intended by their manufacturer and shall be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose. They shall be safe and effective and shall not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art.	
2.	The requirement in this Annex to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio.	
3.	Manufacturers shall establish, implement, and maintain a risk management system. Risk management shall be understood as a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating. In carrying out risk management manufacturers shall: (a) establish and document a risk management plan for each device; (b) identify and analyse the known and foreseeable hazards associated with each device; (c) estimate and evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse; (d) eliminate or control the risks referred to in point (c) in accordance with the requirements of Section 4; (e) evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, the benefit-risk ratio and risk acceptability; and (f) based on the evaluation of the impact of the information referred to in point (e), if necessary amend control measures in line with the requirements of Section 4.	
4.	Risk control measures adopted by manufacturers for the design and manufacture of the devices shall conform to safety principles, taking account of the generally acknowledged state of the art. To reduce risks, the manufacturers shall manage risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable. In selecting the most appropriate solutions, manufacturers shall, in the following order of priority:` (a) eliminate or reduce risks as far as possible through safe design and manufacture; (b) where appropriate, take adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated; and (c) provide information for safety (warnings/precautions/contra-indications) and, where appropriate, training to users. Manufacturers shall inform users of any residual risks.	

	GENERAL SAFETY & PERFORMANCE REQUIREMENT	COMMENTS / REFERENCES
5.	In eliminating or reducing risks related to use error, the manufacturer shall: (a) reduce as far as possible the risks related to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety), and (b) give consideration to the technical knowledge, experience, education, training and use environment, where applicable, and the medical and physical conditions of intended users (design for lay, professional, disabled or other users).	
6.	The characteristics and performance of a device shall not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.	
7.	Devices shall be designed, manufactured and packaged in such a way that their characteristics and performance during their intended use are not adversely affected during transport and storage, for example, through fluctuations of temperature and humidity, taking account of the instructions and information provided by the manufacturer.	
8.	All known and foreseeable risks, and any undesirable effects shall be minimised and be acceptable when weighed against the evaluated potential benefits to the patients and/or the user arising from the intended performance of the device during normal conditions of use.	

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9	**Performance characteristics**	
9.1	Devices shall be designed and manufactured in such a way that they are suitable for the purposes referred to in point (2) of Article 2, as specified by the manufacturer, and suitable with regard to the performance they are intended to achieve, taking account of the generally acknowledged state of the art. They shall achieve the performances, as stated by the manufacturer and in particular, where applicable: (a) the analytical performance, such as, analytical sensitivity, analytical specificity, trueness (bias), precision (repeatability and reproducibility), accuracy (resulting from trueness and precision), limits of detection and quantitation, measuring range, linearity, cut-off, including determination of appropriate criteria for specimen collection and handling and control of known relevant endogenous and exogenous interference, cross-reactions; and (b) the clinical performance, such as diagnostic sensitivity, diagnostic specificity, positive predictive value, negative predictive value, likelihood ratio, expected values in normal and affected populations.	
9.2	The performance characteristics of the device shall be maintained during the lifetime of the device as indicated by the manufacturer.	
9.3	Where the performance of devices depends on the use of calibrators and/or control materials, the metrological traceability of values assigned to calibrators and/or control materials shall be assured through suitable reference measurement procedures and/or suitable reference materials of a higher metrological order. Where available, metrological traceability of values assigned to calibrators and control materials shall be assured to certified reference materials or reference measurement procedures.	
9.4	The characteristics and performances of the device shall be specifically checked in the event that they may be affected when the device is used for the intended use under normal conditions: a) for devices for self-testing, performances obtained by laypersons; b) (b) for devices for near-patient testing, performances obtained in relevant environments (for example, patient home, emergency units, ambulances).	
10	**Chemical, physical and biological properties**	
10.1	Devices shall be designed and manufactured in such a way as to ensure that the characteristics and performance requirements referred to in Chapter I are fulfilled. Particular attention shall be paid to the possibility of impairment of analytical performance due to physical and/or chemical incompatibility between the materials used and the specimens, analyte or marker to be detected (such as biological tissues, cells, body fluids and micro-organisms), taking account of the intended purpose of the device.	

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10.2	Devices shall be designed, manufactured and packaged in such a way as to minimise the risk posed by contaminants and residues to patients, taking account of the intended purpose of the device, and to the persons involved in the transport, storage and use of the devices. Particular attention shall be paid to tissues exposed to those contaminants and residues and to the duration and frequency of exposure.	
10.3	Devices shall be designed and manufactured in such a way as to reduce to a level as low as reasonably practicable the risks posed by substances or particles, including wear debris, degradation products and processing residues, that may be released from the device. Special attention shall be given to substances which are carcinogenic, mutagenic or toxic to reproduction ('CMR'), in accordance with Part 3 of Annex VI to Regulation (EC) No 1272/2008 of the European Parliament and of the Council[21], and to substances having endocrine disrupting properties for which there is scientific evidence of probable serious effects to human health and which are identified in accordance with the procedure set out in Article 59 of Regulation (EC) No 1907/2006 of the European Parliament and of the Council[22].	
10.4	Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks posed by the unintentional ingress of substances into the device, taking into account the device and the nature of the environment in which it is intended to be used.	
11	**Infection and microbial contamination**	
11.1	Devices and their manufacturing processes shall be designed in such a way as to eliminate or reduce as far as possible the risk of infection to the user or, where applicable, other persons. The design shall: (a) allow easy and safe handling; (b) reduce as far as possible any microbial leakage from the device and/or microbial exposure during use; and, where necessary (c) prevent microbial contamination of the device during use and, in the case of specimen receptacles, the risk of contamination of the specimen.	
11.2	Devices labelled either as sterile or as having a specific microbial state shall be designed, manufactured and packaged to ensure that their sterile condition or microbial state is maintained under the transport and storage conditions specified by the manufacturer until that packaging is opened at the point of use, unless the packaging which maintains their sterile condition or microbial state is damaged.	

[21] Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 (OJ L 353, 31.12.2008, p. 1).

[22] Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) (OJ L 136, 29.5.2007, p. 3).

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11.3	Devices labelled as sterile shall be processed, manufactured, packaged and, sterilised by means of appropriate, validated methods.	
11.4	Devices intended to be sterilised shall be manufactured and packaged in appropriate and controlled conditions and facilities.	
11.5	Packaging systems for non-sterile devices shall maintain the integrity and cleanliness of the product and, where the devices are to be sterilised prior to use, minimise the risk of microbial contamination; the packaging system shall be suitable taking account of the method of sterilisation indicated by the manufacturer.	
11.6	The labelling of the device shall distinguish between identical or similar devices placed on the market in both a sterile and a non-sterile condition additional to the symbol used to indicate that devices are sterile.	
12	**Devices incorporating materials of biological origin**	
	Where devices include tissues, cells and substances of animal, human or microbial origin, the selection of sources, the processing, preservation, testing and handling of tissues, cells and substances of such origin and control procedures shall be carried out so as to provide safety for user or other person. In particular, safety with regard to microbial and other transmissible agents shall be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process. This might not apply to certain devices if the activity of the microbial and other transmissible agent are integral to the intended purpose of the device or when such elimination or inactivation process would compromise the performance of the device.	
13	**Construction of devices and interaction with their environment**	
13.1	If the device is intended for use in combination with other devices or equipment, the whole combination, including the connection system, shall be safe and shall not impair the specified performances of the devices. Any restrictions on use applying to such combinations shall be indicated on the label and/or in the instructions for use.	
13.2	Devices shall be designed and manufactured in such a way as to remove or reduce as far as possible: (a) the risk of injury, in connection with their physical features, including the volume/pressure ratio, dimensional and where appropriate ergonomic features; (b) risks connected with reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, temperature, variations in pressure and acceleration or radio signal interferences; (c) the risks associated with the use of the device when it comes into contact with materials, liquids, and substances, including gases, to which it is exposed during normal conditions of use; (d) the risks associated with the possible negative interaction between software and the IT environment within which it operates and interacts;	

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	(e) the risks of accidental ingress of substances into the device; (f) the risk of incorrect identification of specimens and the risk of erroneous results due to, for example, confusing colour and/or numeric and/or character codings on specimen receptacles, removable parts and/or accessories used with devices in order to perform the test or assay as intended; (g) the risks of any foreseeable interference with other devices.	
13.3	Devices shall be designed and manufactured in such a way as to minimise the risks of fire or explosion during normal use and in single fault condition. Particular attention shall be paid to devices the intended use of which includes exposure to or use in association with flammable or explosive substances or substances which could cause combustion.	
13.4	Devices shall be designed and manufactured in such a way that adjustment, calibration, and maintenance can be done safely and effectively.	
13.5	Devices that are intended to be operated together with other devices or products shall be designed and manufactured in such a way that the interoperability and compatibility are reliable and safe.	
13.6	Devices shall be designed and manufactured in such a way as to facilitate their safe disposal and the safe disposal of related waste substances by users, or other person. To that end, manufacturers shall identify and test procedures and measures as a result of which their devices can be safely disposed after use. Such procedures shall be described in the instructions for use.	
13.7	The measuring, monitoring or display scale (including colour change and other visual indicators) shall be designed and manufactured in line with ergonomic principles, taking account of the intended purpose, users and the environmental conditions in which the devices are intended to be used.	
14	**Devices with a measuring function**	
14.1	Devices having a primary analytical measuring function shall be designed and manufactured in such a way as to provide appropriate analytical performance in accordance with point (a) of Section 9.1 of Annex I, taking into account the intended purpose of the device.	
14.2	The measurements made by devices with a measuring function shall be expressed in legal units conforming to the provisions of Council Directive 80/181/EEC.[23]	
15	**Protection against radiation**	

[23] [23] Council Directive 80/181/EEC of 20 December 1979 on the approximation of the laws of the Member States relating to units of measurement and on the repeal of Directive 71/354/EEC (OJ L 39, 15.2.1980, p. 40).

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15.1	Devices shall be designed, manufactured and packaged in such a way that exposure of users or other persons to radiation (intended, unintended, stray or scattered) is reduced as far as possible and in a manner that is compatible with the intended purpose, whilst not restricting the application of appropriate specified levels for diagnostic purposes.	
15.2	When devices are intended to emit hazardous, or potentially hazardous, ionizing and/or non-ionizing radiation, they shall as far as possible be: (a) designed and manufactured in such a way as to ensure that the characteristics and the quantity of radiation emitted can be controlled and/or adjusted; and (b) fitted with visual displays and/or audible warnings of such emissions.	
15.3	The operating instructions for devices emitting hazardous or potentially hazardous radiation shall contain detailed information as to the nature of the emitted radiation, the means of protecting the user, and on ways of avoiding misuse and of reducing the risks inherent to installation as far as possible and appropriate. Information regarding the acceptance and performance testing, the acceptance criteria, and the maintenance procedure shall also be specified.	
16	**Electronic programmable systems — devices that incorporate electronic programmable systems and software that are devices in themselves**	
16.1	Devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, shall be designed to ensure repeatability, reliability and performance in line with their intended use. In the event of a single fault condition, appropriate means shall be adopted to eliminate or reduce as far as possible consequent risks or impairment of performance.	
16.2	For devices that incorporate software or for software that are devices in themselves, the software shall be developed and manufactured in accordance with the state of the art taking into account the principles of development life cycle, risk management, including information security, verification and validation.	
16.3	Software referred to in this Section that is intended to be used in combination with mobile computing platforms shall be designed and manufactured taking into account the specific features of the mobile platform (e.g. size and contrast ratio of the screen) and the external factors related to their use (varying environment as regards level of light or noise).	
16.4	Manufacturers shall set out minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorised access, necessary to run the software as intended.	
17	**Devices connected to or equipped with an energy source**	
17.1	For devices connected to or equipped with an energy source, in the event of a single fault condition, appropriate means shall be adopted to eliminate or reduce as far as possible consequent risks.	

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17.2	Devices where the safety of the patient depends on an internal power supply shall be equipped with a means of determining the state of the power supply and an appropriate warning or indication for when the capacity of the power supply becomes critical. If necessary, such warning or indication shall be given prior to the power supply becoming critical.	
17.3	Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks of creating electromagnetic interference which could impair the operation of the device in question or other devices or equipment in the intended environment.	
17.4	Devices shall be designed and manufactured in such a way as to provide a level of intrinsic immunity to electromagnetic interference such that is adequate to enable them to operate as intended.	
17.5	Devices shall be designed and manufactured in such a way as to avoid as far as possible the risk of accidental electric shocks to the user, or other person both during normal use of the device and in the event of a single fault condition in the device, provided the device is installed and maintained as indicated by the manufacturer.	
18	**Protection against mechanical and thermal risks**	
18.1	Devices shall be designed and manufactured in such a way as to protect users and other persons against mechanical risks.	
18.2	Devices shall be sufficiently stable under the foreseen operating conditions. They shall be suitable to withstand stresses inherent to the foreseen working environment, and to retain this resistance during the expected lifetime of the devices, subject to any inspection and maintenance requirements as indicated by the manufacturer.	
18.3	Where there are risks due to the presence of moving parts, risks due to break-up or detachment, or leakage of substances, then appropriate protection means shall be incorporated. Any guards or other means included with the device to provide protection, in particular against moving parts, shall be secure and shall not interfere with access for the normal operation of the device, or restrict routine maintenance of the device as intended by the manufacturer.	
18.4	Devices shall be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from vibration generated by the devices, taking account of technical progress and of the means available for limiting vibrations, particularly at source, unless the vibrations are part of the specified performance.	
18.5	Devices shall be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from the noise emitted, taking account of technical progress and of the means available to reduce noise, particularly at source, unless the noise emitted is part of the specified performance.	
18.6	Terminals and connectors to the electricity, gas or hydraulic and pneumatic energy supplies which the user or other person has to handle, shall be designed and constructed in such a way as to minimise all possible risks.	
18.7	Errors likely to be made when fitting or refitting certain parts which could be a source of risk shall be made impossible by the design and construction of such parts or, failing this, by information given on the parts themselves and/or their housings.	

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	The same information shall be given on moving parts and/or their housings where the direction of movement needs to be known in order to avoid a risk.	
18.8	Accessible parts of devices (excluding the parts or areas intended to supply heat or reach given temperatures) and their surroundings shall not attain potentially dangerous temperatures under normal conditions of use.	
19	**Protection against the risks posed by devices intended for self-testing or near-patient testing**	
19.1	Devices intended for self-testing or near-patient testing shall be designed and manufactured in such a way that they perform appropriately for their intended purpose taking into account the skills and the means available to the intended user and the influence resulting from variation that can be reasonably anticipated in the intended user's technique and environment. The information and instructions provided by the manufacturer shall be easy for the intended user to understand and apply in order to correctly interpret the result provided by the device and to avoid misleading information. In the case of near-patient testing, the information and the instructions provided by the manufacturer shall make clear the level of training, qualifications and/or experience required by the user.	
19.2	Devices intended for self-testing or near-patient testing shall be designed and manufactured in such a way as to: (a) ensure that the device can be used safely and accurately by the intended user at all stages of the procedure if necessary after appropriate training and/or information; and (b) reduce as far as possible the risk of error by the intended user in the handling of the device and, if applicable, the specimen, and also in the interpretation of the results.	
19.3	Devices intended for self-testing and near-patient testing shall, where feasible, include a procedure by which the intended user:	

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20	***LABEL AND INSTRUCTIONS FOR USE***	
20.1	**General requirements regarding the information supplied by the manufacturer**	
20.1	Each device shall be accompanied by the information needed to identify the device and its manufacturer, and by any safety and performance information relevant to the user or any other person, as appropriate. Such information may appear on the device itself, on the packaging or in the instructions for use, and shall, if the manufacturer has a website, be made available and kept up to date on the website, taking into account the following: a) The medium, format, content, legibility, and location of the label and instructions for use shall be appropriate to the particular device, its intended purpose and the technical knowledge, experience, education or training of the intended user(s). In particular, instructions for use shall be written in terms readily understood by the intended user and, where appropriate, supplemented with drawings and diagrams. b) The information required on the label shall be provided on the device itself. If this is not practicable or appropriate, some or all of the information may appear on the packaging for each unit. If individual full labelling of each unit is not practicable, the information shall be set out on the packaging of multiple devices. c) Labels shall be provided in a human-readable format and may be supplemented by machine-readable information, such as radio-frequency identification or bar codes. d) Instructions for use shall be provided together with devices. However, in duly justified and exceptional cases instructions for use shall not be required or may be abbreviated if the device can be used safely and as intended by the manufacturer without any such instructions for use. e) Where multiple devices, with the exception of devices intended for self-testing or near-patient testing, are supplied to a single user and/or location, a single copy of the instructions for use may be provided if so agreed by the purchaser who in any case may request further copies to be provided free of charge. f) When the device is intended for professional use only, instructions for use may be provided to the user in non-paper format (e.g. electronic), except when the device is intended for near-patient testing. g) Residual risks which are required to be communicated to the user and/or other person shall be included as limitations, contra-indications, precautions or warnings in the information supplied by the manufacturer.	

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20.1	h) Where appropriate, the information supplied by the manufacturer shall take the form of internationally recognised symbols, taking into account the intended users. Any symbol or identification colour used shall conform to the harmonised standards or CS. In areas for which no harmonised standards or CS exist, the symbols and colours shall be described in the documentation supplied with the device. i) In the case of devices containing a substance or a mixture which may be considered as being dangerous, taking account of the nature and quantity of its constituents and the form under which they are present, relevant hazard pictograms and labelling requirements of Regulation (EC) No 1272/2008 shall apply. Where there is insufficient space to put all the information on the device itself or on its label, the relevant hazard pictograms shall be put on the label and the other information required by Regulation (EC) No 1272/2008 shall be given in the instructions for use. j) The provisions of Regulation (EC) No 1907/2006 on the safety data sheet shall apply, unless all relevant information, as appropriate, is already made available in the instructions for use.	
20.2	**Information on the label**	
20.2	The label shall bear all of the following particulars: a) the name or trade name of the device; b) the details strictly necessary for a user to identify the device and, where it is not obvious for the user, the intended purpose of the device; c) the name, registered trade name or registered trade mark of the manufacturer and the address of its registered place of business; d) if the manufacturer has its registered place of business outside the Union, the name of its authorised representative and the address of the registered place of business of the authorised representative; e) an indication that the device is an in vitro diagnostic medical device, or if the device is a 'device for performance study', an indication of that fact; f) the lot number or the serial number of the device preceded by the words LOT NUMBER or SERIAL NUMBER or an equivalent symbol, as appropriate; g) the UDI carrier as referred to in Article 24 and Part C of Annex VI; h) an unambiguous indication of the time limit for using the device safely, without degradation of performance, expressed at least in terms of year and month and, where relevant, the day, in that order;	

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20.2	i) where there is no indication of the date until when it may be used safely, the date of manufacture. This date of manufacture may be included as part of the lot number or serial number, provided the date is clearly identifiable; j) where relevant, an indication of the net quantity of contents, expressed in terms of weight or volume, numerical count, or any combination of thereof, or other terms which accurately reflect the contents of the package; k) an indication of any special storage and/or handling condition that applies; l) where appropriate, an indication of the sterile state of the device and the sterilisation method, or a statement indicating any special microbial state or state of cleanliness; m) warnings or precautions to be taken that need to be brought to the immediate attention of the user of the device or to any other person. This information may be kept to a minimum in which case more detailed information shall appear in the instructions for use, taking into account the intended users; n) if the instructions for use are not provided in paper form in accordance with point (f) of Section 20.1, a reference to their accessibility (or availability), and where applicable the website address where they can be consulted; o) where applicable, any particular operating instructions; p) if the device is intended for single use, an indication of that fact. A manufacturer's indication of single use shall be consistent across the Union; q) if the device is intended for self-testing or near-patient testing, an indication of that fact; r) where rapid assays are not intended for self-testing or near-patient testing, the explicit exclusion hereof; s) where device kits include individual reagents and articles that are made available as separate devices, each of those devices shall comply with the labelling requirements contained in this Section and with the requirements of this Regulation; t) the devices and separate components shall be identified, where applicable in terms of batches, to allow all appropriate action to detect any potential risk posed by the devices and detachable components. As far as practicable and appropriate, the information shall be set out on the device itself and/or, where appropriate, on the sales packaging; u) the label for devices for self-testing shall bear the following particulars: i. the type of specimen(s) required to perform the test (e.g. blood, urine or saliva); ii. the need for additional materials for the test to function properly; iii. (contact details for further advice and assistance. The name of devices for self-testing shall not reflect an intended purpose other than that specified by the manufacturer.	

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20.3	**Information on the packaging which maintains the sterile condition of a device ('sterile packaging'):**	
	The following particulars shall appear on the sterile packaging: a) an indication permitting the sterile packaging to be recognised as such, b) a declaration that the device is in a sterile condition, c) the method of sterilisation, d) the name and address of the manufacturer, e) a description of the device, f) the month and year of manufacture, g) an unambiguous indication of the time limit for using the device safely, expressed at least in terms of year and month and, where relevant, the day, in that order, h) (h) an instruction to check the instructions for use for what to do if the sterile packaging is damaged or unintentionally opened before use.	
20.4	**Information in the instructions for use**	
20.4.1	The instructions for use shall contain all of the following particulars: (a) the name or trade name of the device; (b) the details strictly necessary for the user to uniquely identify the device; (c) the device's intended purpose: (i) what is detected and/or measured; (ii) its function (e.g. screening, monitoring, diagnosis or aid to diagnosis, prognosis, prediction, companion diagnostic); (iii) the specific information that is intended to be provided in the context of: — a physiological or pathological state; — congenital physical or mental impairments; — the predisposition to a medical condition or a disease; — the determination of the safety and compatibility with potential recipients; — the prediction of treatment response or reactions; — the definition or monitoring of therapeutic measures; (iv) whether it is automated or not; (v) whether it is qualitative, semi-quantitative or quantitative; (vi) the type of specimen(s) required;	

	(vii) where applicable, the testing population; and (viii) for companion diagnostics, the International Non-proprietary Name (INN) of the associated medicinal product for which it is a companion test. (d) an indication that the device is an in vitro diagnostic medical device, or, if the device is a 'device for performance study', an indication of that fact; (e) the intended user, as appropriate (e.g. self-testing, near patient and laboratory professional use, healthcare professionals); (f) the test principle; (g) a description of the calibrators and controls and any limitation upon their use (e.g. suitable for a dedicated instrument only); (h) a description of the reagents and any limitation upon their use (e.g. suitable for a dedicated instrument only) and the composition of the reagent product by nature and amount or concentration of the active ingredient(s) of the reagent(s) or kit as well as a statement, where appropriate, that the device contains other ingredients which might influence the measurement; (i) a list of materials provided and a list of special materials required but not provided; (j) for devices intended for use in combination with or installed with or connected to other devices and/or general purpose equipment: — information to identify such devices or equipment, in order to obtain a validated and safe combination, including key performance characteristics, and/or — information on any known restrictions to combinations of devices and equipment. (k) an indication of any special storage (e.g. temperature, light, humidity, etc.) and/or handling conditions which apply; (l) in-use stability which may include the storage conditions, and shelf life following the first opening of the primary container, together with the storage conditions and stability of working solutions, where this is relevant; (m) if the device is supplied as sterile, an indication of its sterile state, the sterilisation method and instructions in the event of the sterile packaging being damaged before use; (n) information that allows the user to be informed of any warnings, precautions, measures to be taken and limitations of use regarding the device. That information shall cover, where appropriate: (i) warnings, precautions and/or measures to be taken in the event of malfunction of the device or its degradation as suggested by changes in its appearance that may affect performance,	

	(ii) warnings, precautions and/or measures to be taken as regards the exposure to reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, or temperature, (iii) warnings, precautions and/or measures to be taken as regards the risks of interference posed by the reasonably foreseeable presence of the device during specific diagnostic investigations, evaluations, therapeutic treatment or other procedures such as electromagnetic interference emitted by the device affecting other equipment, (iv) precautions related to materials incorporated into the device that contain or consist of CMR substances, or endocrine disrupting substances or that could result in sensitisation or an allergic reaction by the patient or user, (v) if the device is intended for single use, an indication of that fact. A manufacturer's indication of single use shall be consistent across the Union, (vi) if the device is reusable, information on the appropriate processes to allow reuse, including cleaning, disinfection, decontamination, packaging and, where appropriate, the validated method of re-sterilisation. Information shall be provided to identify when the device should no longer be reused, such as signs of material degradation or the maximum number of allowable reuses; (o) any warnings and/or precautions related to potentially infectious material that is included in the device; (p) where relevant, requirements for special facilities, such as a clean room environment, or special training, such as on radiation safety, or particular qualifications of the intended user; (q) conditions for collection, handling, and preparation of the specimen; (r) details of any preparatory treatment or handling of the device before it is ready for use, such as sterilisation, final assembly, calibration, etc., for the device to be used as intended by the manufacturer; (s) the information needed to verify whether the device is properly installed and is ready to perform safely and as intended by the manufacturer, together with, where relevant: — details of the nature, and frequency, of preventive and regular maintenance, including cleaning and disinfection; — identification of any consumable components and how to replace them; — information on any necessary calibration to ensure that the device operates properly and safely during its intended lifetime;	

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	— methods for mitigating the risks encountered by persons involved in installing, calibrating or servicing devices. (t) where applicable, recommendations for quality control procedures; (u) the metrological traceability of values assigned to calibrators and control materials, including identification of applied reference materials and/or reference measurement procedures of higher order and information regarding maximum (self-allowed) batch to batch variation provided with relevant figures and units of measure; (v) assay procedure including calculations and interpretation of results and where relevant if any confirmatory testing shall be considered; where applicable, the instructions for use shall be accompanied by information regarding batch to batch variation provided with relevant figures and units of measure; (w) analytical performance characteristics, such as analytical sensitivity, analytical specificity, trueness (bias), precision (repeatability and reproducibility), accuracy (resulting from trueness and precision), limits of detection and measurement range, (information needed for the control of known relevant interferences, cross-reactions and limitations of the method), measuring range, linearity and information about the use of available reference measurement procedures and materials by the user; (x) clinical performance characteristics as defined in Section 9.1 of this Annex; (y) the mathematical approach upon which the calculation of the analytical result is made; (z) where relevant, clinical performance characteristics, such as threshold value, diagnostic sensitivity and diagnostic specificity, positive and negative predictive value; (aa) where relevant, reference intervals in normal and affected populations; (ab) information on interfering substances or limitations (e.g. visual evidence of hyperlipidaemia or haemolysis, age of specimen) that may affect the performance of the device; (ac) warnings or precautions to be taken in order to facilitate the safe disposal of the device, its accessories, and the consumables used with it, if any. This information shall cover, where appropriate: (i) infection or microbial hazards, such as consumables contaminated with potentially infectious substances of human origin; (ii) (ii) environmental hazards such as batteries or materials that emit potentially hazardous levels of radiation); (iii) physical hazards such as explosion. (ad) the name, registered trade name or registered trade mark of the manufacturer and the address of its registered place of business at which he can be contacted and its location be established, together with a telephone number and/or fax number and/or website address to obtain technical assistance;	

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	(ae) date of issue of the instructions for use or, if they have been revised, date of issue and identifier of the latest revision of the instructions for use, with a clear indication of the introduced modifications; (af) a notice to the user that any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established; (ag) where device kits include individual reagents and articles that may be made available as separate devices, each of these devices shall comply with the instructions for use requirements contained in this Section and with the requirements of this Regulation; (ah) for devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorised access, necessary to run the software as intended.	
20.4.2	In addition, the instructions for use for devices intended for self-testing shall comply with all of the following principles: (a) details of the test procedure shall be given, including any reagent preparation, specimen collection and/or preparation and information on how to run the test and interpret the results; (b) specific particulars may be omitted provided that the other information supplied by the manufacturer is sufficient to enable the user to use the device and to understand the result(s) produced by the device; (c) the device's intended purpose shall provide sufficient information to enable the user to understand the medical context and to allow the intended user to make a correct interpretation of the results; (d) the results shall be expressed and presented in a way that is readily understood by the intended user; (e) information shall be provided with advice to the user on action to be taken (in case of positive, negative or indeterminate result), on the test limitations and on the possibility of false positive or false negative result. Information shall also be provided as to any factors that can affect the test result such as age, gender, menstruation, infection, exercise, fasting, diet or medication; (f) the information provided shall include a statement clearly directing that the user should not take any decision of medical relevance without first consulting the appropriate healthcare professional, information on disease effects and prevalence, and, where available, information specific to the Member State(s) where the device is placed on the market on where a user can obtain further advice such as national helplines, websites; (g) for devices intended for self-testing used for the monitoring of a previously diagnosed existing disease or condition, the information shall specify that the patient should only adapt the treatment if he has received the appropriate training to do so.	

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