Guidance on the health institution exemption under Article 5(5) of the Regulations on medical devices and *in vitro* diagnostic medical devices.

1 Scope and target audience

Health institutions can manufacture and use medical devices in-house and thereby address, on a non-industrial scale, the specific needs of target patient groups which cannot be met at the appropriate level of performance by an equivalent CE marked device available on the market. In-house medical devices are exempted from most of the provisions of Regulations (EU) 2017/745 (medical devices Regulation, MDR) and (EU) 2017/746 (*in vitro* diagnostic medical devices Regulation, IVDR) provided they adhere to the conditions laid out in Article 5(5) of both Regulations. In order to ensure the highest level of health protection, Article 5(5) sets a number of rules regarding the manufacture and use of such in-house medical devices.

The provisions in Article 5(5) are the basis for the regulatory control and overview of in-house devices. This document provides guidance on the application of some of these rules. It is written for health care professionals and researchers of health institutions wishing to continue using in-house devices or aiming to design, manufacture and use new in-house devices. In addition, this guidance document intends to foster harmonised application of Article 5(5) by the national competent authorities.

The exemption provision from Article 5(5) is applicable to health institutions within the Union only. According to Article 6(2), health institutions outside the Union that offer diagnostic or therapeutic services through distance sales to patients in the Union must use devices that comply with the MDR or IVDR, without having the possibility of applying the in-house exemption.

While most recommendations in this document pertain to both medical devices and *in vitro* diagnostic medical devices (IVDs), some are specific to IVDs, in which case this is explicitly mentioned.

2 Clarification of commonly used terms in this guidance document

- **General safety and performance requirements**: the general safety and performance requirements of the MDR and the IVDR are applicable to in-house devices and are laid down in Annex I of both Regulations.
- **Health institution:** an organisation the primary purpose of which is the care or treatment of patients or the promotion of public health. Health institutions include hospitals as well as institutions, such as laboratories and public health institutions that support the health care system and/or address patient needs, but which do not treat or care for patients directly. The concept of health institution does not cover establishments primarily claiming to pursue health interests or healthy lifestyles, such as gyms, spas, wellness and fitness centres.
- **In-house device:** a device that is manufactured only within a health institution established in the Union and that meets all conditions set in Article 5(5) of the MDR or IVDR and is used within that same health institution.

- **IVDR:** Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on *in vitro* diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU.
- **MDR**: Regulation (EU) 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.

3 Guidance on terms used in Article 5(5) of the MDR and the IVDR

With the exception of the relevant general safety and performance requirements set out in Annex I, the requirements of the MDR and IVDR shall not apply to **devices** manufactured and used only within health institutions established in the Union, provided that specific conditions are met.

3.1 Which devices are referred to in Article 5(5)?

MDR

According to Article 1(4) of the MDR: the term 'devices' means (1) medical devices, (2) accessories for medical devices, and (3) products listed in Annex XVI.

(1) 'medical device' is defined in Article 2(1) of the MDR.

(2) 'accessory for a medical device' is defined in Article 2(2) of the MDR.

(3) 'products listed in Annex XVI' refers to the groups of products without an intended medical purpose that are listed in Annex XVI of the MDR. Applicability of the MDR for these products, and therefore application of Article 5(5), will be effective from the date of application of common specifications for these products.

IVDR

According to Article 1(2) of the IVDR: the term 'devices' means (1) IVDs, and (2) accessories for IVDs.

(1) 'IVD' is defined in Article 2(2) of the IVDR.

(2) 'accessory for an IVD' is defined in Article 2(4) of the IVDR.

General

Remarks:

- A protocol in the form of a written procedure that is shared between health institutions, patient samples and results are not considered as being devices according to the definitions above. Consequently, the MDR and IVDR do not apply to these.
- Any product or a combination of products which meets the definition of 'device' must comply with the MDR or IVDR, *i.e.* either be CE marked, or be manufactured in-house and thus comply

with Article 5(5), or be an investigational device or a device for performance study, or be a custom-made device, or be exceptionally allowed a derogation from CE marking by a competent authority.

- According to the second paragraph of Article 5(5), member states shall retain the right to restrict the manufacture and the use of any specific type of in-house devices. Health institutions are advised to contact their competent authority or consult national legislations for possible restrictions in their country.

3.2 How to understand the terms 'manufactured and used'?

A device must be **manufactured and used** within the same health institution in order for Article 5(5) to apply.

3.2.1 How to understand the term '**manufactured**'?

Manufacturing a device by a health institution can include:

- manufacturing a device from raw materials or parts or components;
- combining devices or products for a medical purpose, when the devices do not bear the CE marking or where the combination of devices is not in line with their original intended purpose;
- significantly modifying an existing device. A significant modification is a modification made by a health institution that was not intended by the manufacturer and has an impact on the conformity of the product (for example, a significant change of a medical device as described in the guidance document MDCG 2020-3).

3.2.2 How to understand the term '**used**'?

- Devices can only be defined as in-house devices when their manufacture and use is limited to health institutions established in the Union. This use within health institutions can either be physically or, for instance for medical device software, remotely, provided they are not made available to another legal entity. The act of using an in-house manufactured device is performed within the health institution when the device is used in the care or diagnosis of a patient. If, during the lifecycle of the device, the device is used outside the health institution's premises, it cannot be in-house manufactured.

Examples:

- PCR master mix: a health institution orders primers based on scientific literature and manufactures its own in-house master mix containing buffer, primers, dNTPs, cofactors and enzymes to run PCRs on human DNA/RNA samples.

- A health institution develops in-house a medical device software that is used on site by its medical staff.

Examples of devices that do not fall under in-house devices:

- Medical device applications where patients can enter medical data outside the health institution.
- Orthopaedic braces that can be adapted by patients themselves outside the health institution.
- Self-tests cannot fall under Article 5(5) if used outside the health institution's premises. However, an in-house manufactured self-test can be used within the health institution by lay users. Also, an in-house device can be used in the health institution's laboratory for the analysis of a sample that is collected by a patient himself and consecutively sent to the laboratory.
- Manufacturing a device purely for economic reasons/financial interests.

Note:

The MDR and IVDR do not regulate any possible off-label use of devices by healthcare practitioners.

3.3 Legal entity

In-house devices **shall not be transferred to another legal entity**.

Healthcare systems are organised differently in different member states. Therefore, the concept of legal entity can differ. The national competent authority can clarify how legal entity is understood nationally. Here are some examples:

- One hospital can be one legal entity when there is only one health institution (one organiser) within the hospital.
- One hospital can accommodate several legal entities when there are different health institutions (different organisers) within the same hospital. The different health institutions can have different organisational numbers and different quality management systems.
- Several hospitals (a hospital network) can belong to the same legal entity when they are all part of one health institution (one organiser). They share the same organisational number and quality management systems even though they might be spread over different locations.

3.4 What is an appropriate quality management system?

The manufacture and use of in-house devices must occur under **appropriate quality management systems** (QMS).

MDR

Article 10(9) of the MDR describes the minimal aspects that a QMS for manufacturing medical devices should cover. This Article can be used as guidance on how to implement an appropriate QMS for manufacturing in-house devices. Below are some examples of provisions of Article 10(9) that could be relevant and adapted to in-house manufacturing.

- 10(9) (a) 'compliance with conformity assessment procedures':

  Health care institutions must determine how the requirements of Article 5(5) will be met. A declaration must be published confirming compliance with the general safety and performance requirements (see Article 5(5) (e)).

- 10(9) (b) 'identification of applicable general safety and performance requirements and exploration of options to address those requirements':

  As the general safety and performance requirements set out in Annex I do apply to in-house devices, compliance with applicable requirements must be documented.

- 10(9) (f) 'clinical evaluation in accordance with Article 61 and Annex XIV, including PMCF':

  According to 5(5) (c), (f) and (h), there is a need for proper scientific data and analysis of that data to justify that the target patient group´s specific needs cannot be met in another way than by manufacturing and using the health institution´s device. The experience gained from clinical use of the device should be used to review the device performance.

- 10(9) (h) 'verification of the UDI assignments...':

  There is no obligation to implement a UDI (unique device identification) system. However, pursuant to Article 5(5) (h), the health institution shall take all necessary corrective actions. Therefore, some form of a product tracking system must be established to identify the affected products and involved patients. Additionally, according to 5(5) (e) (ii), health institutions shall make publicly available the details necessary to identify the devices.

- 10(9) (i) 'setting-up, implementation and maintenance of a post-market surveillance system, in accordance with Article 83':

  According to 5(5) (h), the health institution shall review experience gained from clinical use of the device and take all necessary corrective actions.

IVDR

Article 10(8) of the IVDR describes the minimal aspects that a QMS for manufacturing medical devices should cover. This Article can be used as a guidance on how to implement an appropriate QMS for manufacturing in-house devices. Below are some examples of provisions of Article 10(8) that could be relevant and adapted to in-house manufacturing.

- 10(8) (a) 'compliance with conformity assessment procedures':

  Health care institutions must determine how the requirements of Article 5.5 will be met. A declaration must be published confirming compliance with the general safety and performance requirements (see Article 5.5 (f)).

- 10(8) (b) ‘identification of applicable general safety and performance requirements and exploration of options to address those requirements’:

  As the general safety and performance requirements set out in Annex I do apply to in-house devices, compliance with applicable requirements must be documented.

- 10(8) (f) ‘performance evaluation in accordance with Article 56 and Annex XIII, including PMPF’:

  According to 5(5) (d), (g)* and (i), there is a need for proper scientific data and analysis of that data to justify that the target patient group´s specific needs cannot be met in another way than by manufacturing and using the health institution´s device. The experience gained from clinical use of the device should be used to review the performance of the in-house device.

  * applies only to class D devices unless regulated otherwise by national provisions.

- 10(8) (h) ‘verification of the UDI assignments...’:

  There is no obligation to implement a UDI system. However, pursuant to Article 5(5) (i), the health institution shall take all necessary corrective actions. Therefore, some form of a product tracking system must be established to identify the affected products and involved patients. Additionally, according to 5(5) (f) (ii), health institutions shall make publicly available the details necessary to identify the devices.

- 10(8) (i) ‘setting-up, implementation and maintenance of a post-market surveillance system, in accordance with Article 78’:

  According to 5(5) (i), the health institution shall review experience gained from clinical use of the device and take all necessary corrective actions.

Note:

- For in-house IVDs, the laboratory of the health institution should be in compliance with the standard EN ISO 15189 (or with national provisions regarding QMS, including national provisions regarding accreditation). However, as the manufacturing process of a device is not in the scope of this standard, compliance with EN ISO 15189 alone does not constitute an appropriate QMS for the manufacture of in-house IVDs.

General

For both medical devices and IVDs, the QMS can cover the whole health institution or parts of the health institution involved in the manufacturing or modification of the device. A QMS should include a process for obtaining information about equivalent CE marked devices that become available on the market.

3.5 Justification 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.

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**. The health institution should consult relevant national legislation and/or guidance on this point.

Target patient group's specific needs

In this context, the **target patient group** should be understood as a group of patients who have in common the same disease, condition or characteristics, that could benefit from using the device.

The specific needs should be understood as needs for:

- a specific device with one or more of the intended purposes specified in Article 2(1) of the MDR and, for IVDs, Article 2(2) of the IVDR, and;
- a specified level of performance of that device for certain performance characteristics.

Equivalent device in the context of the justification

MDR

Annex XIV.3 of the MDR describes device characteristics that should be taken into consideration for the demonstration of (non-)equivalence. These characteristics are divided into technical, biological and clinical aspects.

- Technical: the device is of similar design, is used under similar conditions, has similar specifications and properties including physicochemical properties, uses similar deployment methods, has similar principles of operation and critical performance characteristics.
- Biological: the device uses the same materials or substances in contact with the same human tissues or body fluids for a similar kind and duration of contact, has similar release characteristics of substances, including degradation products and leachables.
- Clinical: the device is used for the same clinical condition or purpose, including similar severity and stage of disease, at the same site in the body, in a similar population, has the same kind of user, has a similar relevant critical performance in view of the expected clinical effect for a specific intended purpose.

Note the different usage of the terms 'similar' and 'same'.

The health institution should consult the 'MDCG 2020-5 guidance on Clinical Evaluation – Equivalence' for further guidance on the subject.

Non-equivalence should be based on scientific or clinical justifications.

IVDR

The IVDR does not provide a description of equivalent devices. However, some of the equivalence characteristics listed in the MDR are also applicable to IVDs (see above). Justification that the patient groups specific needs cannot be met, or cannot be met at the appropriate level of performance, by an equivalent device available on the market can be based on technical or clinical aspects e.g. different intended purpose, different clinical conditions, different patient group, different conditions of use, different principles of operation. Non-equivalence should be based on scientific or clinical justifications.

Process for producing and reviewing the justification

Before manufacturing an in-house device for the first time, a health institution should examine the market for the presence and availability of equivalent CE marked devices. It is appropriate to describe this process in the documentation for the in-house device. The European database on medical devices, EUDAMED, could serve as one of the sources of information for the identification of equivalent CE marked alternatives (e.g. for higher risk class devices, a summary of safety and (clinical) performance is publicly available in EUDAMED). On the basis of its findings, the health institution should justify why 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.

The health institution should continue gathering information about the availability on the market and performance of potentially equivalent CE-marked devices in order to keep their in-house device manufacturing up-to-date with market developments. The health institution should review its justification on a regular basis, in view of its findings.

Once the in-house device is in use, a possible subsequent availability on the market of an equivalent device does not invalidate the initial justification regarding the fulfilment of the requirements set out in Article 5(5) at moment of the start of the in-house manufacturing. However, in such a case the health institution should review and update its justification.

Availability on the market

Market in this context should be understood as the market of CE marked devices that is accessible to the health institution according to national and local rules and regulations.

3.6 What kind of information can be requested from health institutions by competent authorities?

The health institution provides **information upon request** on the manufacture and use of in-house devices to its competent authority, which shall include a justification of their manufacturing, modification and use.

Examples of what information can be requested:

- When an in-house device is put into service:
  - Device type.
  - Intended use.
  - Target patient group.

- A justification for the lack of equivalent CE marked alternatives.
- Description of the manufacturing process.
- Description of modifications carried out.
- Information regarding use: procedures, used in combination with other devices (data on compatibility) etc.

- After the device has been used routinely:
  - All information as described above.
  - Number of units manufactured in a certain period and a justification of the production numbers.
  - Data regarding the performance of the device: performance outcome, incidents or complaints, corrective actions undertaken.

Note:

- Health Institutions should consult national provisions on notifying the competent authority when an in-house device is put into service, modified or its use discontinued.

3.7 Public declaration.

The health institution draws up a **declaration** which it shall make **publicly available**, including: (i) the name and address of the manufacturing health institution, (ii) the details necessary to identify the devices, and (iii) a declaration that the devices meet the general safety and performance requirements set out in the IVDR or MDR and, where applicable, information on which requirements are not fully met with a reasoned justification thereof.

Health institutions should consult possible national legislation, rules or guidance regarding the exact declaration format, language requirements and the publication conditions that need to be fulfilled (e.g. publication on the health institution's website and/or on a dedicated webpage from the competent authority). A proposed declaration format is provided in Annex A of this guidance. Health institutions should regularly review their public declaration and update it as necessary.

3.8 Documentation requirements.

For all medical devices and for class D IVDs (or any other IVD class if deemed necessary by national legislation), 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 Annex I of the MDR and IVDR are met. Health Institutions should consult national provisions regarding possible documentation requirements for class A, B and C IVDs.

The following aspects (non-exhaustive list of examples that might be applicable) should be taken into account when drafting documentation for in-house devices.

- **Manufacturing facility:** description of the infrastructure, the services and the work environment needed to safely manufacture the device in a way that fulfils the product requirements, listing of the equipment that is essential for production etc.
- **Manufacturing process:** explanation of the manufacturing processes, including a description of the raw materials, control of suppliers, final product testing etc.
- **Design:** principles of operation of the device and its mode of action, technical specifications including chemical, physical and biological properties, listing of applied standards, common specifications and guidelines that are essential to meet the relevant general safety and performance requirements etc.
- **Performance data:** according to Annex I of the IVDR/MDR, devices shall be designed and manufactured in such a way that they are suitable with regard to the performance they are intended to achieve, taking account of the generally acknowledged state of the art. A description of, where applicable, **the analytical and the clinical performance data** supporting the intended purpose should be provided.
- **Intended purpose of the device:** specification of indications and contra-indications, the patient target group or groups, information provided by an IVD device, function of an IVD device (e.g. screening, monitoring, …), what type of specimen is used by an IVD device etc.

All information should be presented in a clear, organised, readily searchable and unequivocal way. An appropriate format is described in detail in Annex II of the MDR/IVDR and can be used as guidance for documentation purposes. The documentation must be kept up to date.

3.9 Vigilance, incidents and corrective actions.

The health institution reviews experience gained from clinical use of the devices and takes all **necessary corrective actions**.

Health institutions should have a documented procedure in place to collect clinical data (please be aware that collecting clinical data under Article 5(5) activities does not replace clinical investigations/performance studies) and to process incidents and corrective actions for in-house devices. They should consult national legislation on possible requirements regarding reporting of incidents and corrective actions.

3.10 Industrial scale.

The last sentence of Article 5(5) of both Regulations, states that the exemption provisions do not apply to devices manufactured on an **industrial scale**. Furthermore, the recitals of the Regulations state that healthcare institutions should be able to manufacture, modify and use devices in-house and thus meet, on a non-industrial scale, the specific needs of a patient group that cannot be met at an appropriate level of performance by an equivalent device available on the market.

Industrial scale is not simply defined by the number of devices manufactured, but it is also related to commercial aspects. Therefore, if the manufacturing activity of an in-house device is carried out for commercial purposes, it should be considered as production on an industrial scale.

The exemption provisions in Article 5(5) of the Regulations should only be applicable to devices that are produced by the health institutions in order to meet the patient groups' specific needs, and therefore, the manufacturing process should not produce more than the estimated number of required devices.

Note:

- 'Industrial scale' is not synonymous to 'mass-produced' as defined in the IMDRF/PMD WG/N49:2018 document.
- In case of IVDs, the analysis of a large number of patient samples does not automatically render an in-house IVD to a device produced on an industrial scale.

Annex A

Public declaration regarding the manufacture and use of in-house devices by health institutions.

Name of health institution:

Address:

-the health institution- declares that the devices described in the accompanying table are only manufactured and used in *-the health institution-* and do meet the applicable general safety and performance requirements (GSPR) of the medical devices Regulation (EU 2017/745) or of the *in vitro* diagnostic medical devices Regulation (EU 2017/746). A reasoned justification is provided in case applicable general safety and performance requirements are not fully met.

Date and location:

Name, function and signature of responsible person(s):

Table of in-house devices:

Device identification (e.g. name, description, reference number)	Device type (IVD/ MD)	Device class	Intended purpose	Applicable GSPR met? (Y/N)	Information on and justification for applicable GSPR that are not fully met (using the numbering as in Annex I of the IVDR/MDR)