Home-Brew Assays and the New In Vitro-Diagnostic Reglementation

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On behalf of the SSMG
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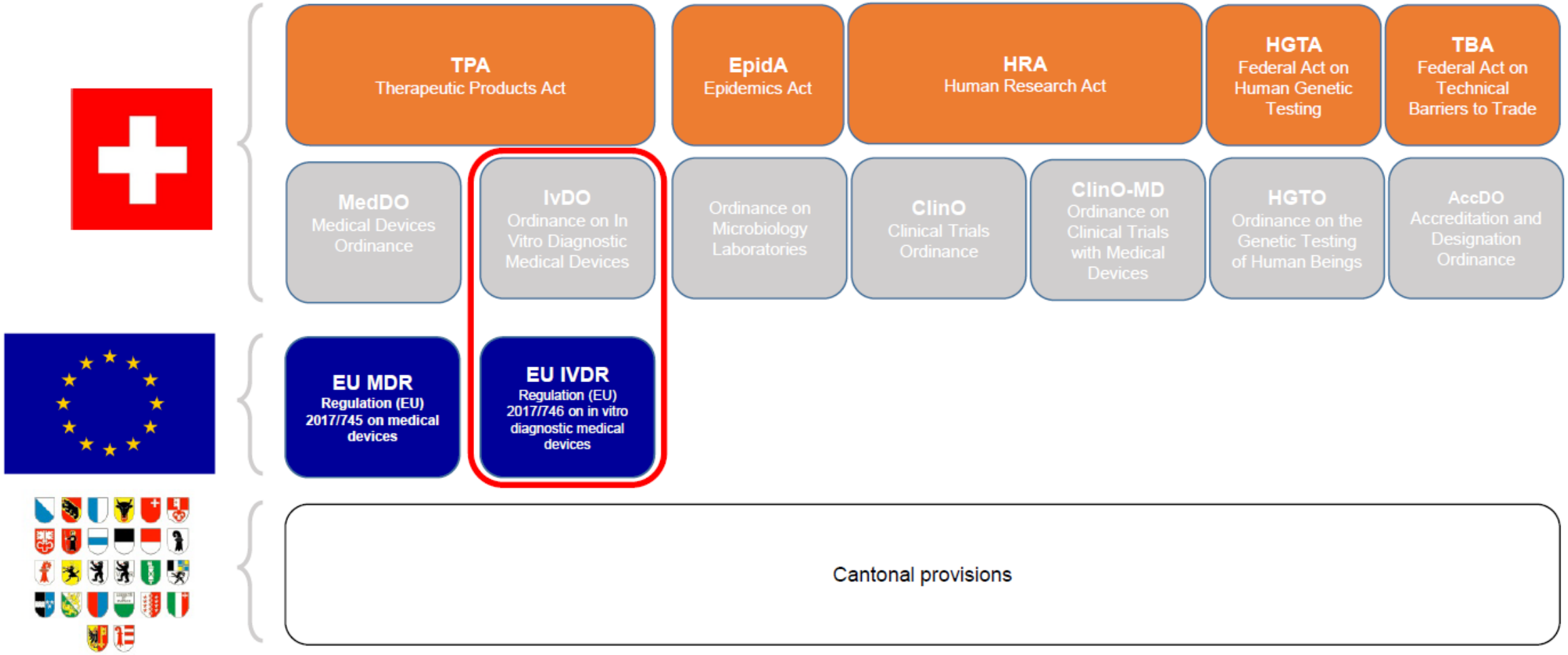
Laws, ordinances and international agreements

- TPA: Therapeutic Products Act SR 812.21
- HRA: Human Research Act SR 810.30
- MedDO: Medical Devices Ordinance SR812.213
- ClinO-MD: Ordinance on Clinical Trials with Medical Devices SR 810.306
- IvDO: Ordinance on In Vitro Diagnostic Medical Devices SR 812.219
- MDR: Regulation (EU) on Medical Devices 2017/745
- IVDR: Regulation (EU) on In vitro Diagnostic Medical Devices 2017/746
- IVDD: In Vitro Diagnostics Medical Devices Directive (98/79/EC)
- MRA-2017: Mutual Recognition Agreement (not updated): SR 0.946.526.81

Overview of applicable regulation



Yann Amstutz, SwissMedic, Inspector, Medical Devices Surveillance

IVDR

- Since 2001, the regulation of medical devices in Switzerland has been equivalent to that in the EU.

- On May 4th 2022, the Federal Council adopted the new IvDO and the amendment to the Ordinance on Clinical Trials with Medical Devices.

- Aim: improve patient safety by means of stricter requirements for conformity assessment and post-market surveillance.

- The new legal requirements entered into force on May 26th 2022, at the same time as the application of the IVDR in the EU.

Transitional periods

- On January 25th 2022, the EU adopted "Regulation (EU) 2022/112 amending Regulation (EU) 2017/746 as regards transitional provisions for certain in vitro diagnostic medical devices and the deferred application of conditions for in-house devices“

- These new transitional periods in the EU have also been taken into account accordingly in the IvDO.

What is an IVD?

- Art. 3 IvDO In vitro diagnostic medical device and its accessories
- In vitro diagnostic medical device = Medical device that generates medical information *in vitro* from specimens taken from humans

Art. 3 In vitro diagnostic medical device and its accessories

[1] An *in vitro diagnostic medical device* means any medical device in accordance with Article 3 paragraphs 1 and 2 MedDO[8] which:

a. 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; and

b. solely or principally for the purpose of providing information on one or more of the following:

   1. concerning physiological or pathological processes or states,
   2. concerning congenital physical or mental impairments,
   3. concerning the predisposition to a particular medical condition or a particular disease,
   4. to determine the safety and compatibility with potential recipients,
   5. to predict treatment response or reactions,
   6. to define or monitor therapeutic measures.

[2] Specimen receptacles shall also be deemed to be in vitro diagnostic medical devices.

[3] *Accessory for an in vitro diagnostic medical device* means an article which, whilst not being itself an in vitro diagnostic medical device, is intended by its manufacturer to be used together with one or more particular in vitro diagnostic medical device(s), to:

What are in-house IVDs?

- Art. 9 IvDO Devices **manufactured** and **used** in healthcare institutions
- Devices that are manufactured and used solely within healthcare institutions
- Devices: In vitro diagnostic medical devices and associated accessories
- Healthcare institutions comprise hospitals and laboratories

- In-house IVDs are also known as laboratory-developed tests (LDTs)

In-house IVDs

- are deemed to have been put into service
- are not deemed to have been placed on the market
- may not be supplied to any other legally autonomous entity
- may not be produced on an industrial scale

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Guidance on the health institution exemption under Article 5(5) of Regulation (EU) 2017/745 and Regulation (EU) 2017/746

January 2023

How to understand the term ‘manufactured’?

Manufacturing a device by a health institution can include:

- manufacturing a device from raw materials, from parts or components of a device or of another type of product or from an existing device or another type of product

- combining a device with another device or another type of product, where the combination creates a new device

- modifying an existing device in order to create a new device

How to understand the term ‘used’?

- Use within health institutions can either be
  - physical
  - remote (medical device software)

- 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 legal entity, it cannot be in-house.

What is a legal entity?

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

- Healthcare systems are organized differently. Therefore, the concept of legal entity can differ. The national competent authority may clarify how legal entity is understood nationally.

  - One hospital[1] can be one legal entity when there is only one health institution (one organiser) within the hospital.
  - One hospital[1] 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[1] can belong to the same legal entity when they are all part of one health institution (one organiser). They share the same organisational number, quality goals and quality management systems and the same healthcare strategy, even though they might be spread over different locations.

Examples of in-house IVDs

- Analytical tests developed for medical purposes by a healthcare institution
  - 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 specimens.
- Standard analytical medical tests that use an institution's proprietary devices (e.g. reagents that are not CE-marked)
- IVD test equipment manufactured in-house
- IVD software developed in-house
  - A health institution develops in-house a medical device software that is used on site by healthcare professionals.

Examples of devices that are **not** in-house IVDs

- When patients can use the device outside the health institution, e.g. by entering or accessing medical data that are subsequently used by the healthcare professional.

- Orthopedic braces that can be adapted by patients themselves outside the health institution.

- Self-tests if used outside the health institution's legal entity.

- Devices manufactured in-house purely for economic motives/financial interests, without clinically relevant reasons.

Compliance with the relevant general safety and performance requirements

Annex I MDR and IVDR

- Chapter I describes the establishment of a risk management system and the regular update of the benefit-risk ratio assessment.

- Chapter II describes requirements regarding design, manufacture and performance of devices.

- Chapter III defines requirements for the information that is supplied with the device. While a number of the provisions in this chapter do not apply to in-house devices, some are relevant to safely use the device in a way that allows it to achieve its intended purpose.

What is an appropriate quality management system?

- Article 10(9) of the MDR describes the minimal aspects that a QMS for manufacturing CE-marked medical devices should cover.

- Article 10(8) of the IVDR describes the minimal aspects that a QMS for manufacturing CE-marked medical devices should cover.

- The laboratory of the health institution must be compliant with standard EN ISO 15189 or where applicable national provisions, including national provisions regarding accreditation and certification.

Examples of areas covered by an appropriate QMS

- Compliance to Article 5(5) and Annex I, MDR and IVDR
- Responsibility of the management
- Risk management
- Identify, generate and appraise data
- Manufacturing
- Traceability
- Monitoring, analysis and continuous improvement
- Communication with competent authorities

Justification on missing equivalent device on the market (1/2)

The health institution must justify 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.

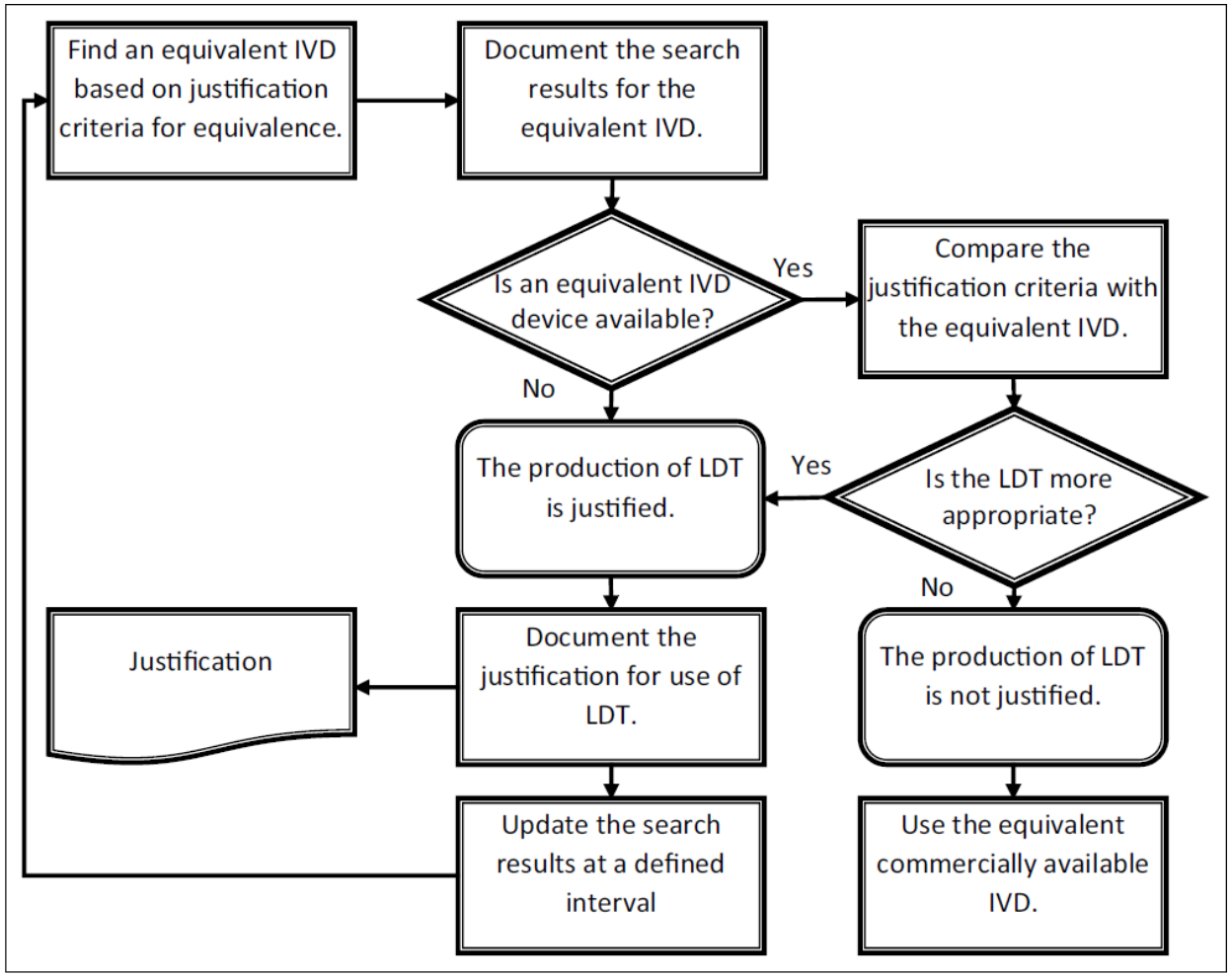
- The **specific needs** should be understood as needs for:
  - a specific device
  - a specified level of performance of a device for certain performance characteristics

Justification on missing equivalent device on the market (2/2)

Equivalent device

- 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.
- The IVDR does not provide a description of equivalent devices.

Search for an equivalent CE-marked IVD and justification for use according to Article 5 (5)



Spitzenberger et al., *Therapeutic Innovation & Regulatory Science (2022) 56:47–64*

Obligations of healthcare institutions (1/3)

Art. 5 para. 5 EU IVDR

a. Devices must not be supplied to any other legally autonomous entity
b. Devices must be **manufactured** and **used** under appropriate quality management systems
c. The healthcare institution's laboratory must comply with EN ISO 15189 or national provisions, including national accreditation provisions
d. Written evidence that no equivalent device is on the market must be provided
e. Healthcare institutions must provide information upon request on the use of such devices to the competent authority

Art. 83 IvDO => applicable from: **26 May 2022** **26 May 2024** **26 May 2028**

Obligations of healthcare institutions (2/3)

f. Healthcare institutions must produce a **publicly accessible declaration** showing:
   i. Name and address of the healthcare institution
   ii. Identifying details for the in-house IVD
   iii. Declaration that the in-house IVD fulfils the general safety and performance requirements. => Any requirements that are not fulfilled must be identified and reasons for non-compliance must be given.

g. Healthcare institutions must produce detailed documents that facilitate understanding of the manufacturing facility, manufacturing process, device design and performance data, including intended purpose.
   - Documents must demonstrate that the general safety and performance requirements are fulfilled

Art. 83 IvDO => applicable from: **26 May 2022** **26 May 2024** **26 May 2028**

Obligations of healthcare institutions (3/3)

h. All necessary steps must be taken to ensure that all devices are manufactured in compliance with the documents referred to in **g** above

i. Experience gained while using the device in clinical practice must be assessed and all necessary corrective actions must be implemented

Art. 83 IvDO => applicable from: **26 May 2022** **26 May 2024** **26 May 2028**

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Requirements for in-house IVDs

The following requirements must be fulfilled (Art. 9 and 10 IvDO):

- The relevant general safety and performance requirements according to Annex I of EU IVDR
- The requirements set out in Art. 5 para. 5 EU IVDR
- In-house IVDs have to be notified to Swissmedic before they are put into service
- Other requirements of EU IVDR do not have to be fulfilled, i.e.
  - Certification by a designated body is not required
  - A UDI does not have to be assigned and affixed to the device
  - In-house IVDs may not carry a conformity marking

How should in-house IVDs be notified?

- Forms are available on www.swissmedic.ch

Home › Medical devices › Market access › Notification of IVDs

The following form must be sent to Swissmedic:

BW630_30_032e FO Notification in accordance with Art. 10 IvDO for devices manufactured in healthcare institutions (PDF, 2 MB, 11.01.2023)

The product list template for notifying a device group can be downloaded here:

Product list template Art. 10 IvDO (XLSX, 11 kB, 26.05.2022)

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)	Risk class of the device[2]	Intended purpose	Applicable GSPR fully 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)

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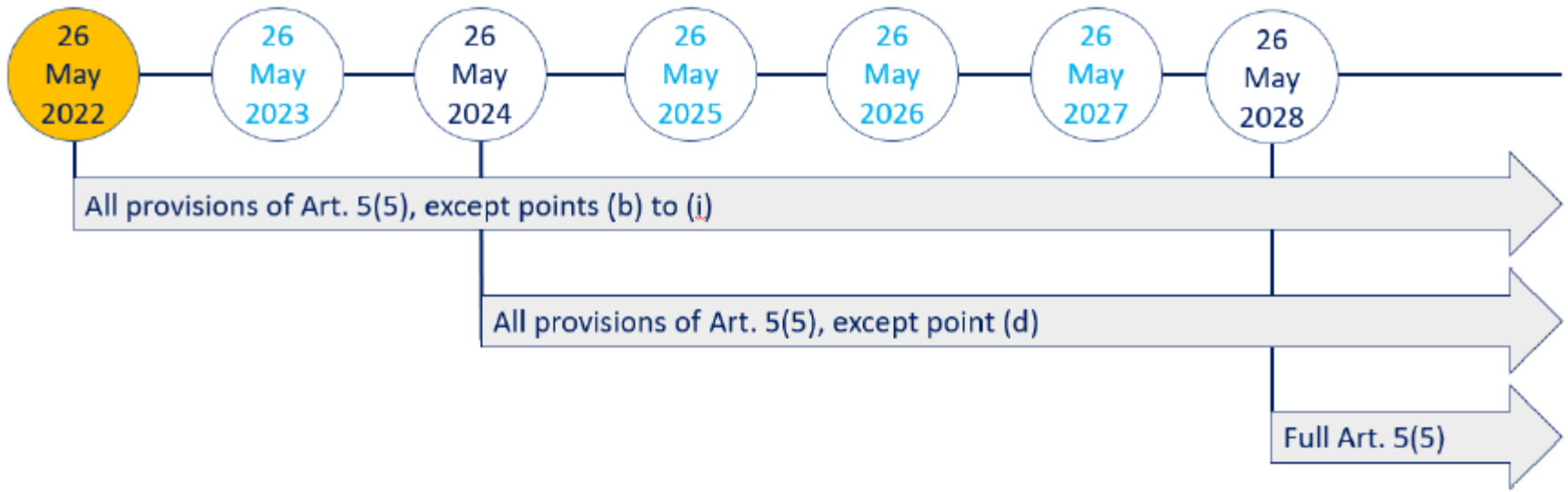
Timeline for the application of the different provisions of IVDR Article 5(5)



Note that the corresponding Article 5(5) of the MDR has been fully applicable since 26 May 2021.

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Useful links / information

- Neue Regulierung über In-vitro-Diagnostika (swissmedic.ch)

https://www.swissmedic.ch/swissmedic/de/home/services/veranstaltungen/online-neue-regulierung-ivd.html#308300180

- The SSMG has a working group led by Dr. Thierry Nouspikel with members of public (academic and non-academic) and private labs