Webinar on IVD Kits

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Alex Laan, Dipl-Ing.
Head of IVD Medical Devices Notified Body BSI

Agenda

Registration

- **Welcome & Opening**
- **Introduction**
- **Definitions under the IVDR and MDR**
- **Qualification and classification of IVD kits, components and accessories**
- **Regulatory requirements for IVD kits, components and accessories**
- **Product configurations and potential certification scenarios**
- **Recommendations and Key takeaway messages**
- **Q&A**

End of Webinar

Introduction

Why this topic is important...

Introduction

The situation so far.

Currently.

The Regulation on in vitro diagnostic medical devices (2017/746) introduced updated and expanded definitions that reflect changes in technology, progress in diagnostics, and improvements in regulatory oversight.

Definitions.

One key definition is Definition 11 in Article 2: 'kit' means a set of components that are packaged together and intended to be used to perform a specific in vitro diagnostic examination, or a part thereof".

The Challenge.

Besides a clear definition, the Regulation has not reserved a dedicated clause to the regulatory requirements applicable to IVD kits in a similar fashion as to the procedure pack counterpart in EU 2017/745 (MDR).

Learning Curve.

The lack of clarity on how to interpret "IVD kits" could generate interpretation issues and, eventually, it could make the certification process very difficult for both the manufacturer and the Notified Body.

Some things to consider, regarding the EU framework…

- It needs to be clear that the EU Medical Device Regulations applies to **finished products**, as defined by the scope of each specific Union harmonisation legislation; yet the concept of “product” varies between different pieces of Union harmonisation legislation.

- The EU Regulations apply to, for instance, as **products, equipment, apparatus, devices, appliances, instruments, materials, assemblies, components or safety components, units, fittings, accessories, systems** or **partly completed machinery**.

- Thus, within the terms of the EU Regulation, components, spare parts or sub-assemblies **may be** regarded as finished products and their end-use may be the assembly or incorporation into a finished product.

- As such, these products must comply with the **applicable legislation** at the time they are placed on the Union market (and/or put into service).

- When a finished product incorporating another product is placed on the Union market, the manufacturer that places the final device on the EU market is responsible for the compliance of the **complete product** with the applicable legislation.

Definitions under the IVDR (and MDR)

Why definitions are so important when it comes down to regulatory compliance...

Regulatory Definitions

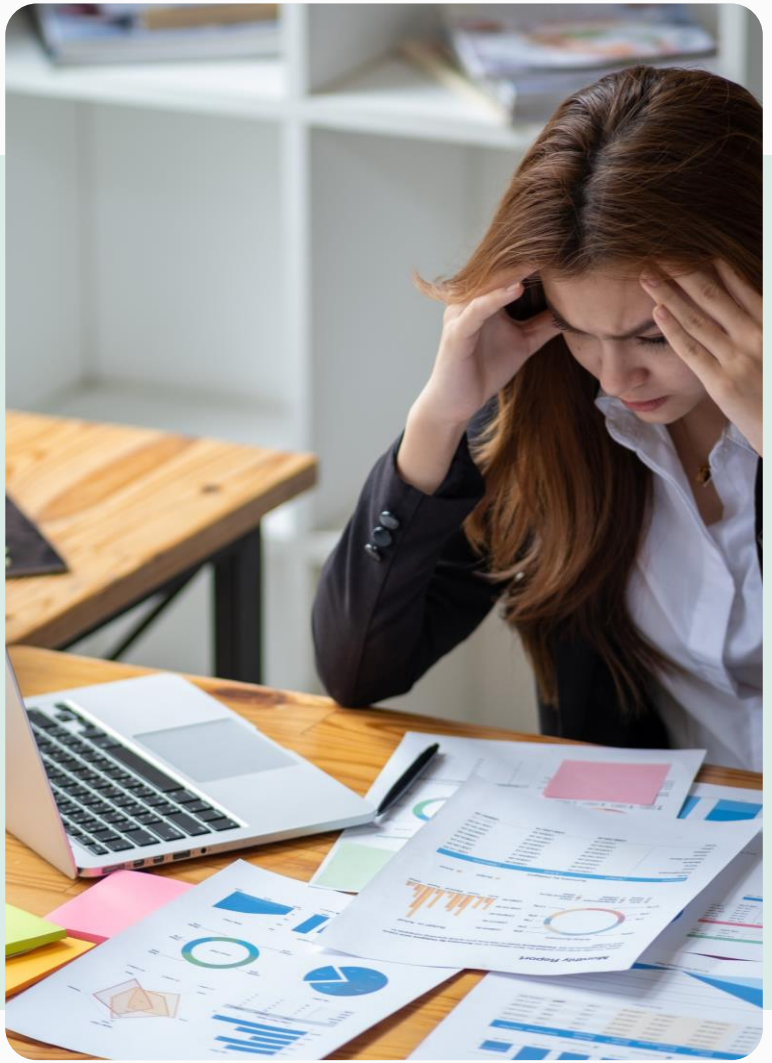
Background

As already mentioned, the IVDR brought in revised and broadened definitions compare to the repealed IVD Directive (98/79/EC). The following definitions clarify the terms “Kit”, “Accessory”, and “Component” as they relate to the in vitro diagnostic medical devices within the scope of the IVDR.

Definitions

Kit (Art 2.11): ‘Kit’ means a **set of components** that are packaged together and intended to be used to perform a specific in vitro diagnostic examination, or a part thereof.

Accessory (Art 2.4): ‘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 several particular in vitro diagnostic medical device(s) to specifically enable the in vitro diagnostic medical device(s) to be used in accordance with its/their intended purpose(s) or to **specifically and directly assist the medical functionality** of the in vitro diagnostic medical device(s) in terms of its/their intended purpose(s).



Regulatory Definitions

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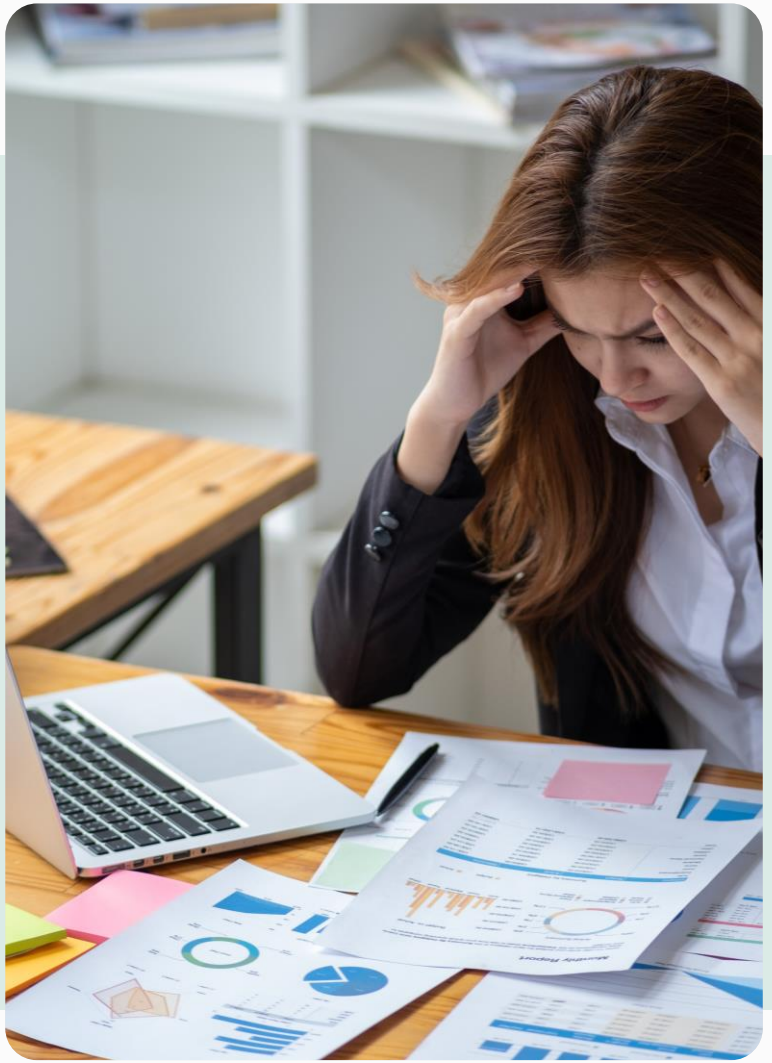
Definitions

Component or part: although this term does not have an assigned definition under Article 2 this can be understood as an article which, in combination with one or more other components or parts, forms an in vitro diagnostic medical device kit.

Compatibility (Art 2.18): is the ability of a device, including software, when used together with one or more other devices in accordance with its intended purpose, to perform without losing or compromising the ability to perform as intended…

Interoperability (Art 2.19): is the ability of two or more devices, including software, from the same manufacturer or from different manufacturers, to exchange information and use the information that has been exchanged for the correct execution of a specified function without changing the content of the data…



Regulatory Definitions

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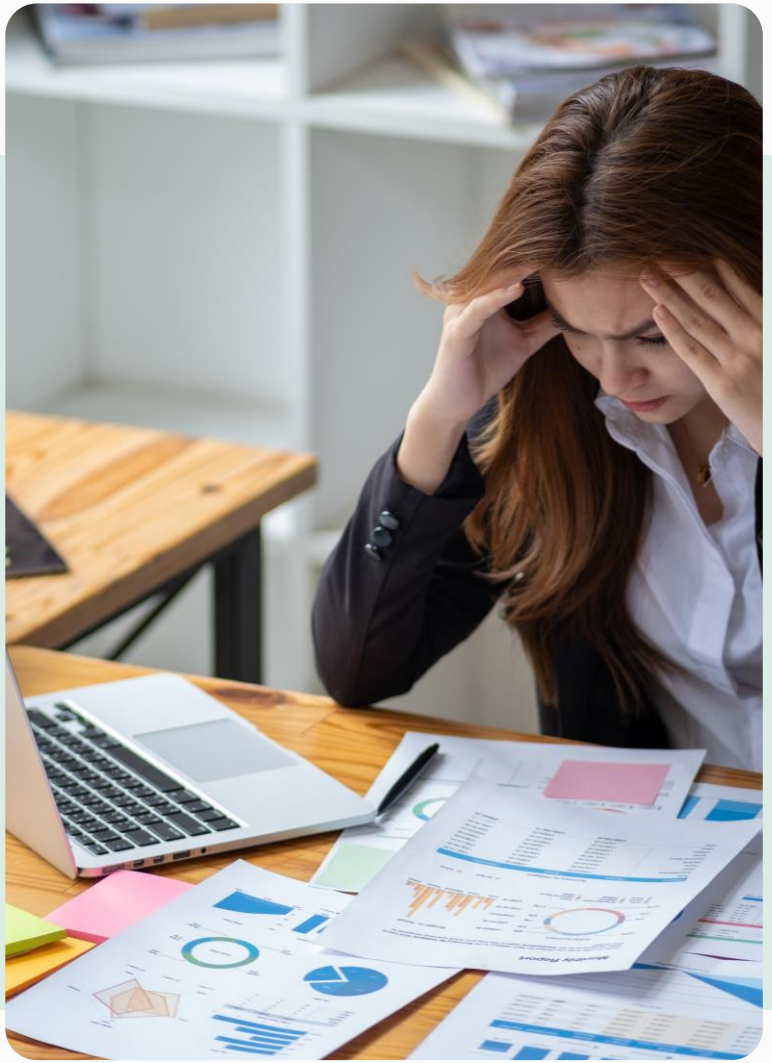
Definitions

Configurable device: A **configurable device** is a device that consists of **several** components which can be assembled by the manufacturer in multiple configurations. Those individual components **may be** devices in themselves.

Configuration: Configuration is a **combination of items of equipment**, as specified by the manufacturer, that operate together as a device to achieve an intended purpose.



Regulatory Definitions

- Just by applying and combining the correct definitions alone, you will not get to a compliant approach…
- Some diagnostic products may not fall under the regime of the IVDR, but under the MDR.
- Some accessories and/or components may not be considered a final device…
- So, before we start deciphering how to start organizing the technical documentation, we first need to establish what the device “is”;

Qualification and classification of IVD kits, components and accessories

Notified Body Discretion is advised...

Qualification and classification of IVD kits

- In order to establish a sound regulatory strategy of a specific device (Art 10.8), the device must **first** qualify as an in vitro medical device in accordance with the definition set out in **Article 2**.
- Once the device is **qualified** as an IVD medical device, classification guides the applicable conformity assessment procedures for it to be CE marked and placed on the EU market.
- IVDs are classified based on their **intended purpose**, **risk**, and the **type of tests** they perform. The classification follows the rules laid out in Annex VIII of the IVDR, which defines the risk classes (Class A, B, C to D) and associated criteria.
- Classification of IVD kits is **not explicitly addressed** in Annex VIII, although clarification on combination of devices, accessories, and kit components (such as control and calibrators) classification is provided.
- The basic principle is that all devices are **generally classified** in their own right based on their separate intended purpose and this also applies when these are to be used in combination with one or more devices, standalone software and accessories.
- There are some very nice MDCG documents available on qualification and classification!

Qualification and classification of IVD kits

- In order to establish a sound regulatory strategy of a specific device (Art 10.8), the device must **first** qualify as an in vitro medical device in accordance with the definition set out in **Article 2**.

However, there are exceptions:

- **Software**, which **drives a device or influences the use of a device**, shall fall within the same class as the device. If the software is **independent of any other device**, it shall be classified in its own right.
- **Calibrators** intended to be used with a device shall be **classified in the same class** as the device.
- **Control materials** with quantitative or qualitative assigned values intended for one specific analyte or multiple analytes shall be **classified in the same class** as the device.

Qualification and classification of IVD kits

- As a consequence, an IVD kit is classified on the basis of the intended purpose assigned to the kit as a whole, by the kit's manufacturer as per Annex VIII, section 1.1.
- A kit's classification may be influenced by the implementing rules in Section 1 of Annex VIII IVDR.
- The IVD kit **could**, in theory, contain software, calibrators or control materials that are **totally independent** from the device component (assay); in other words, they would not drive or influence the use of the device; these would then be separately classified from the IVD in the kit.
- One could however argue whether adding software to an IVD kit would be considered the software to be "integrated into the product"…Many times, this is not, per the regulatory definitions. Software integrated into an IVD is not just a matter of simply adding software data carrier to an IVD kit.

Devices with a diagnostic purpose, qualified under the MDR.

- The MDR is also covering diagnostic products within their scope and definition (article 2 MDR);

(1) 'medical device' means any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:

- *diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,*
- *diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,*
- *investigation, replacement or modification of the anatomy or of a physiological or pathological process or state,*
- *providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations,*

- **invasive sampling products** or products which are directly applied to the human body for the purpose of obtaining a specimen;

- Any device which, when placed on the market or put into service, incorporates, **as an integral part**, a **medical device as defined** in point 1 of Article 2 **of Regulation (EU) 2017/745** shall be **governed by that Regulation**. The requirements of this Regulation shall apply to the in vitro diagnostic medical device part.

- How is this possible???

Devices with a diagnostic purpose, qualified under the MDR.

- This means that some devices that have a clear diagnostic purpose, are not **automatically placed** under the scope of the IVDR. In order for a diagnostic device to fall in the scope of the IVDR, it shall meet the following description:

- The principal intended purpose of an IVD is to solely or principally provide information on one or more medical purposes;

a) Information concerning a physiological process or state
b) Information concerning a pathological process or state
c) Information concerning a congenital physical or mental abnormality
d) Information concerning the predisposition to a medical condition, state or a disease
e) To determine the safety and compatibility with potential recipients
f) To predict treatment response or reactions
g) To monitor therapeutic measures

- The IVD may provide this information either **alone or in combination** with other devices or products
- The IVD is used **in vitro for the examination of a specimen** derived from the human body and where the specimen is never reintroduced into the body.
- The IVD is used in vitro for the examination of a specimen derived from **the human body**.
- The specimen is **never reintroduced** into the body.

Devices with a diagnostic purpose, qualified under the MDR.

- Products cannot be brought into the scope of the IVDR merely by mentioning ‘for in vitro diagnostic use’, since many devices that are governed by the MDR may also be involved in diagnosis, prediction and providing information.
- MRI instruments and CT scanners being the clearest examples.
- Also, when invasive sample taking is part of the testing process and the specimen is reintroduced in the body, this would also place this under the remit of the MDR and not the IVDR.
- What is however important to consider is that when both the medical device part and the IVD part are integrated as a whole, the final device could easily fall under the MDR and not the IVDR.
- A clear definition for an integral product is currently lacking both in the MDR and IVDR, although the **Blue Guide** will give some clear reflections on what is expected…

Kit as a Procedure Pack or Systems governed by article 22 MDR (?)

- The basic principle of intended purpose-based device classification of the IVDR it is also present in Annex VIII of the Medical Device Regulation (MDR).

- However, for **systems and procedure packs** the MDR on the other hand has a dedicated article (Article 22), which deals with systems and procedure packs that are composed of devices and other products but are not devices in their own right. Those are defined in Article 2(10) and 2(11) (as opposite to the IVDR “kit” definition) as follows:
  - **Procedure Pack**: a combination of products packaged together and placed on the market with the **purpose of being used** for a **specific medical purpose**.
  - **System**: a combination of products, either packaged together or not, which **are intended to be interconnected or combined** to achieve a specific medical purpose.

- Procedure Packs or Systems are **not CE marked as per Article 22.5** “ The systems or procedure packs referred to in paragraph 1 of this Article shall not themselves bear an additional CE marking, but they shall bear the name, registered trade name or registered trademark of the person referred to in paragraphs 1 and 3 of this Article as well as the address at which that person can be contacted, so that the person’s location can be established”.

Kit as a Procedure Pack or Systems governed by article 22 MDR (?)

- However, the MDR does treat **systems** and **procedure packs** in a similar way as the IVDR treats a kit in the specific scenario set out in article 22 (4) MDR, which means that the whole system or procedure pack is considered as a device in its own right and therefore **must undergo the relevant conformity assessment** pursuant to Article 52 to gain the **CE-mark as a single device**:
  - When the system or procedure pack **incorporates non-CE-marked** devices.
  - Where the selected combination of devices deviates from the **devices' initial intended purpose**.
  - If **sterilisation processes deviate** from the medical device manufacturer's instructions.

- In all other circumstances the IVDR, however, diverges from the MDR by considering IVD kits as medical devices in their own right and therefore subjecting to the same general requirements and classification rules as other devices under the IVDR.

- It is good to know that the recent update of the MDCG 2020-16 classification guideline (rev.3) has now expanded on IVD kits intended for specimen collection, per rule 5a;

"Kits intended for specimen collection must include at least one IVD (specimen receptacle). The kit may also include devices other than IVDs, such as a medical device or components which are covered neither by the IVDR nor by the MDR.".

Kit as a Procedure Pack or Systems governed by article 22 MDR (?)

- This means, for example, that a kit that is intended for sampling and collecting specimen (IVD), which in addition contains an (invasive) needle (MD), would still need to be qualified an IVD medical device as a whole, falling under the regime of the IVDR. But the medical device part, the needle, would need to be separately qualified (and classified) under the MDR and undergo the appropriate conformity assessment as well.
- Kits intended for specimen collection are classified according to the kit's intended purpose and implementing rule 1.9. Typically, these kits are classified as class A as they contain a specimen receptacle (class A) and other possible IVD components likely to be class A (e.g. buffers). Specimen receptacles and kits intended for specimen collection may be placed on the market separately but intended by the manufacturer to be used in combination with another IVD.
- As a reminder, according to Article 1(3)(b), invasive sampling products or products which are **directly applied to the human body** for the purpose of obtaining a specimen are themselves **NOT IVDs** but fall in the MDR.
- In this case implementing rule 1.2 applies: the **specimen receptacle or kit** intended for **specimen collection** and the other IVD should be **classified independently**.

Parts and components as part of the IVD; is there a difference?

- In essence, there does not seem to be a difference between **parts** and **components** in an IVD, per IVDR.
- The IVDR considers an (IVD) kit as a **set of components that are packaged together** and intended to be used to perform a specific in vitro diagnostic examination, or part thereof; it does not specifically talk about "**parts**". This set of components can only be treated as a "kit", when the intended purpose of the set of components **as a whole fall** within the definition of an IVD, per IVDR.
- The IVDR Article 20, however seems to place a parts or component of an IVD in the same ballpark. Both can be **considered to specifically intend to replace an identical or similar integral part** or component of a device that is defective or worn in order to maintain or restore the function of the device without changing its performance or safety characteristics or its intended purpose.
- Now, the difference is however that when an item is intended to specifically replace a part or component of the device, and this replacement **significantly changes the performance or safety characteristics**, or the intended purpose of the device, this item in turn **shall be considered a device** and, as such, **shall meet the requirements of the IVDR**.
- In that sense, IVD parts and components seem to have a different regulatory position from **IVD accessories** that are not "**being an IVD in themselves**"

Parts and components as part of the IVD; is there a difference?

- Where accessories are considered **“optional**” for an IVD to function and safely perform in accordance with the essential requirements (GSPR), parts and components, however, can impact the safety and performance of the device.
- And if they do, they should be considered “**a device**” per article 20.
- When parts and components **do not impact the safety and performance** of the device, IVDR requirements do not apply to them.

What about general laboratory products and accessories? Are these governed by the IVDR?

- The IVDR takes an interesting stance on **general laboratory products**; in some cases, the IVDR requirements are applicable, in some cases they are not.

- It is however clear that the IVDR **governs these products** under article 3 (a):

This Regulation does not apply to:
(a) products for general laboratory use or research-use only products, unless such products, in view of their characteristics, are specifically intended by their manufacturer to be used for in vitro diagnostic examination;

- Which basically means "**it depends**".

- In this case, it **depends on the intended purpose** that the manufacturer specifically states for the general laboratory product. The MDCG 2020-16 gives further guidance, by giving some examples (pipettes, stain powders, glass microscope slides, centrifuges, pipette tips or instrument liquid collection containers, buffers which usually do not fall under the definition of an IVD medical device).

What about general laboratory products and accessories? Are these governed by the IVDR?

- Consequently, when such products are specifically intended by the manufacturer to be used for in vitro diagnostic examinations, then they are considered as IVDs, making the IVDR requirements applicable again.

- Example:

(- IVDR) if no medical and diagnostic claims are made

(+ IVDR) if medical and diagnostic claims are made

(+ IVDR + Class ⇧ when instrument is dedicated for particular IVD test only

Regulatory requirements for IVD kits...

And parts, components and accessories as well...

Regulatory requirements for IVD kits

- Whilst Article 22 of the MDR defines the obligations of the “natural or legal person” responsible for the placing on the market of a combination of devices as a system or procedure pack, the IVDR does not identify a distinct role for a kit “producer”.
- Hence, they are manufacturers as defined by the Article 2(24) of IVDR and subject to the Article 10 obligations.
- As long as the general principle of IVD kits being devices in their own right applies, kits are:
  - classified according to rules as set out in Annex VIII
  - described in Technical Documentation compliant with Annex II and III of the IVDR
  - assigned a basic UDI as set out in Annex VI
  - subject to a Declaration of Conformity per Annex IV
  - subject to general obligations for Economic Operators
  - subject to requirements regarding information supplied with the device as per Annex I, part III (with special attention to section 20.2 and 20.4)

Regulatory requirements for IVD kits

- **Accessories**, since not IVDs in their own right, should be considered as a **specific category** onto which the IVDR requirements apply and shall be classified in their own right separately from the device with which they are used. Therefore, the IVDR keeps mentioning devices and accessories, throughout the regulation.
- This is also true for **parts and components** as Article 20 of the IVDR indicates that an item, if intended specifically to replace a part or component of a device and if it significantly changes the performance, safety characteristics, or intended purpose of the device, is considered a device in its own right.
- In such cases, the **item must meet the relevant regulatory requirements** specified in the (applicable) regulation. This recognises that certain components can play a critical role in influencing the overall functionality and characteristics of a device, warranting classification and regulatory adherence as an independent device.
- Per the Blue Guide, **spare parts or parts** which are available and marketed separately as products intended for users **in order to be integrated to other products**, such as service parts or components intended for maintenance or repair, must nevertheless **comply with the general safety requirement** set out in the GPSR.

Product configuration and potential certification scenarios in the EU…

Regulatory requirements for IVD kits

- A device manufacturer of a specific “item” should take a **phased approach** before pursuing any conformity assessment to define the correct certification scenario.

- The **first step** would be to clearly qualify the item as a medical device (in general), before determining it is an in vitro diagnostic medical device, per article 2 (1) and article 2 (2) IVDR, consecutively.

- Manufacturers would then need to be able to **determine** whether they are, according to the respective definitions in the Regulation, dealing with an accessory, a part or component, a single device and/or a combination of each and/or every of those.

- In case of a **combination of devices and/or components**, such as a kit or a combination device, this process shall further differentiate, based on the configuration that is followed and the potential certification scenarios that apply.

- In fact, when the configuration sees the IVD device as an **integral part of a medical device** and that medical device falls under the definition provided in Article 2, point 1, of MDR, then the **entire combination** is subject to the regulations outlined in (EU) 2017/745.

Recommendations and Conclusions

Notified Body Discretion is advised…

Recommendations and Takeaway messages

Whoever said this presentation would be easy?

Before a device can be **placed on the EU market**, the manufacturer will first need to define “what the **device is**”. What does the device “do” in relation to the caregiver and what “result” it does intend to give. And what is it intended to provide to the patient.

As a result, it can be **challenging** to determine what regulatory requirements apply to any particular device, especially when the scoping criteria for the regulations are not entirely clear.

Since the moment BSI has been designated as an EU Notified Body for IVD medical devices in 2019, it has received **applications** containing varying views of how IVD devices are qualified and classified. Some may come **not come up in the application stage** of the review but in the review itself…

When taking a closer look at the medical device regulations MDR 2017/745 and IVDR 2017/746, including available MDCG guidance, one can deduct a **regulatory strategy** for the whole product portfolio.

This presentation, in itself, may not provide **more information** than has already been made available through MDCG or MEDDEV documents. As such, these sources of documents are being mentioned.

The contents of this presentation will be further developed into a **BSI whitepaper**, providing more clarifications to manufacturer and examples that will give **more backgrounds**.

Questions, anybody?

Thank you for joining us today