New impacts of the extended transition period for IVDR implementation

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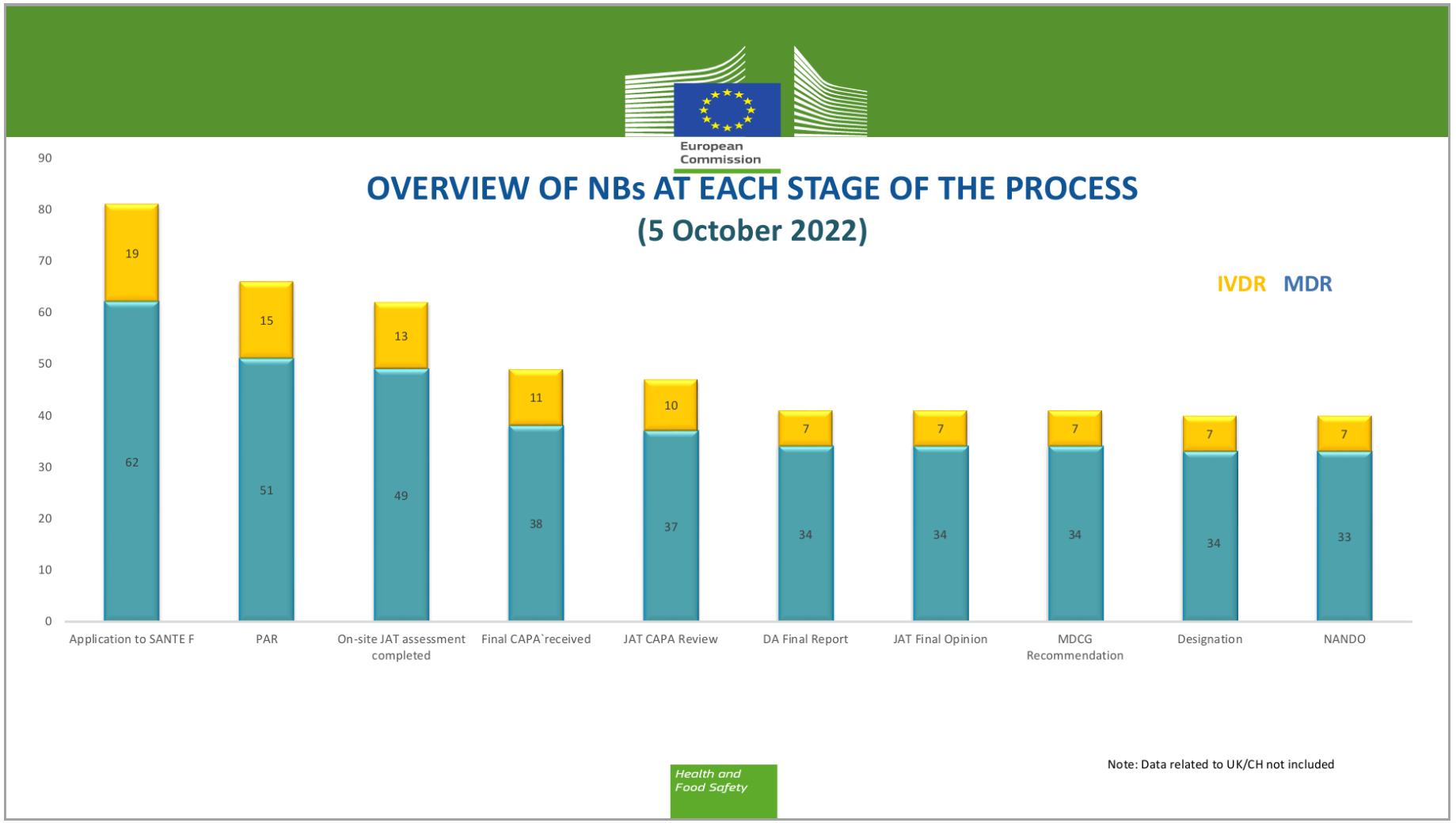
Mehr Sicherheit.
Mehr Wert.

Choose certainty.
Add value.

Agenda

- EU IVDR state of play
- The transition period
- Other guidances & legislation
- Laboratory developed tests
- Conclusions

Notified Body capacity



No new NB designation for IVDR since May 2022

+1 new application
+1 on-site assessment
+1 Final CAPA received
+1 JAT CAPA review

IVDR designated Notified Bodies

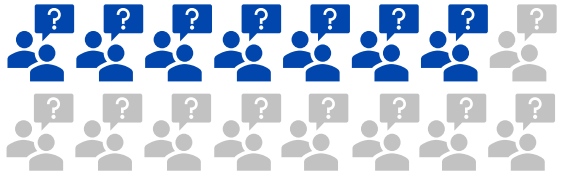
Body type ▲	Name ▲	Country ▲
NB 2265	3EC International a.s.	Slovakia
NB 2797	BSI Group The Netherlands B.V.	Netherlands
NB 0344	DEKRA Certification B.V.	Netherlands
NB 0124	DEKRA Certification GmbH	Germany
NB 0459	GMED SAS	France
NB 0197	TÜV Rheinland LGA Products GmbH	Germany
NB 0123	TÜV SÜD Product Service GmbH	Germany

The Numbers

Notified Bodies

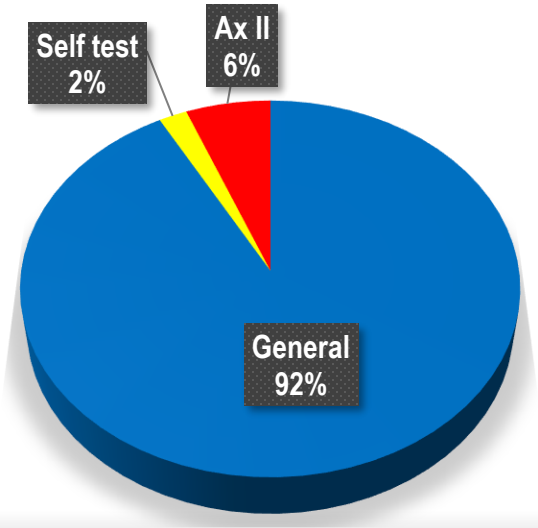
IVDD

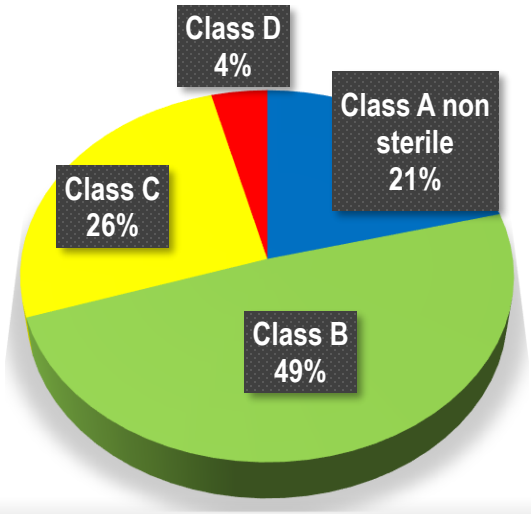
IVDR

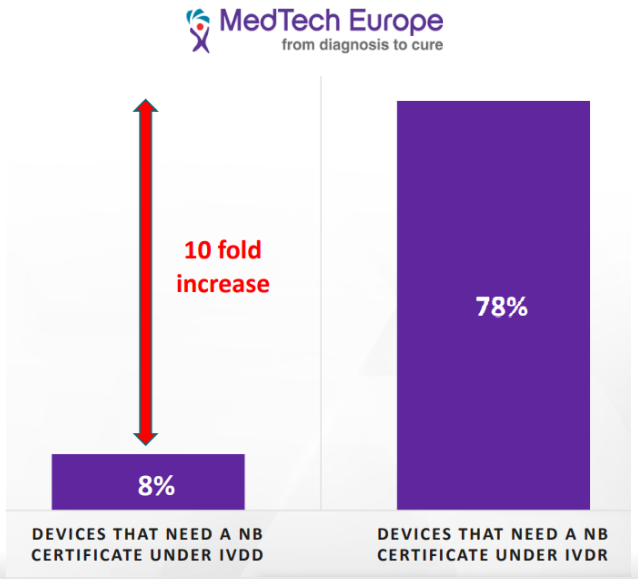


32%

Devices







736%

Preliminary results for 8 – 28 July 2021 Survey Market composition of in vitro diagnostic medical devices (IVDs) EU Competent Authorities for Medical Devices (CAMD) coordinated by MedTech Europe

Enhancing Notified Body capacities – MDCG 2022-14

MDCG suggested actions for NBs:

- Make use of **hybrid audits**, for timely and efficient conformity assessment
- **Leverage evidence from previous assessments** under the IVDD when appropriate
- Make use of flexibility according to MDCG 2022-15 on **appropriate surveillance of legacy devices**
- **Eliminate administrative workload or undue limitations**, based on forthcoming guidance from MDCG
- Foster **capacity-building** of existing and potentially new NBs
- **Rationalise & streamline internal administrative procedures** to ensure timely and efficient conformity assessment
- Organise **structured dialogues with manufacturers** on regulatory aspects, before and during the conformity assessment process
- Work on **common guidelines to assist manufacturers** (e.g. TD preparation and content guideline)

Infrastructure status

- **No European reference laboratories (EURL)** designated yet
  - Applications accepted until DEC 2022
  - First designation expected 2023 Q3

- **Eudamed not fully functional** for IVDR
  - MDCG 2022-12 describes harmonized administrative practices and alternative solutions

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The transition period (Regulation 2022/112 IVDR)

Dealing with changes to products under IVDD – MDCG 2022-6

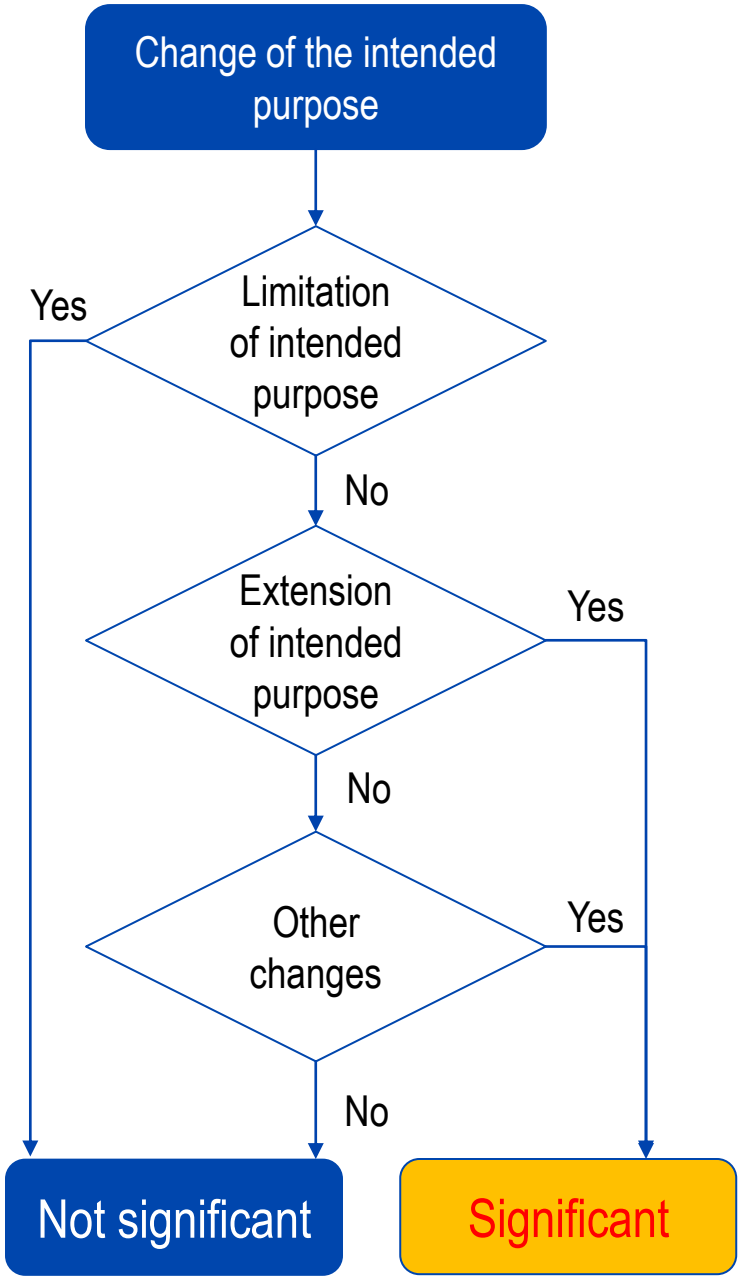
Pre-Conditions	▪ Valid IVDD certificate, or ▪ DoC issued **before** IVDR DoA
Change considerations	▪ No significant changes (design, intended purpose) permitted ▪ New devices need to be certified under IVDR
Manufacturer responsibility	▪ Must have process to evaluate changes ▪ Must report changes to NB for evaluation
Notified Bodies	▪ Verify changes ▪ Cannot amend IVDD certificate, BUT may confirm changes in writing for correction or complementation of certificate information

Changes to the intended purpose

- Limitation of intended purpose, such as restricting the target population, specimen type, specimen location → **Not significant**

- Extension of intended purpose → **Significant**
  - *Addition regarding what is detected or measured*
  - *Additional functions of the device (screening, monitoring, diagnosis)*
  - *Addition of specimen type(s)*
  - *For CDx: extension of associated medicinal product, of target population, or of the tissue type*

- Other major changes of the intended purpose → **Significant**
  - *Change in assay type (e.g. qualitative to quantitative assay)*
  - *Change of the intended user (e.g. professional to lay user)*
  - *Change of operation (e.g. automatic to manual)*
  - *Change of specimen type(s)*

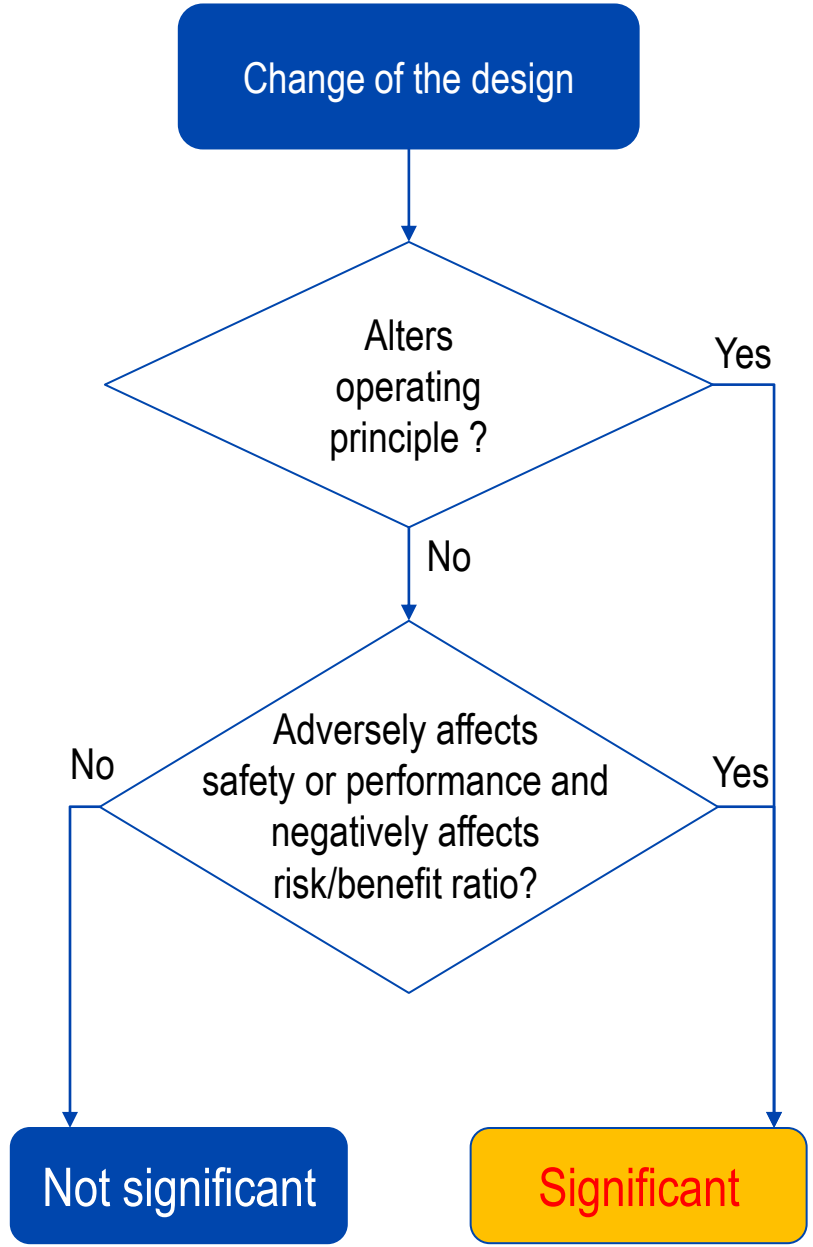


Changes in the design

- Changes that alter the device's operating principle: → **Significant**
  - *Change from immunofluorescence to enzyme-linked immunoabsorbent assay*

- Changes that adversely affect the safety or performance and negatively affect the risk/benefit ratio of the device → **Significant**
  - *Change of IFU to refer to reduced sensitivity of the device (based on PMS)*

- Changes of the design that **DO NOT** alter the device operating principle, that **DO NOT** adversely affect the safety or performance and that **DO NOT** negatively affect the risk/benefit ratio of the device: → **Not Significant**
  - *Use of a new PCR cycler*
  - *Change of IFU to refer to better precision or addition of a new interfering substances (based on post-market surveillance)*



Appropriate surveillance – MDCG 2022-15

Manufacturer of "legacy devices" certified under IVDD	Audit under Directive 98/79/EC	IVDR requirements for legacy devices (MDCG 2022-8)	Audit under Regulation EU 2017/746
Did not apply for certification under IVDR	✓	✓	
Already implemented IVDR requirements & certification application in process			✓
Already certified by same NB under IVDR			✓
Already certified by another NB under IVDR	✓ (If NB_{IVDD} is NOT designated under IVDR)	✓	✓ (If NB_{IVDD} designated under IVDR)

IVDR requirements applicable to legacy devices – MDCG 2022-8

IVDR requirement	Applicable?	Specifics
Post-market surveillance & Vigilance	✓	• PMS system & plan (Articles 78 & 79) • Serious incidents, FSCAs, trend reporting (Articles 82-84) • PMS report (Article 80), OR or Class C & D 'equivalent' – PSUR (Article 81) instead [voluntary]
Economic operator obligations	✓	• Manufacturers: Article 10(9), (11) to (14) • Authorised representatives: Article 11(3)(c) to (g) • Importers: Article 13(2), 2nd subparagraph, (4), (6) to (8), (10) • Distributors: Article 14(2), last subparagraph, (4) to (6)
Person responsible for regulatory compliance	✗	• Article 15
Manufacturer obligations for importers & distributors	✗	• Article 16(3) and (4)
Identification & traceability	✗	• Identification with supply chain (Article 22) • UDI system (Article 24) • Summary of safety and performance, SSP (Article 29)

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Other MDCG guidances

MDCG 2021-22 rev.1 EN ●●●	Clarification on "first certification for that type of device" and corresponding procedures to be followed by notified bodies, in context of the **consultation of the expert panel** referred to in Article 48(6) of Regulation (EU) 2017/746	September 2022
MDCG 2022-10 EN ●●●	Q&A on the interface between Regulation (EU) 536/2014 on clinical trials for medicinal products for human use (CTR) and Regulation (EU) 2017/746 on in vitro diagnostic medical devices (IVDR)	May 2022
MDCG 2022-9 EN ●●●	Summary of safety and performance template	May 2022

Borderline and classification manual

Manual on Borderline	Manual on borderline and classification under Regulations (EU) 2017/745 and 2017/746 v1 EN Background note EN on the use of the Manual on borderline and classification for medical devices under the Directives.	September 2022

Recent legislation

COMMISSION IMPLEMENTING REGULATION (EU) 2022/1107

of 4 July 2022

laying down common specifications for certain class D *in vitro* diagnostic medical devices in accordance with Regulation (EU) 2017/746 of the European Parliament and of the Council

COMMISSION IMPLEMENTING REGULATION (EU) 2022/944

of 17 June 2022

laying down rules for the application of Regulation (EU) 2017/746 of the European Parliament and of the Council as regards the tasks of and criteria for European Union reference laboratories in the field of *in vitro* diagnostic medical devices

COMMISSION NOTICE

The 'Blue Guide' on the implementation of EU product rules 2022

(Text with EEA relevance)

(2022/C 247/01)

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LDT - The “US perspective” – What, Who and How?

- FDA definition: *A laboratory developed test (LDT) is a type of **in vitro diagnostic test** that is designed, manufactured and used within a **single laboratory***.
- A **single laboratory** – Development and performance of the test. The use of the LDT cannot be extended to multiple laboratories
- The **laboratory must be certified under the CLIA program** to perform high-complexity testing. (A single laboratory for test development refers to single **CLIA certification**).
- Test must be performed under the **instruction of an authorized physician or healthcare professional**. The physician ordering the test must be **independent from the laboratory** offering the LDT. LDT **cannot be offered direct-to-consumer**.
- **CLIA certification** (performed by the Centers for Medicare and Medicaid Services – CMS) **focuses on procedure and personnel but not on products**, which are the focus for the FDA. Analytical validity is required and reviewed by two-yearly survey. There are no CLIA requirements for clinical validity.

US LDTs under EU ruling

- Article 5(5): *With the exception of the **relevant general safety and performance requirements** set out in Annex I, the requirements of this Regulation shall not apply to devices manufactured and used only within health institutions **established in the Union**.*

- Article 6: Distance sales
  - 1. *A device offered by means of information society services, as defined in **point (b) of Article 1(1) of Directive (EU) 2015/1535**, to a natural or legal person established in the Union **shall comply with this Regulation**.*
  - 2. *Without prejudice to national law regarding the exercise of the medical profession, a device that is not placed on the market but used in the context of a commercial activity, whether in return for payment or free of charge, for the provision of a diagnostic or therapeutic service offered by means of information society services, as defined in **point (b) of Article 1(1) of Directive (EU) 2015/1535**, or by other means of communication, directly or through intermediaries, to a natural or legal person established in the Union **shall comply with this Regulation**.*

US LDTs under EU ruling

Directive (EU) 2015/1535, Article 1(1) point (b)

- *'service' means any Information Society service, that is to say, any service normally provided for remuneration, at a distance, by electronic means and at the individual request of a recipient of services*.

- *For the purposes of this definition:*
  - (i) *'at a distance' means that the service is provided* ***without the parties being simultaneously present***;
  - (ii) *'by electronic means' means that the* ***service is sent initially and received at its destination by means of electronic equipment*** *for the processing (including digital compression) and storage of data, and entirely transmitted, conveyed and received by wire, by radio, by optical means or by other electromagnetic means*;
  - (iii) *'at the individual request of a recipient of services' means that the service is provided through the* ***transmission of data on individual request***.

US LDTs under EU ruling

- Additional requirements applicable to LDT developers
  - Certification of Quality management system
  - Develop Technical Documentation
  - Obtain Clinical Performance data
  - Implement adverse event reporting system
  - Labeling requirements

- Article 5(4): *Devices that are manufactured and used within health institutions,* ***with the exception of devices for performance studies****, shall be considered as having been put into service*.

- Open question: Is it possible to share testing protocol with health institutions?

CONCLUSION: LDT developers will have become IVD manufacturers to provide services to the EU market

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Conclusions

- Over the past year, significant progresses have been made (by the Commission, NBs, manufacturers) in transition to the IVDR
- However several challenges remain as the regulatory infrastructure is still being built
- Although Regulation 2022/112 extended the transition times for the majority of IVDs, it is critical to progress the transfer to IVDR as soon as possible

? QUESTIONS ?

спасибо
GRACIAS 谢谢
THANK YOU
ありがとうございました MERCI
DANKE धन्यवाद
شُكراً OBRIGADO
Gracie
감사합니다

Stay informed and Updated

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