ENTOURAGE
RESOURCE & EXPERTISE IN LIFE SCIENCES

AMDM
2023 Annual IVD Regulatory Meeting

IVDR Updates and lessons learned - Industry Perspective

Sven Hoffmann – Head of IVD and Principal Consultant

SVEN HOFFMANN

Professional Career.

Entourage GmbH (as of 10/2022)

- Head of IVD and Principal Consultant
- Member of the RAPS European Council

TÜV Rheinland (2007 to 2022)

- Global Head Business Segment IVD
- Global Head Technical Competence Center IVD
- Department Head IVD, Germany
- Lead Auditor, Technical Expert and Certification Officer
- Member of the TeamNB IVD working group and MDCG IVD Mirror Group

Abbott Diagnostics, Germany (2004 to 2007)

- Head Product Specialist

Agenda.

	Topic
1	EU regulatory landscape – updates
2	EU regulatory landscape – outlook
3	IVDR Transition – state of play
4	Transition tips – NBOG code impact
5	Transition tips – Clinical Evidence
6	Transition tips - In-house assays

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EU Notified Bodies designated under IVDR (Nando)

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 0483	MDC MEDICAL DEVICE CERTIFICATION GMBH	Germany
NB 0050	National Standards Authority of Ireland (NSAI)	Ireland
NB 2962	QMD Services GmbH	Austria
NB 0197	TÜV Rheinland LGA Products GmbH	Germany
NB 0123	TÜV SÜD Product Service GmbH	Germany

Harmonized standards:

published in the Official Journal , as of May 12th 2022

Most relevant standards harmonized so far:

- EN ISO 13485:2016
- EN ISO 14971:2019

Harm. Standards do NOT represent the state of the art

New MDCG Documents for IVDs since 05/2022 (if not NB specific)

MDCG 2022-12 **07/2022**

- **Guidance** on harmonised administrative practices and alternative technical solutions **until Eudamed is fully functional**

MDCG 2022-19 **12/2022**

- **Performance study application**/notification documents under Regulation (EU) 2017/746

MDCG 2022-20 **12/2022**

- **Substantial modification of performance study** under Regulation (EU) 2017/746

MDCG 2022-16 **10/2022**

- **Guidance on Authorised Representatives** Regulation (EU) 2017/745 and Regulation (EU) 2017/746

MDCG 2022-15 **09/2022**

- Guidance on **appropriate surveillance regarding the transitional provisions under Article 110** of the IVDR with regard to devices covered by certificates according to the IVDD

MDCG 2023-1 **01/2023**

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

New MDCG Documents for IVDs since 05/2022 (if not NB specific)

MDCG 2022-10 05/2022

- 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)

MDCG 2022-9 05/2022

- Summary of safety and performance template

MDCG 2022-8 05/2022

- Regulation (EU) 2017/746 - **application of IVDR requirements to 'legacy devices'** and to devices placed on the market prior to 26 May 2022 in accordance with Directive 98/79/EC

MDCG 2022-6 05/2022

- **Guidance on significant changes** regarding the transitional provision under Article 110(3) of the IVDR

MDCG 2020-16 Rev.2 02/2023

- **Guidance on Classification Rules** for in vitro Diagnostic Medical Devices under Regulation (EU) 2017/746

MDCG 2021-22 Rev.1 09/2022

- **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

TeamNB Position Papers:

- “Conformity Assessment of multiplex assays” 07/2022
- “IVDR Significant Changes” V1 12/2022
- “Modifications Sampling Plan” V1 12/2022
- “Best Practice Guidance Submission of TechDoc under Annex II and III IVDR” 02/2023

MedTech Europe:

- eBook “Clinical Evidence Requirements under IVDR ” Edition 3 02/2023

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MDCG Documents planned

IVD common specifications (CS).

- CS development for hepatitis E — **Adoption end 2023**
- CS development for Plasmodium+Toxoplasma — **Adoption end 2023**
- CS development for Arboviruses (Zika, WNV, Chikungunya, dengue) — **Mature Draft end 2023**

Performance Studies.

- Q&A on performance studies — **Q3 2023**
- Template and guidance on serious adverse event reporting in performance studies — **Q3 2023**
- Minor revision SSP template MDCG 2022-9* — **Q2 2023**
  *only specific IVD-related aspects

Guidance on Classification MDCG 2020-16.

- Minor revision of 2022-16 — **End 2023**

IVD Qualification.

- Guidance on IVD borderline issues (transposition of MEDDEV 2. 14/1) — **Q2 2023**

Interplay CTR/IVDR.

- Minor revision of MDCG 2022-10 — **Q2/Q3 2023**

MDCG Documents planned (cont.)

Health crisis preparedness.

- Analyze the IVDR in context of hypothetical scenarios of an urgent response to a health crisis — **Q1/Q2 2023**

Notified body codes – joint with NBO

- Minor revision of MDCG 2021-14 Explanatory note on IVDR codes — **2023**

Distance sales

- Poss. Work on Q&A/guidance on distance sales — **Q3 2023**

Interaction with IMDRF on IVD-specific matters

- Contribution to group on IVD clinical evidence — **Suspended**

EU Reference Laboratories (Class D)

- Designation foreseen Q3 2023
- Labs will **need time to be fully operational post-designation**

Other MDCG 2023 work items

Post-market surveillance and vigilance

- Guidance on post-market surveillance
- Revision on trend report form
- Q&A document on vigilance terms and concepts
- PSUR (transposition to IVDR)

Market Surveillance.

- Minor revision of MDCG 2019-7 (Person Responsible for Regulatory Compliance)
- Minor revision of MDCG 2021-16 (UDI obligations)
- Minor revision of MDCG 2021-27 (importers/distributors)

Borderline & Classification.

- Procedures for notification of decision on dispute

Notified bodies.

- Revision of MDCG 2019-13 guidance on sampling of devices for the assessment of the technical documentation
- Guidance on substantial changes

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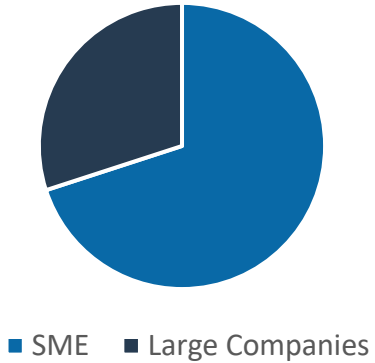
IVD survey among European companies (30.09. - 27.10.2023).

Who participated?

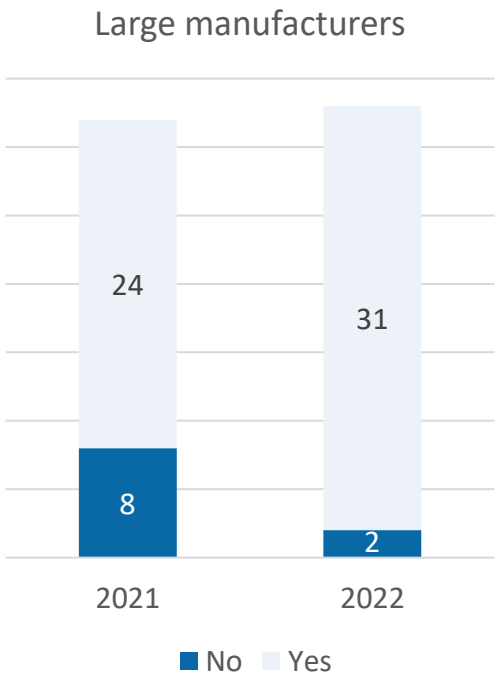
Total	110
SME	77
Large companies	33

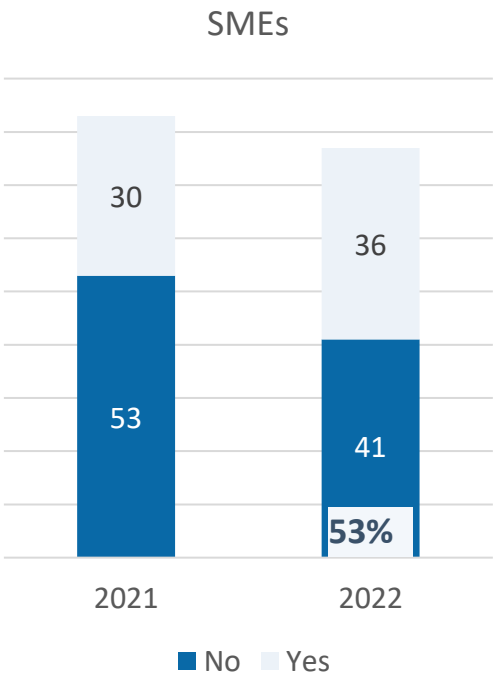
corresponds to the ratio in the EU

Participants represent approx. 75% market share



Agreement with a Notified Bodylarge companies vs. SMEs.



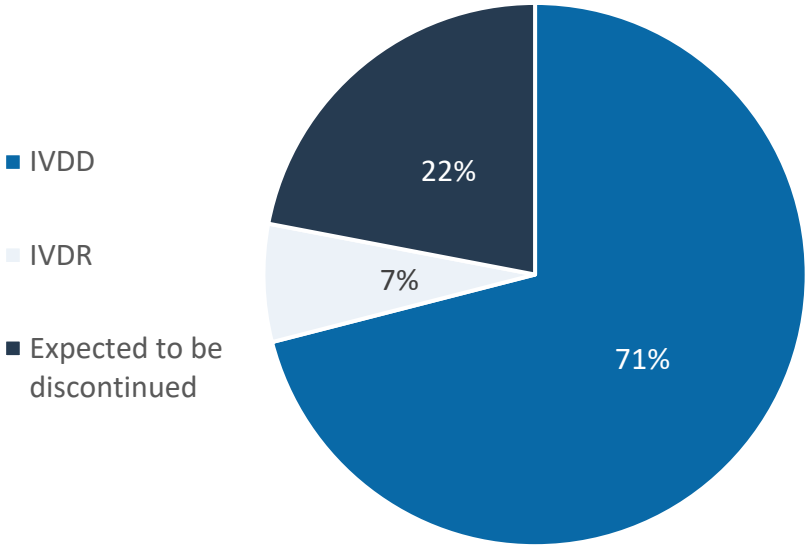


- 53% SMEs do **not** have an agreement with a NB compared with 6% of large companies.
- Having an agreement is a significant first step in transitioning to the IVDR
- Agreements may or may not cover the full products portfolio

Survey Results 2021 vs. 2022.

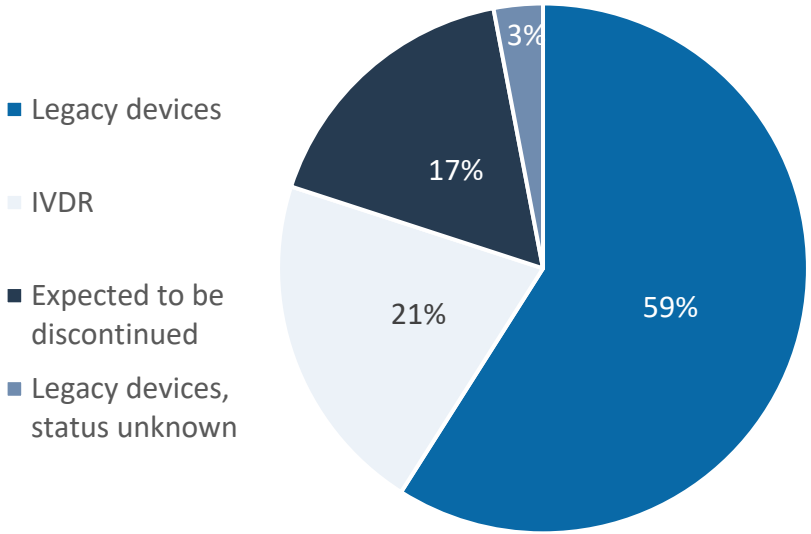
IVD Market 2021

(90% Market Revenue Coverage)

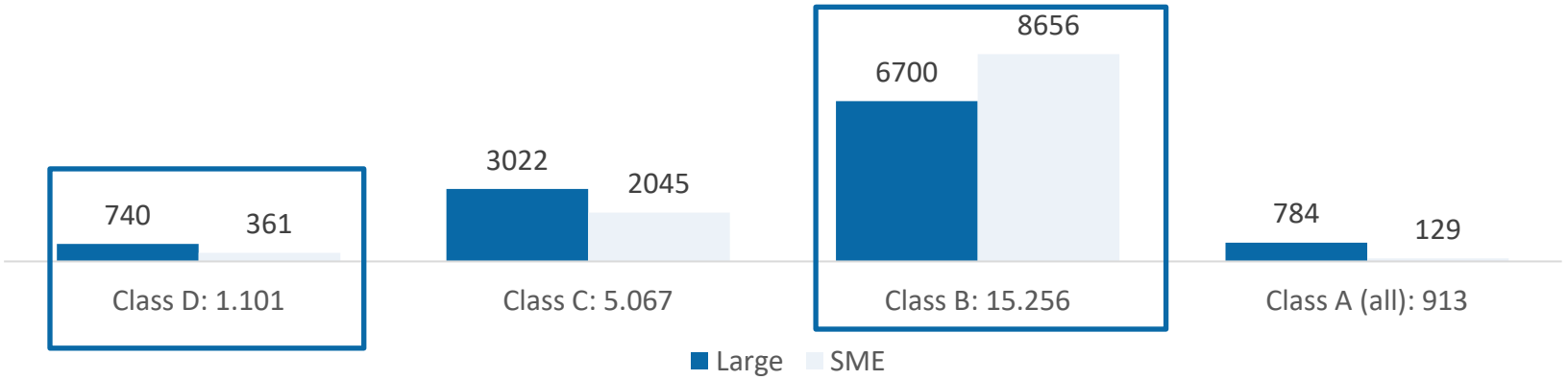


IVD Market 2022

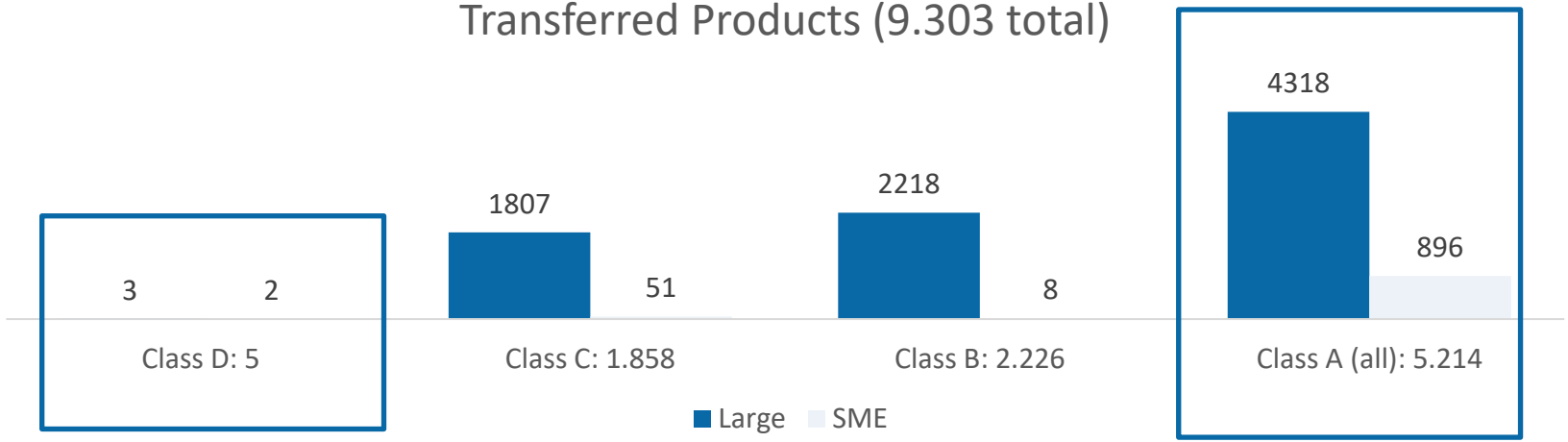
(75% Market Revenue Coverage)



Legacy Devices on the Market (22.437 total)



Transferred Products (9.303 total)

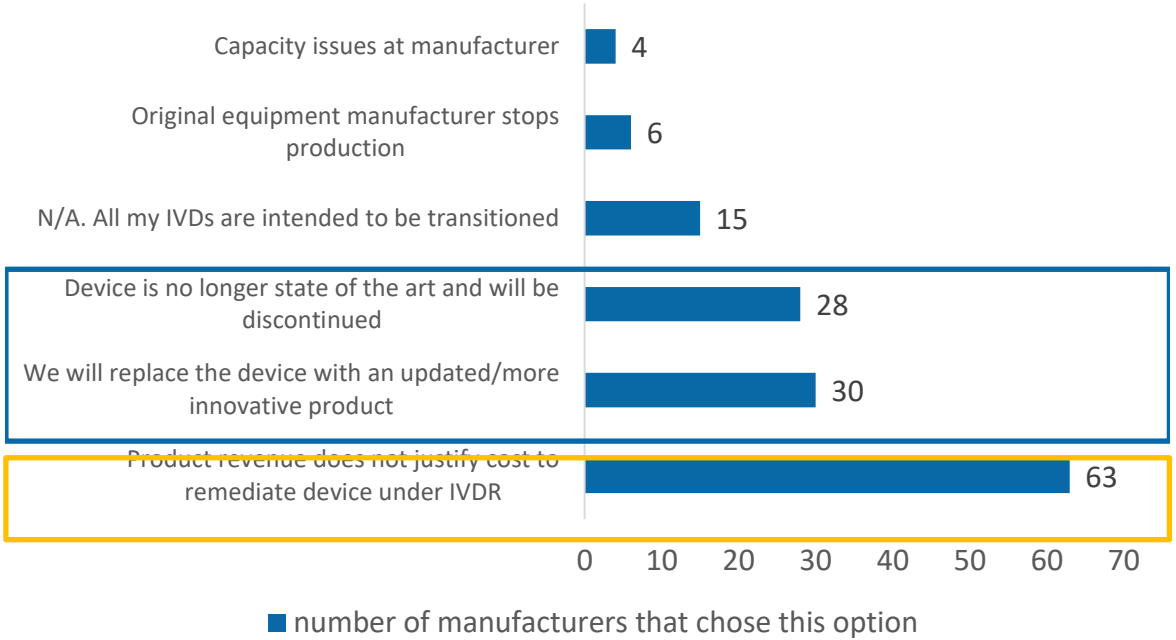


Process of NB Certification and its lead times.

Typical duration in months from review start until the issuance of the recommendation for certification?													
months	1	2	3	5	6	7	8	9	11	12	14	16	18
responses	**28%**					**18%**			**55%**				

	Calculation of #months to issue the EU QMS Certificate following recommendation for certification*					
Number of months	0	1	2	3	6	8
% manufacturers (total 10 responses)	10%	10%	10%	20%	40%	10%

Reasons for discontinuing a device*



*Respondents could choose more than one option

Revision of IVDR / MDR ?

Health Commissioner **Stella Kyriakides** on 9 December 2022 to Health Ministers (EPSCO)

“I also believe that this must be accompanied by additional measures to address the structural problems of the regulation we are now seeing.”

Study on ‚Governance and Innovation‘

EU4Health: 2022 Work Programme

Description:

- Examine the current regulatory governance for medical devices …..
- Assess how the current regulatory framework supports innovation, identify challenges and trigger discussion on possible solutions…
- Gathering feedback from MS authorities and other relevant stakeholders to assess the current regulatory governance…

Timeline: Launch in Q1/Q2 2023 – 18 months

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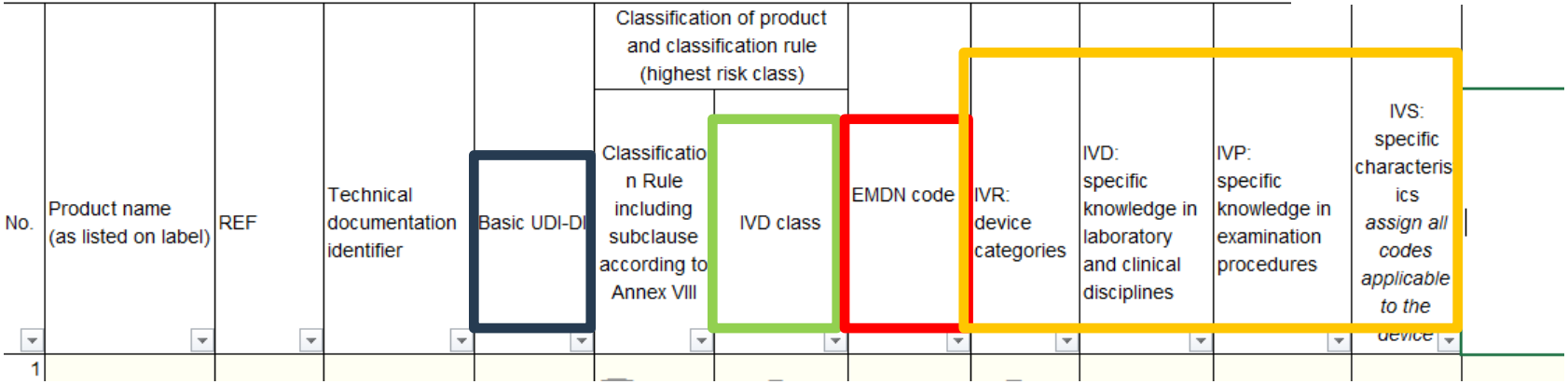
The application according Annex IX Chapter I and II

- **Defines the "device„** as per MDCG 2019-13
- Further guidance documents existing, e.g. MDCG 2018-1rev4 and MDCG 2019-1

- Defined as per rules stipulated in Annex VIII IVDR
- Guidance given by MDCG 2020-16

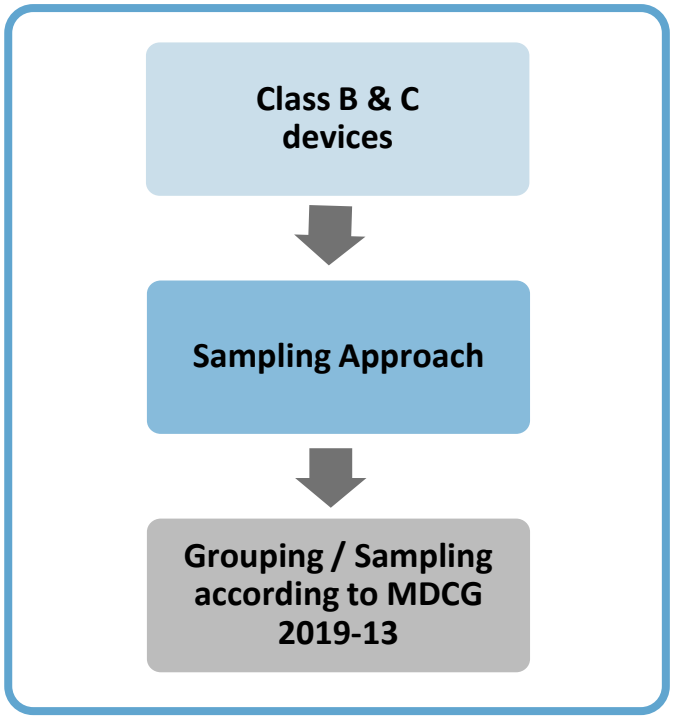
- **Basic EUDAMED nomenclature** (see MDCG 2018-2)
- Also **utilized for the grouping / sampling of products** according to MDCG 2019-13

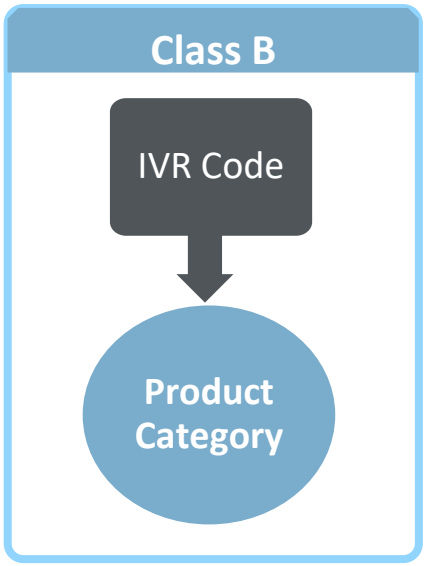
- **Basic competency (designation) codes for NB** (see NBOG F 2017-4)
- Also **utilized for the grouping / sampling of products** according to MDCG 2019-13
- „Explanatory note" MDCG 2021-14

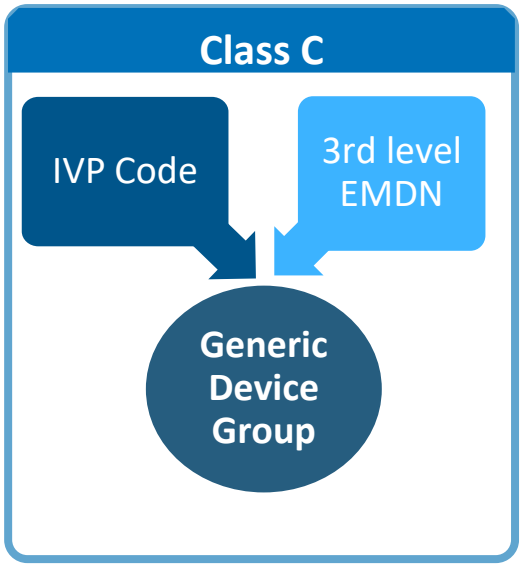


Application review, grouping and sampling

Grouping and Sampling – Basics



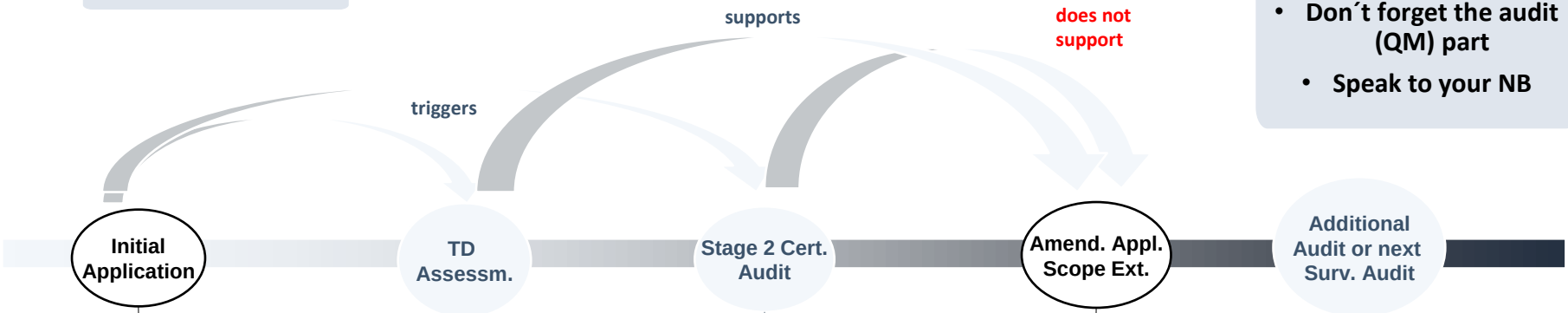




Transition pitfall – NBOG code impact

Case Study

- **Take all relevant codes into consideration**
- **Don´t forget the audit (QM) part**
- **Speak to your NB**



Initial product scope:
1 Generic Device Group (class C):
W0106 + IVP3011
IVR0403

(At least) **1 TD assessment covering the single Generic Device Group:**
W0106 + IVP3011

Audit team covering relevant IVTcode(s): and IVR code:
IVR040(3)
→ **Depending on NB**

Scope Extension: same generic device group (class C):
W0106 + IVP3011
IVR0201

Audit team covering new IVR code:
IVR0201

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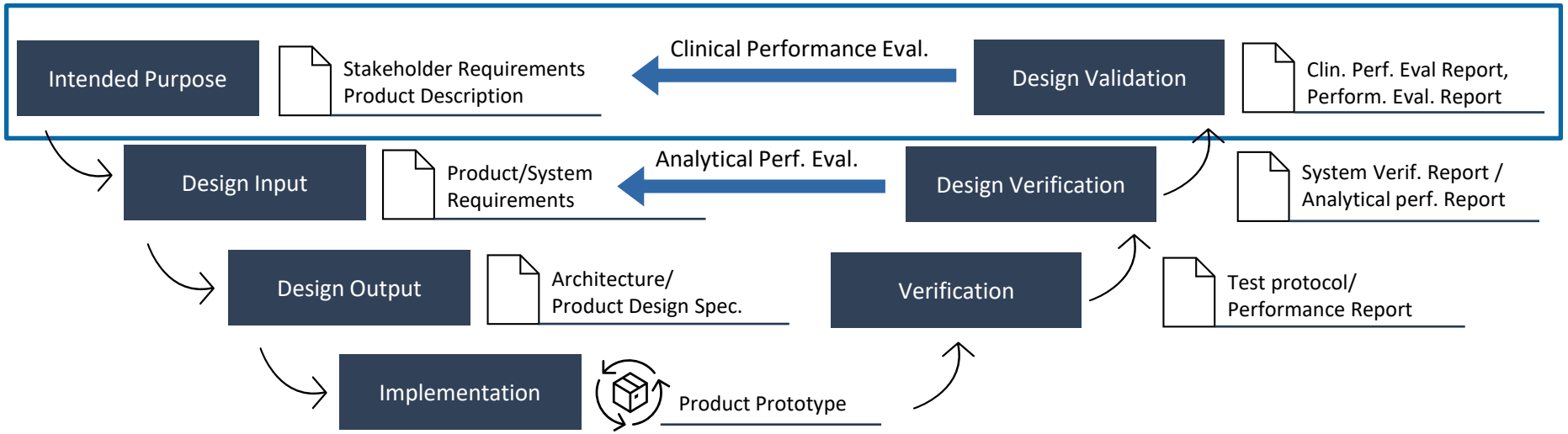
Clinical Evidence

Characteristics to be established:

- diagnostic sensitivity
- diagnostic specificity
- positive predictive value
- negative predictive value
- likelihood ratio
- expected values in normal and affected populations

Design Control – V-Model



Population Equivalence EU vs non-EU

IVDR allows use of non-EU data

Equivalency to EU population to be shown

Top	Criterion	
1	race/ancestry, age, genetic origin	Intrinsic
2	epidemiology (prevalence)	
3	Target population (e.g. blood donors)	
4	Interferences (e.g. drugs, diet)	Extrinsic
5	clinical practice (e.g. cut-off definition, pre-analytical aspects)	

For legacy devices:
PMS data

For gaps:
Bridging study

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In-house (IVD) device: a device that is manufactured and used only **within a health institution** established in the Union and that meets all conditions set in **Article 5(5) of the IVDR.**

Source: MDCG 2023-1

„for a product to be categorized as an **RUO product** it must have **no intended medical purpose**
or objective.“

Source: MEDDEV 2.14/2 rev.1

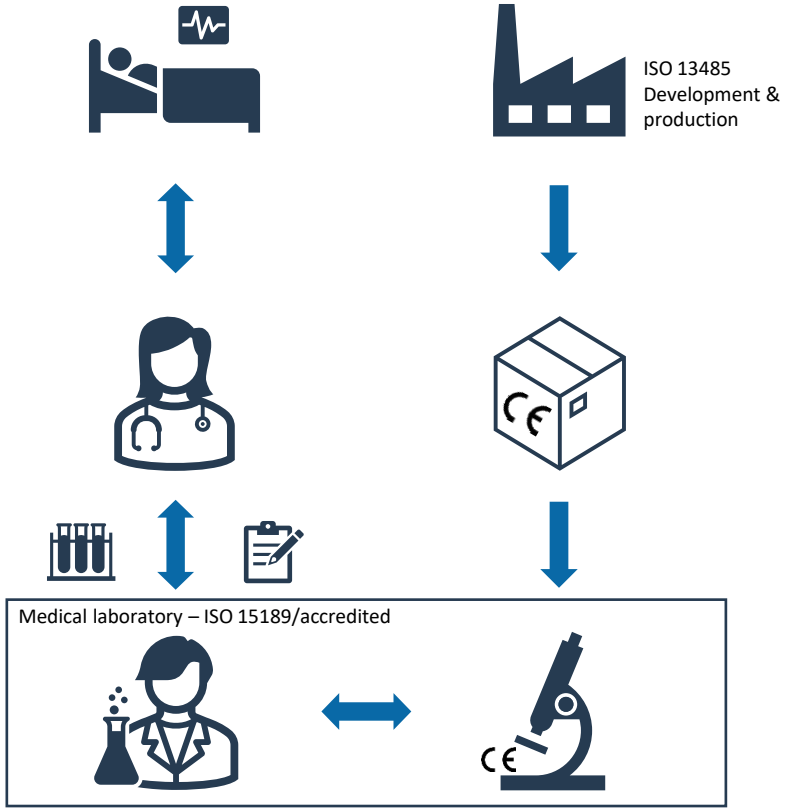
A **‘Laboratory developed Test (LDT)’** is an IVD that is intended for clinical use and designed, manufactured and used within single laboratory.

Source: FDA Draft Guidance „Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs)“

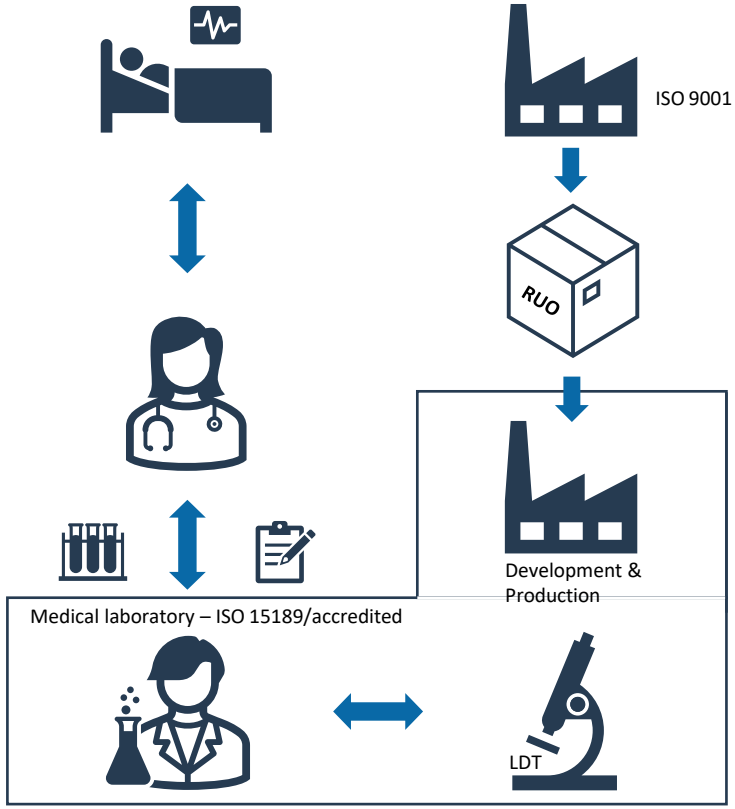
„IVD product that is in the **laboratory research phase** of development and is being shipped or delivered for an investigation […]”

Source: FDA Guidance „Distribution of In Vitro Diagnostic Products Labeled for Research Use Only or Investigational Use Only“

Basic scenarios – medical laboratories



CE-IVD device from the manufacturer in regular use



Use of an IVD procedure developed in-house

Requirements of Article 5(5) IVDR.

Art. 5(5): Lab Developed Tests (LDT) must comply with Annex I AND:

Amending Regulation 25. January 2022 (Art. 113)

(a) No transfer allowed!

(b) Proper QMS required: ISO 13485

(c) laboratory must comply with ISO 15189 or national accreditation solution

(d) Comparison to CE-IVD: my LDT:

(e) Provide information and rationale to authorities, Regarding manufacturing, modification and use

(f) Publish name and address and identification of the products and declare conformity to Annex I

(g) extensive documentation on manufacturing, design, performance and compliance to Annex I for Class D* products

(h) products are manufactured in accordance with the documents referred to in (g)

(i) Collect experience gained from clinical use and apply corrective actions

26. May 2022 | **26. May 2024** | **26. May 2028**

* Member States may apply this provision also to class A, B or C devices in accordance with the rules set out in Annex VIII;

Thank you for listening.

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