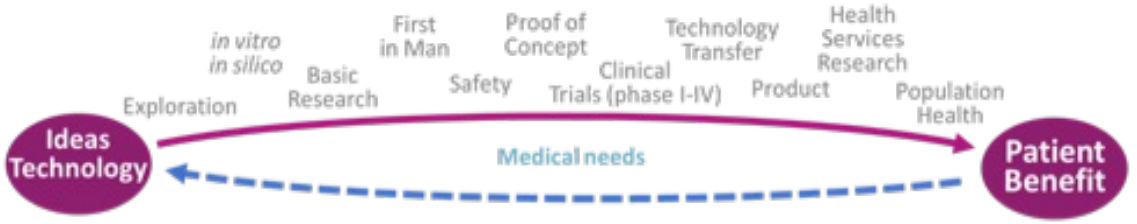
Biomedical Alliance in Europe

Elizabeth Macintyre, IVDR Task Force chair and President-elect

Diagnostic Hematologist, Necker Hospital and Université Paris Cité, FR

European Hematology Association President (2021-23)



In-Vitro Diagnostic Regulations : Present status

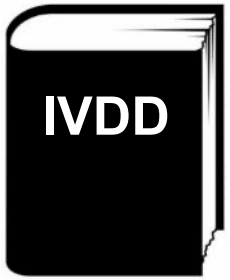
ESCCA, Belfast, UK, 23/09/2022

Committees & Task Forces

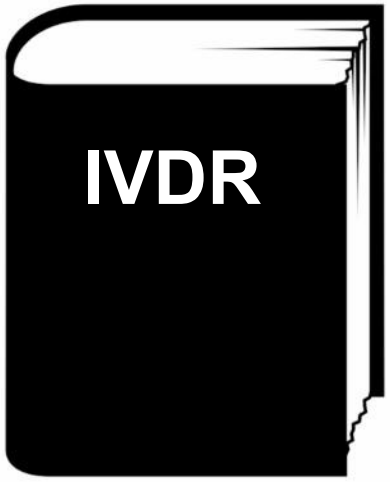
- CME Experts Permanent Committee
- Academic Clinical Trials Task Force
- Regulatory Affairs Committee
  - Medical Devices Task Force
  - **In Vitro Diagnostics Task Force**
  - Health data Task Force (European Health Data Space)
- Policy Officers Committee
- BioMedScape Working Group
- Code of Conduct & Declaration of Interest Working Group

IVDR: What impact for health care professionals & laboratories?

- IVD**D** regulates commercial IVDs (CE-IVDs)
- IVD**R** regulates CE-IVDs and IH-IVD (LDT)
- Intention to improve clinical value of IVD use, including with post-market surveillance
  - Managed similarly to Medical Device regulation (MDR) and Digital Health (EHDS)



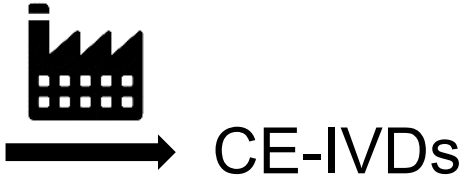
1998 - 2022

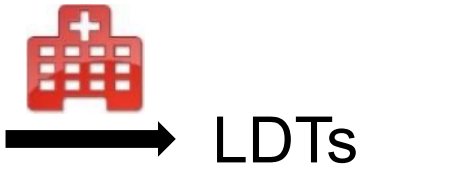


Entry into force: 2017

5 years for Implementation

Initial Date of application: May 26th, 2022





Laboratory-developed tests / In-house devices

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EFLM
EUROPEAN FEDERATION OF CLINICAL CHEMISTRY AND LABORATORY MEDICINE

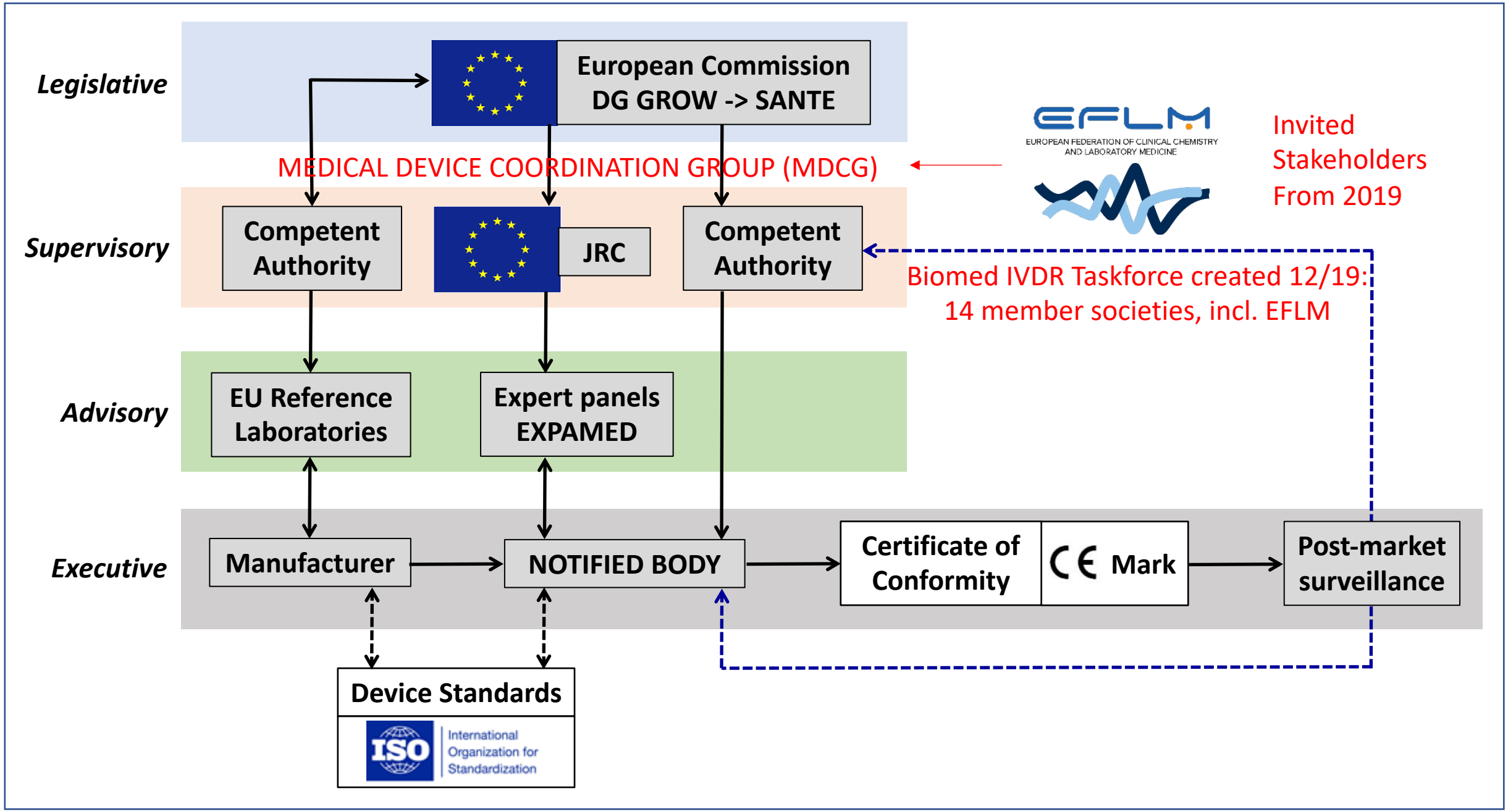
ESHG

EHA EUROPEAN HEMATOLOGY ASSOCIATION

Slide from Van Dongen, 9th ESLHO Symposium, Zoom webinar, 5 November 2020

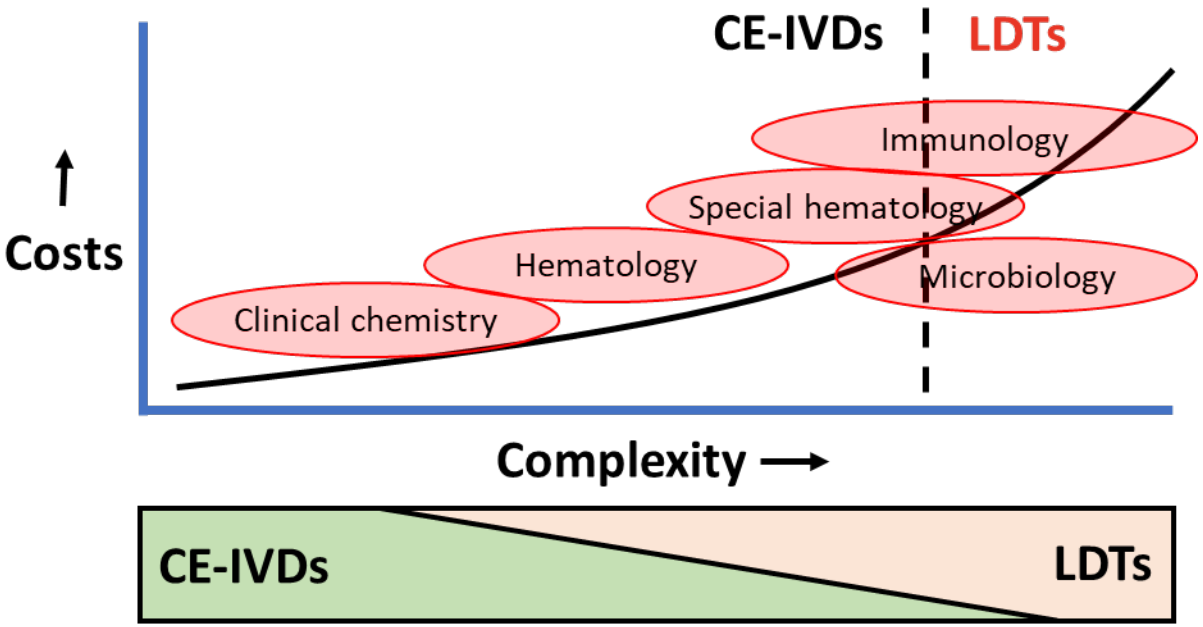
2 Complementary presentations on IVDR

- E Macintyre
  - How European health care professionals and Medical Specialists (Societies) and regulators can learn progressively to understand each other
  - How this might lead to more pragmatic EU legislation
  - How to manage such communication between our varied health systems
  - How to plan for and contribute to construction of the European Health Space
- I. Dombrink
  - How to understand and apply IVDR in your laboratory/discipline/country



Adapted from: Cobbaert C et al. Clin Chem Lab Med. 2022;60(1):33-43.

High complexity assays are frequently LDTs/In-House



Cellular, Protein and Molecular

RISKS of IVDR 2020-21

Loss of CE-IVDs from lack of preparedness on 26/5/22

Fragility of the translational diagnostic value chain

Difficulty in maintainance of innovative diagnostics

Risk of monopolies

- Assays with higher complexity are more difficult to commercialize
- To provide optimal healthcare, diagnostic laboratories depend on development of LDT/IH-IVDs for many (complex) applications
- This dependence differs significantly per diagnostic field

Slide from Van Dongen, 9th ESLHO Symposium, Zoom webinar, 5 November 2020

Highlights in 2021

April 2021: EC STOA Workshop on the IVDR and its consequences for the EU health sector: system not in place (eg EUDAMED), loss of CE-marked kits, threats to in-house / laboratory developed tests (IHD/LDTs)…..

August 2021: Launch of the IVDR questionnaire (July-Sept. 2021).

September 2021: High-level meeting with the European Commission (DG Santé) to discuss IVDR postponement

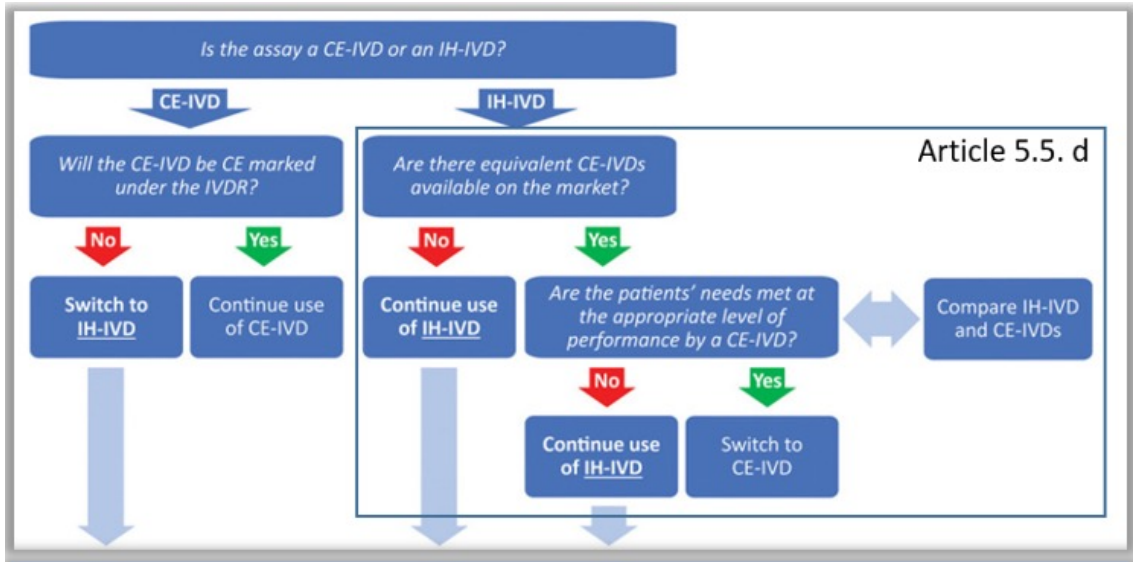
October 2021: Welcoming the amending act and extended transitional provisions. As a result of the BioMed Alliance advocacy efforts, extended provisions are provided for in-house devices as well (Article 5.5).

November 2021: BioMed Alliance input on the draft guidance on in-house tests. "*IVDR and NCA dictate what we must do but diagnostic specialists must define and accompany how we do it*"

November 2021: Promoting the IVDR questionnaire findings.

December 2021: BioMed Alliance welcomes the adoption of the European Commission's proposal amending the IVDR transition periods

IVDR and IH-IVD – Art. 5.5d



May 2022

- Fulfillment Annex I (general safety and performance requirements)
- Not manufactured on an industrial scale
- Manufactured and used only within health institutions established in the Union

May 2024

- Fulfillment Article 5.5 b,c; e-I

May 2028

- Fulfillment Article 5.5. d

Art. 5.5d prevents use of IH-IVD if an equivalent CE-IVD is available on the market.

Guidelines on IH-IVD use are being prepared by the MDCG (Danish CA):

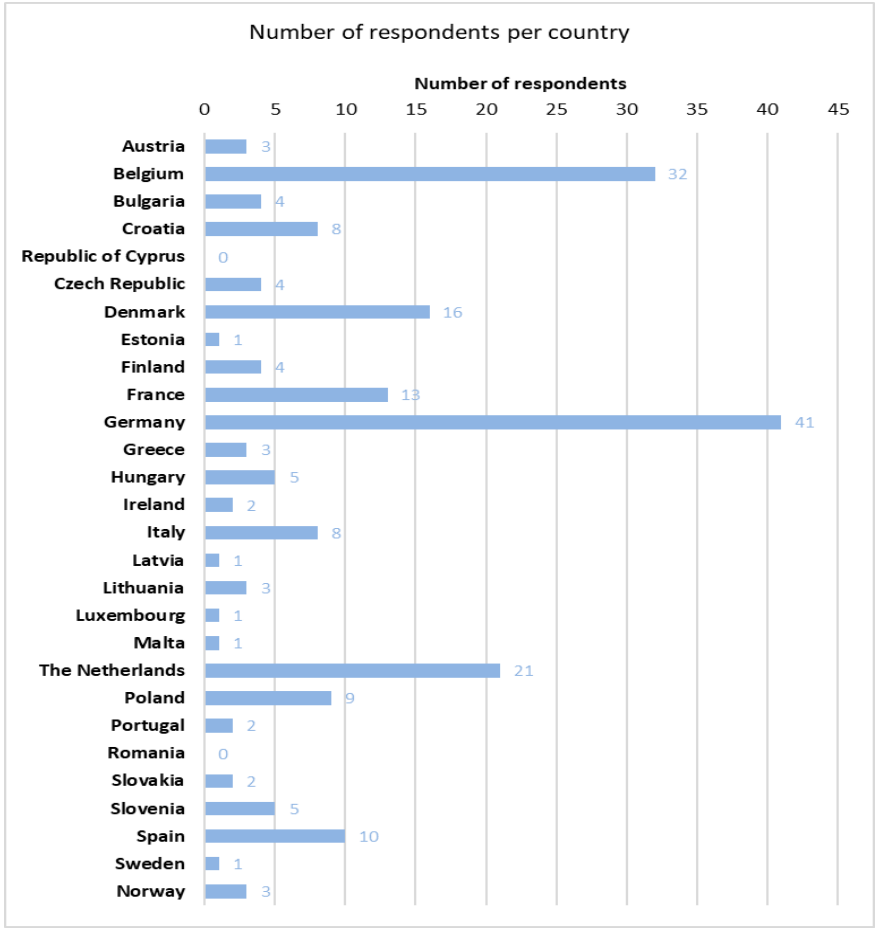
« What we have to do rather than how to do it »

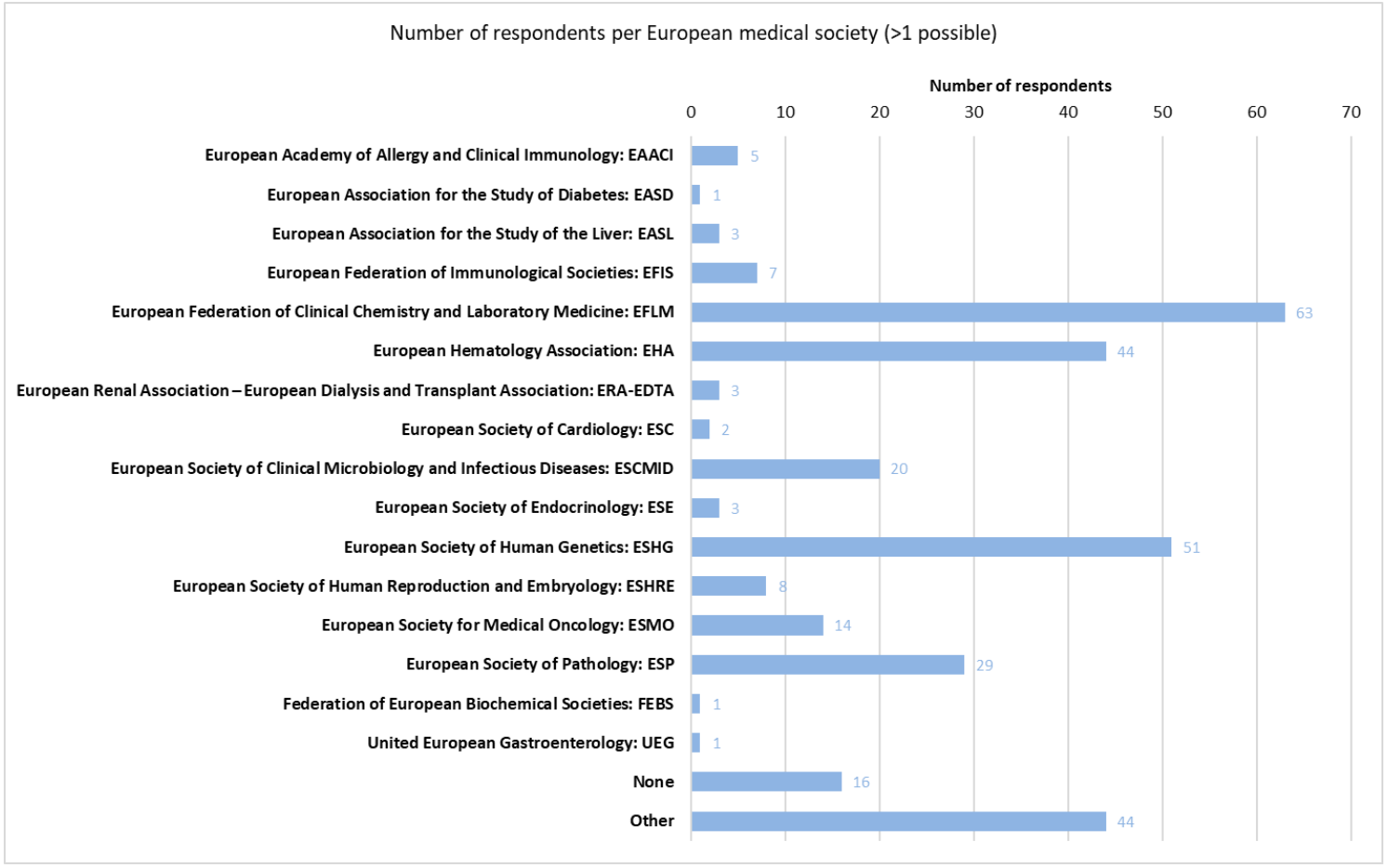
IVDR preparedness and IH-IVD activity in the EU July-Oct 2021: EHA/EFLM/Biomed Alliance survey

- Questionnaire completed by 203 laboratories, from 25/27 EU member states

Dombrink, I et al. HemaSphere vol. 6,6 e724. 20 May. 2022, doi:10.1097/HS9.0000000000000724

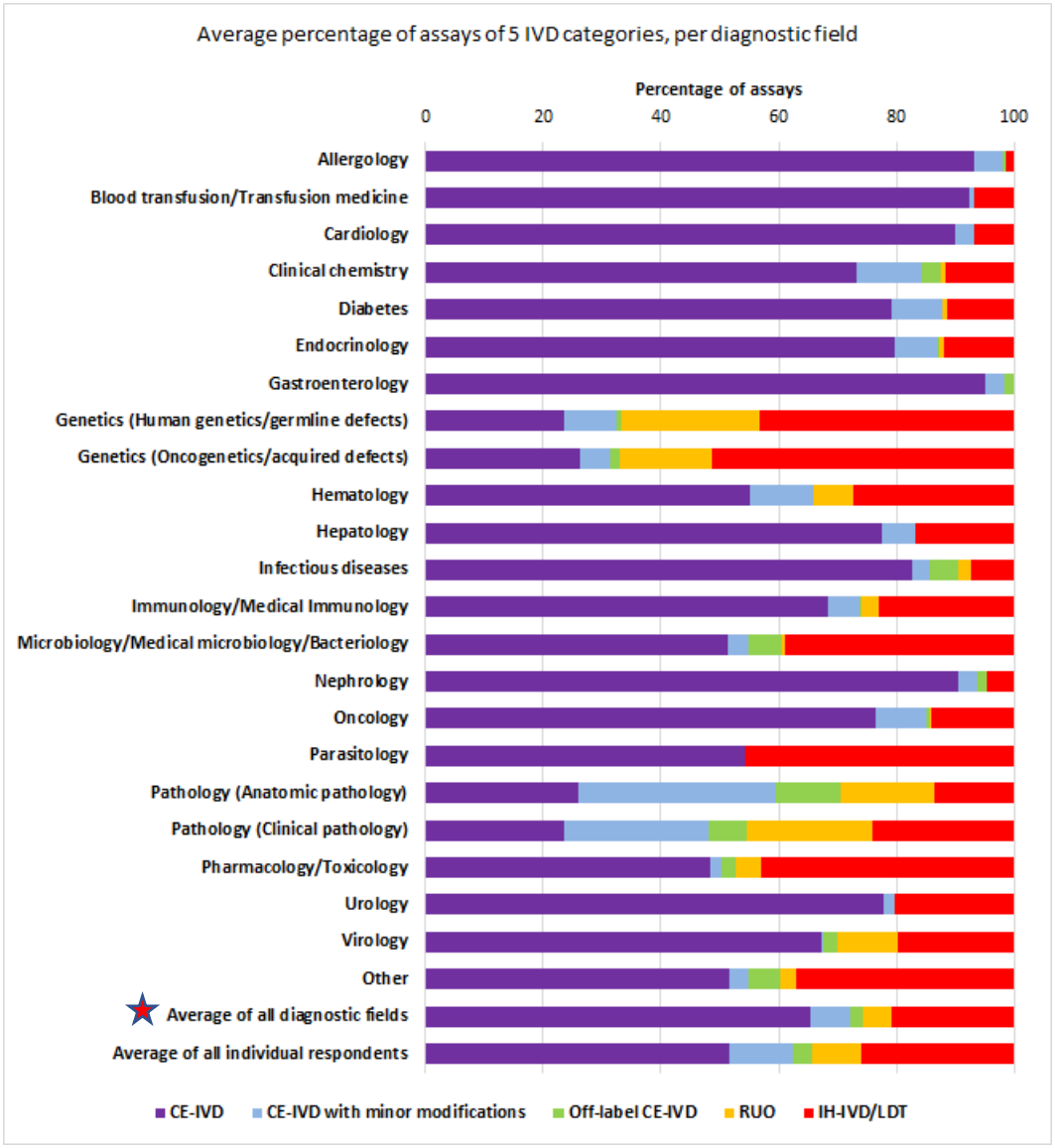
- No attempt was made to assure exhaustivity or balanced representativity of responses or diagnostic specialties, for whom labels, and clustering tends to vary between countries





IH-IVDs, RUO and modified/off-label CE-IVDs currently represent half of the tests offered by 203, predominantly academic, EU laboratories in 25/27 member states

On average, the respondents use (range):
52% (23-95%) CE-IVDs
11% (0-34%) CE-IVDs with minor modifications
3% (0-11%) off-label CE-IVDs
8% (0-24%) RUOs (Research use only)
26% (0-51%) IH-IVDs.

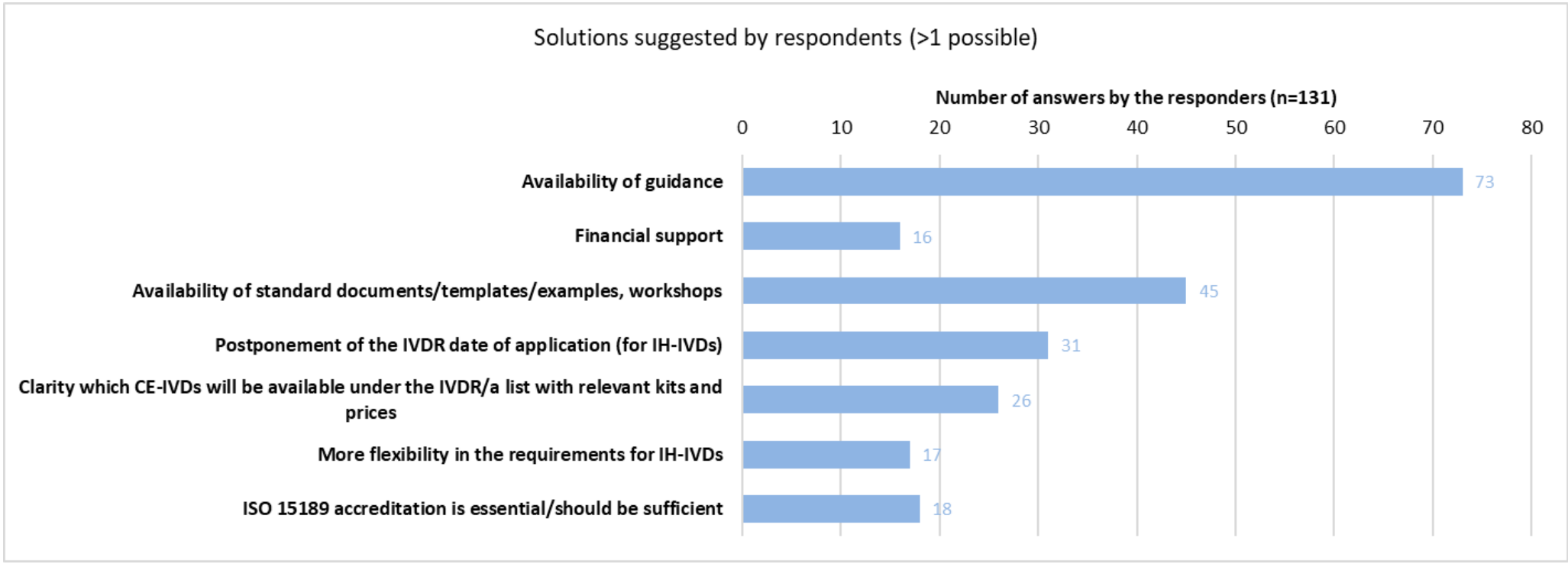


HemaSphere
EHA EUROPEAN HEMATOLOGY ASSOCIATION
HemaPolicy
Open Access

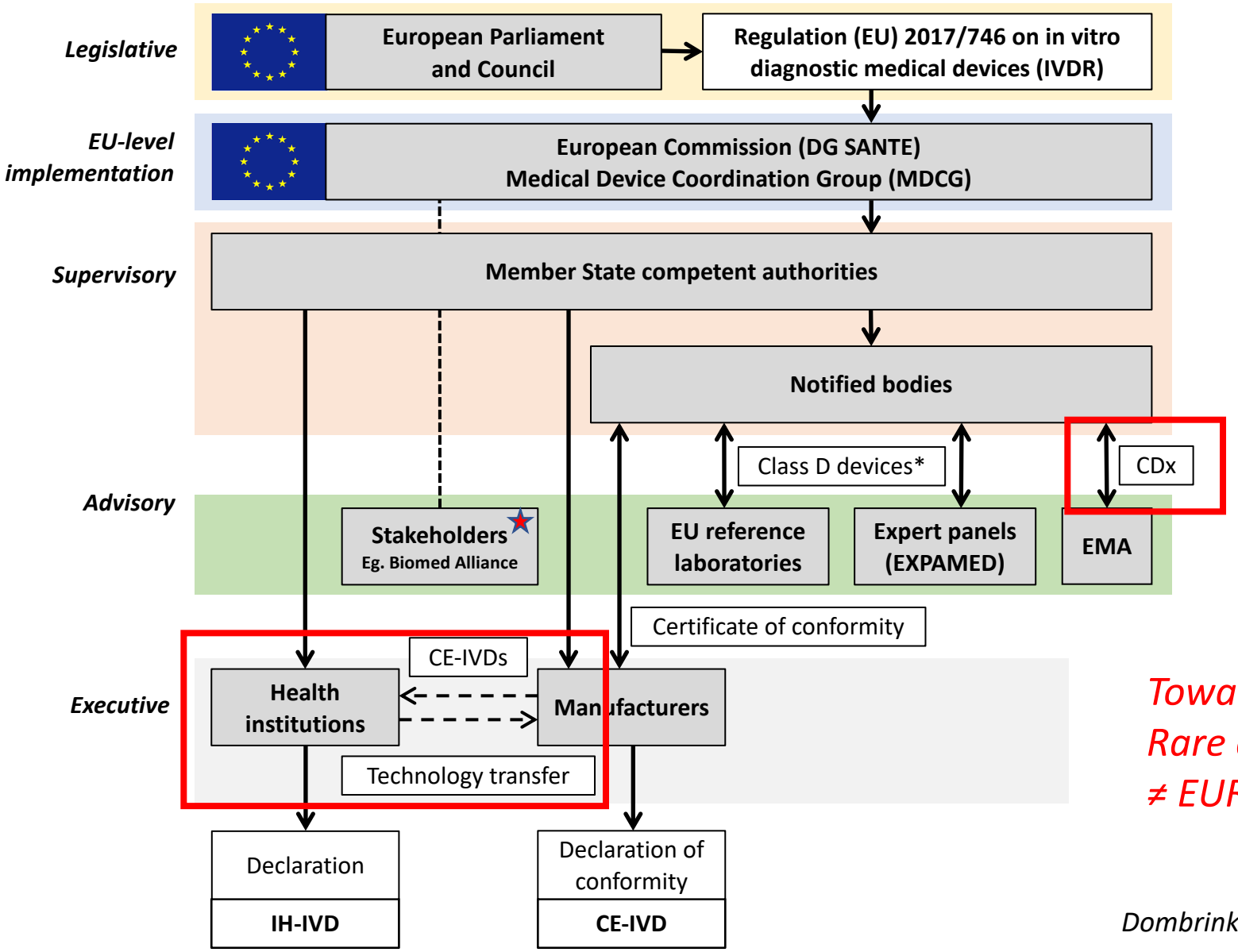
Critical Implications of IVDR for Innovation in Diagnostics: Input From the BioMed Alliance Diagnostics Task Force

Isabel Dombrink[1–3], Bart R. Lubbers[1,4,5], Loredana Simulescu[1], Robin Doeswijk[1,5], Olga Tkachenko[6], Elisabeth Dequeker[1,7,8], Alan G. Fraser[1,9], Jacques J. M. van Dongen[1,4,5,10,11], Christa Cobbaert[1,12,13], Monika Brüggemann[1–3,5], Elizabeth Macintyre[1,5,14]

Which solutions are needed to support diagnostic laboratories with timely and appropriate preparations for the IVDR?



Inclusion of IH-IVDs into the EU IVDR Regulatory Framework



Towards ERN-like/linked Rare diagnostic networks ?
≠ EURL

Dombrink I. et al. HemaSphere 2022

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The GOALS of IVDR
1. Enhance the quality of diagnostics
2. Harmonise EU-wide access

MDCG IVD WG session 5/7/2022

Messages from EFLM and Biomed Alliance from recent (virtual) dissemination activities :

EFLM IVDR Strategic Conference on 26/5/2022

European Hematology Association (EHA) on 17/6/2022: >90 participants (50% EU), 29 countries

European Society for Human Genetics (ESHG) on 22/6/2022: 350 participants, 27 countries (free)

Spokespersons : Isabel Dombrink, Elizabeth Macintyre, Florent van Stapel

Conclusion 1: Diversity in Awareness

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- Information about IVDR needs to reach EVERY laboratory aiming to supply digital-medecine era diagnostics
- Guidance is needed in an understandable, doable manner
  - This support will differ for CE-IVD (manufacturers) and IH-IVD
- IVDR discussions are mainly with ISO 15189 compliant labs, with those furthest from compliance absent/unaware
  - Training and support at national/regional/local level is needed
  - EU-level training of trainers is desirable, in addition to manufacturing sector support

Conclusion 2: Concerns from the aware

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- Need for further clarification on
  - Overlap/difference between IVDR (product) and ISO 15189 (process)
  - Legal responsibilities regarding modified CE-IVD use
- Will the benefits of IVDR outweigh the increased costs?
- Who will fill the gap of lost CE-IVD tests?
- What will the effect of IVDR be on international competitivity?
- What interaction should there be between Notified Bodies and diagnostic specialists?
- How will post-market surveillance be realised?
- IVDR must not stifle or discourage innovation
  - Pragmatism needs to balance zeal, while maintaining/reinforcing diagnostic medical expertise, including for innovation

Next steps and Challenges:

- Encourage Guidance workshops at national and European levels
  - Different solutions are required for CE-IVD (Industry) and IH-IVD (academic networks)
- Help national CA and multidisciplinary academic diagnostic specialists to communicate
  - eg AWMF in DE https://www.awmf.org, but federal system
  - Create such structures if necessary (LBMR in FR?)
  - Clarify overlap/differences with IVDR and ISO 15189
  - Defend innovative diagnostics at member state level
- Communicate with national/European stakeholders
  - Biotech federations (MedTech Europe/SIDIV),
  - EMA and EFPIA/LEEM
    - Understand the place of “Companion Diagnostics” in personalized/precision medical care
  - Notified Bodies and their Coordinating groups
  - Involve patient associations in defending innovative diagnostics
- Work with the EC and DG-Santé/EMA to integrate national and European initiatives
- Minimize the risk of regulatory exhaustion and the explosion of diagnostic costs
- Train an appropriate cohort of Medical Regulatory Scientists, nb. ≠ Regulatory Officers

Thankyou to

Isabel Dombrink and Bart Lubbers

Loredana Simulescu and Robin Doeswijk

Alan Fraser

Elisabeth Dequeker, Jacques J.M. van Dongen, Monika Brüggemann, Florent Vanstapel, Christa Cobbaert

- European Hematology Association
- European Society of Cardiology
- European Society of Human Reproduction and Embryology
- European Academy of Allergy and Clinical Immunology
- European Society of Pathology
- European Federation of Clinical Chemistry and Laboratory Medicine
- European Society of Clinical Microbiology and Infectious Diseases
- European Federation of Immunological Societies
- European Renal Association – European Dialysis and Transplant Association
- Federation of European Biochemical Societies
- European Association for the Study of Diabetes
- United European Gastroenterology
- European Association for the Study of the Liver
- European Society of Human Genetics

EuroFlow

EuroMRD

NGS EuroClonality