IVDR: Implications for diagnostic laboratories

Jacques J.M. van Dongen & Bart Lubbers

Department of Immunology,
Leiden University Medical Center, Leiden, NL

on behalf of

Leiden University Medical Center and ESLHO
european scientific foundation of laboratory hemato oncology

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Overview

- Use of CE-IVDs vs in-house devices (IH-IVDs)
- IVDR requirements for IH-IVDs
- Concerns regarding CE-IVDs and IH-IVDs

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Transition from Directive to Regulation

- IVD**D** regulates commercial IVDs (CE-IVDs)
- IVD**R** regulates CE-IVDs and in-house devices (IH-IVDs)

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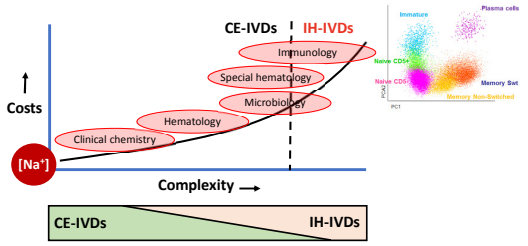
Diagnostic labs depend on CE-IVDs and IH-IVDs



- To provide optimal diagnostic healthcare, labs depend on development of IH-IVDs for many (complex) applications
- This dependence significantly differs per diagnostic field

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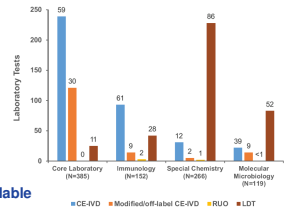
IH-IVDs form a crucial part of the assay portfolio of many (specialized) diagnostic laboratories (1)

Pieter. Vermeersch*, Tobias Van Aelst and Elisabeth M.C. Dequeker

The new IVD Regulation 2017/746: a case study at a large university hospital laboratory in Belgium demonstrates the need for clarification on the degrees of freedom laboratories have to use lab-developed tests to improve patient care



- 41,8% of **tests**: CE-IVD
- 71,9% of LDTs: **no CE-IVD available**
  - Rare diseases
  - High complexity

Vermeersch et al., Clin Chem Lab Med, 2020; doi: 10.1515/cclm-2020-0804

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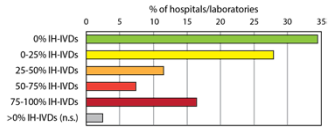
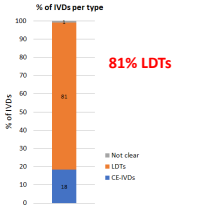
IH-IVDs form a crucial part of the assay portfolio of many (specialized) diagnostic laboratories (2)





- 2 in 3 labs use IH-IVDs
- 1 in 4 labs use >50% IH-IVDs

Based on data from Dutch National Institute for Public Health and the Environment (RIVM), 2015

European Hematology Association (EHA) questionnaire among selected (special) hematology labs, 2019

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IVDR Art. 5.5: Conditions & Requirements for IH-IVDs
(Health Institution exemption)

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, provided that all of the following conditions are met:

a. **No transfer** of devices to other legal entities
b. Manufacture and use under an appropriate **quality management system**
c. Compliance with **EN ISO 15189** and applicable national provisions
d. **Justification** that the patient group's specific needs cannot be met at the **appropriate level of performance** by an **equivalent** device available on the market
e. Upon request, providing **information to the competent authority**
f. **Publicly available declaration** of conformity:
- the name and address of the manufacturing health institution,
- the details necessary to identify the devices,
- a declaration that the devices meet the general safety and performance requirements set out in Annex I to this Regulation and, where applicable, information on which requirements are not fully met with a reasoned justification therefor;

g. Extra strict requirements for **class D devices**
h. Devices are manufactured in accordance with (g)
i. **Evaluation of experience** gained from clinical use and taking necessary corrective actions

This paragraph shall **not** apply to devices that are manufactured on an **industrial scale**.

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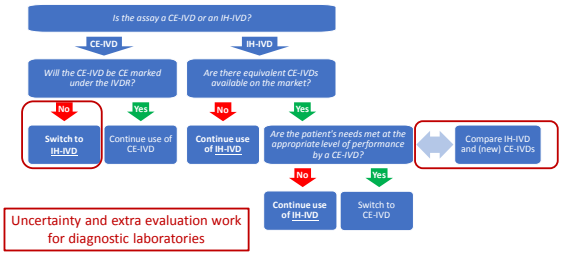
1. Which assays will I run after May 2022?

- Continuity of diagnostics is essential!
- An assay inventory helps to plan future assay portfolio



Uncertainty and extra evaluation work for diagnostic laboratories

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2. Will all my CE-IVDs continue to be available?

Depends on EU implementation, notified bodies, manufacturers:
- Critical infrastructure (notified bodies, EU reference labs)
- MDCG* guidance documents
- Timely preparation (e.g. collection of sufficient clinical evidence) and submission of files by manufacturers
- Commercial viability of assays under the IVDR

Labs need:
- **Realistic timelines/date of application for all stakeholders**
- **Reliable information from manufacturers**

* Medical Device Coordination Group

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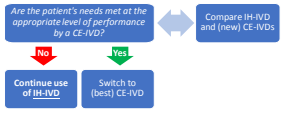
3. How will I select the best assay for each application?

- Clinical evidence (performance data) is key information when comparing CE-IVDs with each other and with IH-IVDs
(see also Fraser et al., Lancet, 2018; 392: 521-530 on data transparency under the MDR)



Labs need:
- **Public availability of clinical evidence/performance data of CE-IVDs in order to select the optimal assay repertoire**

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4. What happens when a manufacturer tries to exploit a monopoly?

- Best IVD is a CE-IVD; no competitors on the market
- Mechanism to control the price?

Labs need:
- **Fair prices, also in case of a monopoly**

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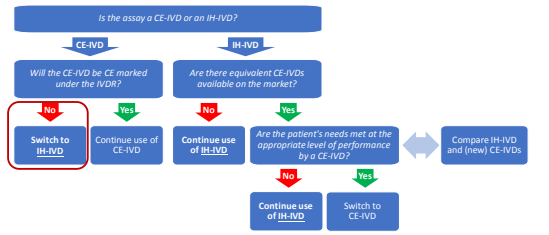

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5. Which of my assays are in-house devices/IH-IVDs?

- Do modified/off-label CE-IVDs fall under the scope of IH-IVDs?
- Extent of modifications allowed?
- Do research use only (RUO) kits fall under the scope of IH-IVDs?
- Is IH-IVDs a good term to refer to in-house devices?

Labs need:

- **Clarity about the scope of the term IH-IVD: which assays are regulated by the IVDR?**
- **What are the rules for critical assays that fall outside of the scope?**
- **Preferably high-quality (GMP) RUOs as basis of IH-IVDs**

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6. What is a valid justification for use of IH-IVDs?

Art. 5.5d: *"Justification that the patient group's specific needs cannot be met at the appropriate level of performance by an equivalent device available on the market"*

- Definition "*equivalent device*"?
- Definition "*patient group's specific needs cannot be met at the appropriate level of performance*"?
- Better performance (benefit for patient)
  - Sensitivity, specificity
  - Broader applicability
  - Turn-around time (when relevant)
- Lower sample volume needed (when relevant)?
- Expertise/equipment/space limitations?
- Unreliable availability/supply of CE-IVD?
- Costs are not a factor, but who will pay for more expensive tests, more CE-IVDs, more quality management?

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7. When will official guidance on IH-IVDs be available?

- IH-IVDs outside of scope IVDD; IVDR is completely new for labs
- MDCG *"Guidance on conditions for in-house devices"* in preparation; planned to be published Q3 2021
- Sufficient consultation of relevant stakeholders?

Labs need:

- **Rules for IH-IVDs that facilitate optimal diagnostic healthcare (use of CE-IVDs when possible, use of IH-IVDs when necessary)**
- **Sufficient time for preparation**

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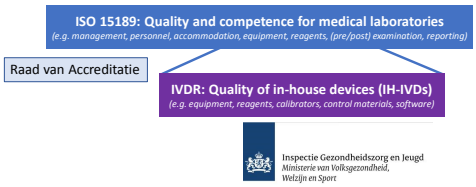
8. What is the optimal way to comply to the IVDR and ISO 15189 in parallel?

- Proposal by the Dutch Taskforce IVDR in *Handvat gebruik Lab-Developed Tests* *(Bank et al., Clin Chem Lab Med, 2020; doi: 10.1515/cclm-2020-1384)*
- What will be the official guidance? (i.e. is it safe to follow this proposal?)



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9. What are the implications of the IVDR for my international collaborations?

- Member states have relative freedom to implement the exemption for health institutions
- Can I continue to develop, validate and evaluate IVDs with my international research networks (e.g. for rare diseases)?
- Are we allowed to partly prepare for the IVDR as a collective (i.e. look for information, share advice, templates, guidance, etc.)?

Labs need:

- **Harmonization of rules for IH-IVDs on EU level: limited differences between member states**
- **International collaboration that underlies high-quality diagnostics**

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10. Is the new regulatory system crisis-proof?

- Sufficient speed/flexibility for development of IH-IVDs and CE-IVDs?

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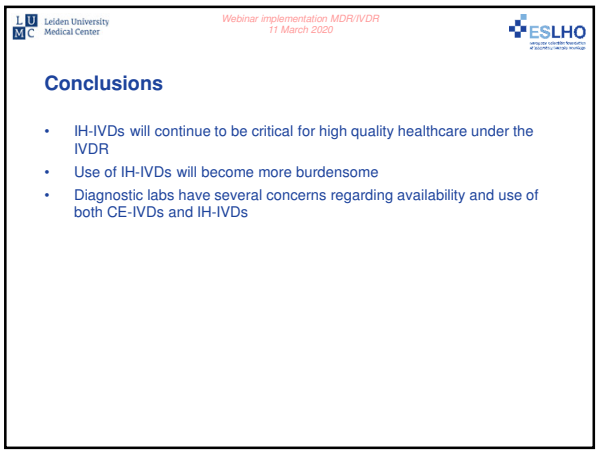
Leiden University Medical Center
Webinar implementation MDR/IVDR
11 March 2020
ESLHO
Conclusions
• IH-IVDs will continue to be critical for high quality healthcare under the IVDR
• Use of IH-IVDs will become more burdensome
• Diagnostic labs have several concerns regarding availability and use of both CE-IVDs and IH-IVDs

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