IVDR Implementation– Industry perspective

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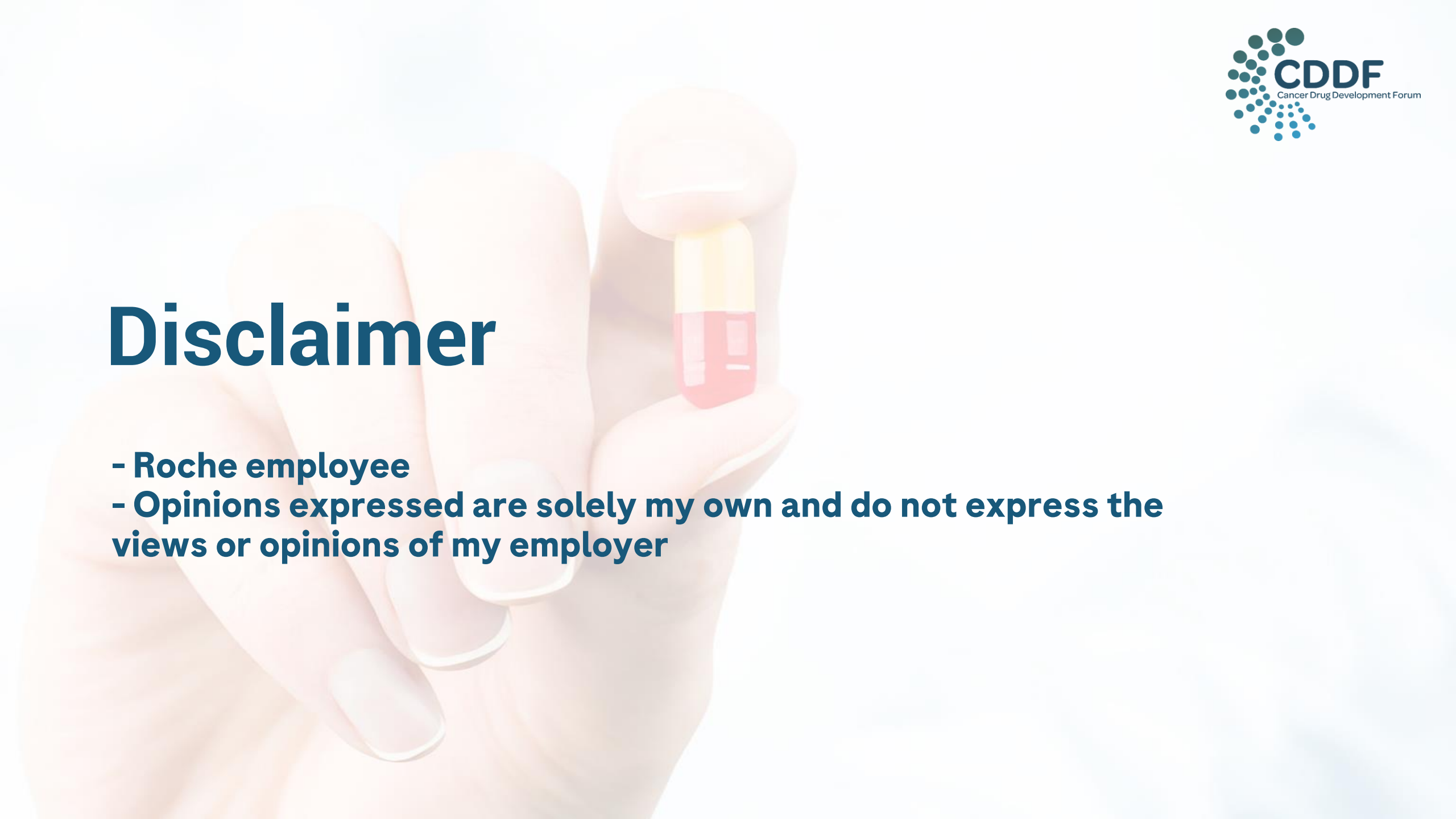


Disclaimer

- Roche employee
- Opinions expressed are solely my own and do not express the views or opinions of my employer

Short IVDR re-cap

New Changes introduced with IVDR in May 2022

- Definition of Companion Diagnostics introduced
- New risk-based classification system
- Performance Evaluation/ Interventional clinical performance study introduced
- Consultation procedure EMA-Notified Bodies
- Transparency via EUDAMED for patients and caregivers
- Exception of health institutions-in house tests (Art 5.5)

Requirement for CE certification: Performance evaluation

Scientific validity + Analytical performance + Clinical performance = Clinical evidence

Art 2 (46) Interventional clinical performamce study

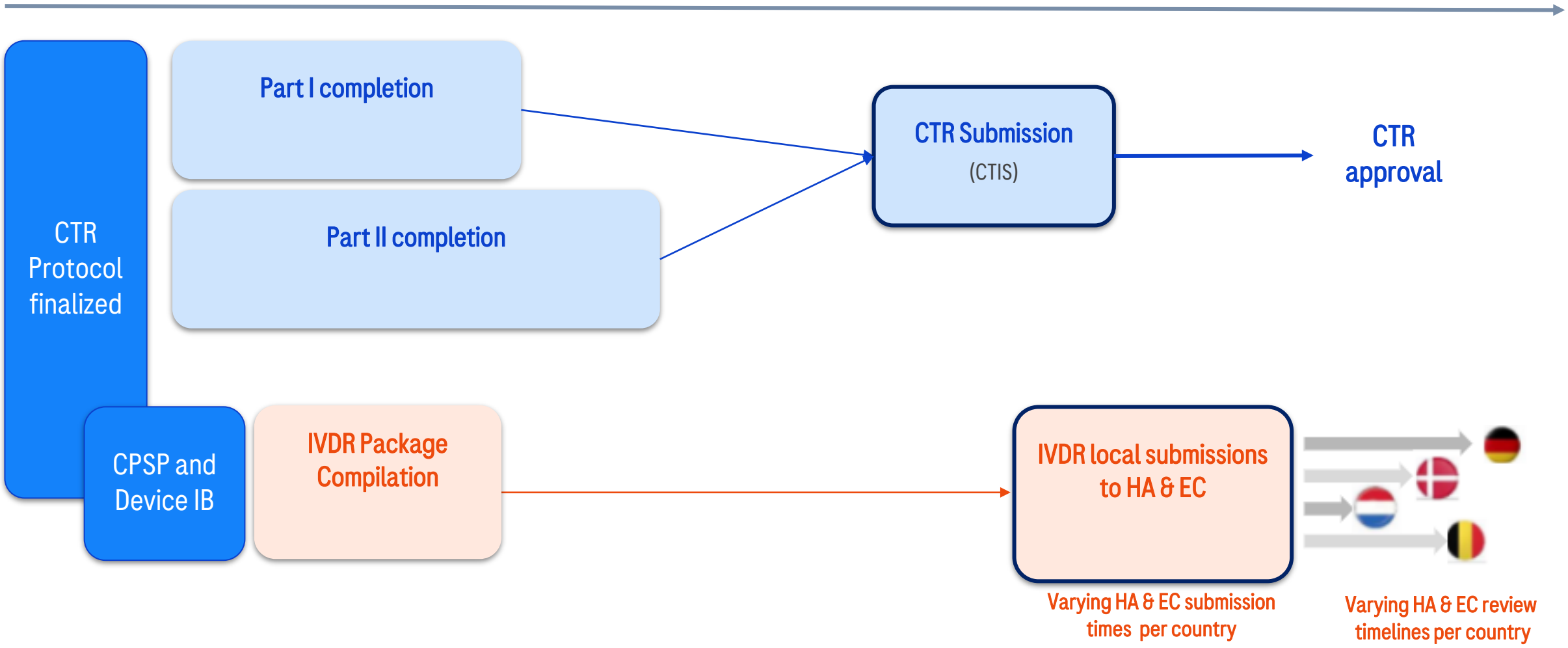
A performance Evaluation Study Submission under the IVDR is needed for all combined studies (drug + IVD) with any medical decision making in case
- a diagnostic test has no CE marking
- a diagnostic test is used outside the approved intended use.

This adds complexity: *EPFIA survey* showed that **approx. 42`000 pts** are negatively impacted in Europe by IVDR link

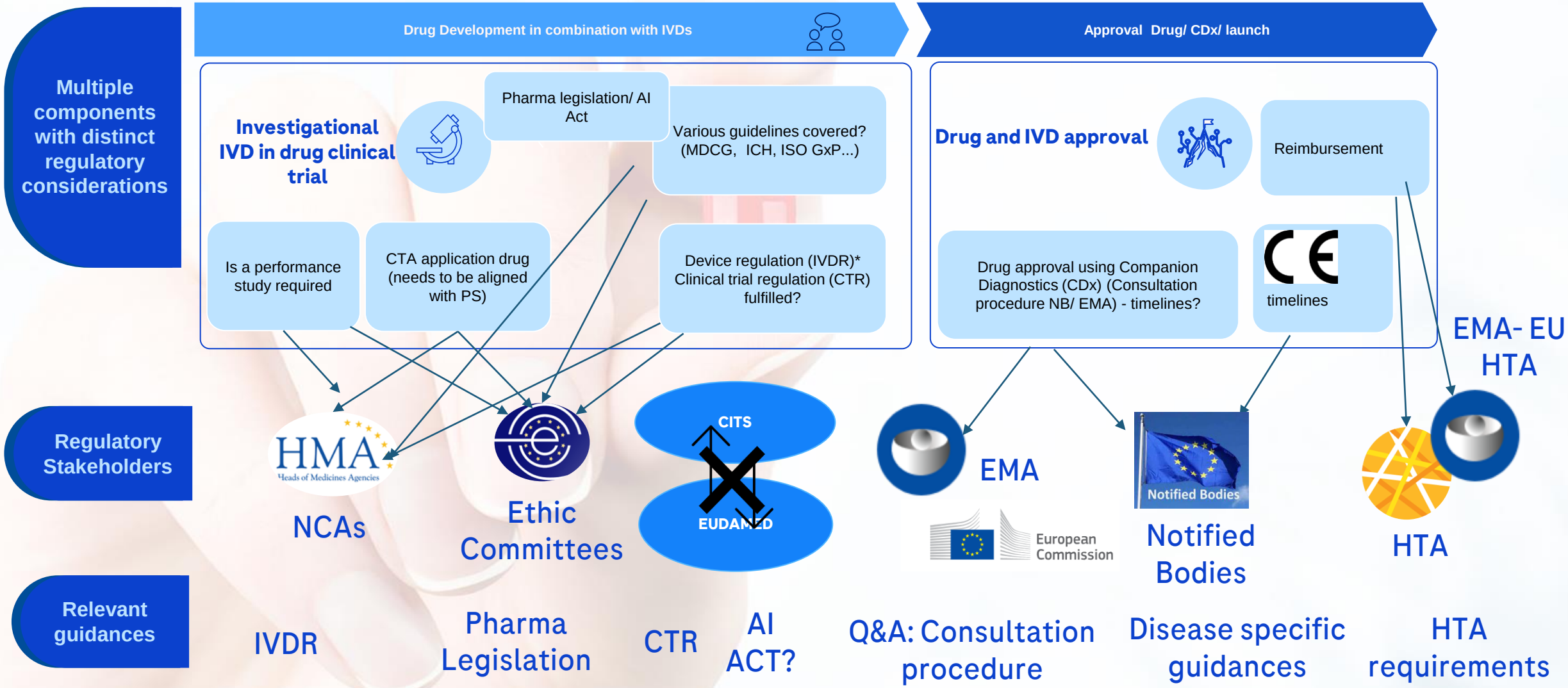
What are the key challenges?

- Classification- is the submission of a performance study required?
- National Competent Authorities/ Ethic committees- different requirements
- No harmonised approval process for performance studies –EUDAMED delayed
- Uncertainties regarding the consultation process
- Timelines / Difficulties to synchronise CTR/IVDR
- No possibility for scientific consultation EMA/ Notified Bodies

Approach for Synchronisation (timeline and flow of CTR + IVDR)



Use of Biomarkers- Points to consider



CTA = Clinical Trial application; AI = Artificial Intelligence; PS= Performance study; EC= Ethic Committees; EMA= European Medicines Agency; HTA= Health Technology Assessment Body; NCA= National Competent Authority

EFPIA proposed complementary solutions until coordinated process is in place

Proposal	Challenge(s) addressed	Impact level (H/M/L)	Timelines (short/ long-term)	Lead
1. Postpone application of IVDR to clinical trials using an IVD	All – provides the opportunity to implement other solutions until coordinated process is available	H	Short term	**European Commission**
2. Voluntary Coordination Process across Member States	PSA submissions to each Member state, inconsistent process, timelines	H	Long term	**HMA, MDCG**
3. Common Set of Principles for Performance Study Submission and Review	Divergence & lack of clarity, inconsistency of approach Role & Responsibilities not clear	H	Medium term	**MDCG (guidance drafted)**
4. Risk-based Approach to Performance Studies	Infrastructure challenges; Burden of PSA	M	Long term	**European Commission**
5. Under Article 92: Temporarily Accept Non-conformity to PSA Requirements	PSA submissions to each MS in absence of needed infrastructure and coordination	M	Medium term	**MDCG**
6. Clarify Definitions of In-House Test to Broaden Scope	Burden of PSA, Enrolling early phase studies in Europe	M	Short term	**MDCG**

Combine Project: analysing the regulatory landscape for combined studies on the IVDR/MDR/CTR interface

CDDF Cancer Drug Development Forum

Analysis phase - understanding challenges and obstacles

1 Issue List

Clarify problems that cause delays in combined studies in terms of 'scientific, procedural, legal' issues – with input from stakeholders.

2 Mapping of EU Landscape

Mapping of competent authority landscape for the different regulations on MS level and parameters relevant to the CT/PS/CI application processes.

3 Mapping of Relevant Activities

Mapping of work potentially related to the MDR/IVDR/CTR interface
(e.g. poss. update of Q&A on interface IVDR/CTR (DK)
devt of Q&A on performance studies (lead: SE), etc.)

4 Proposals for Solutions

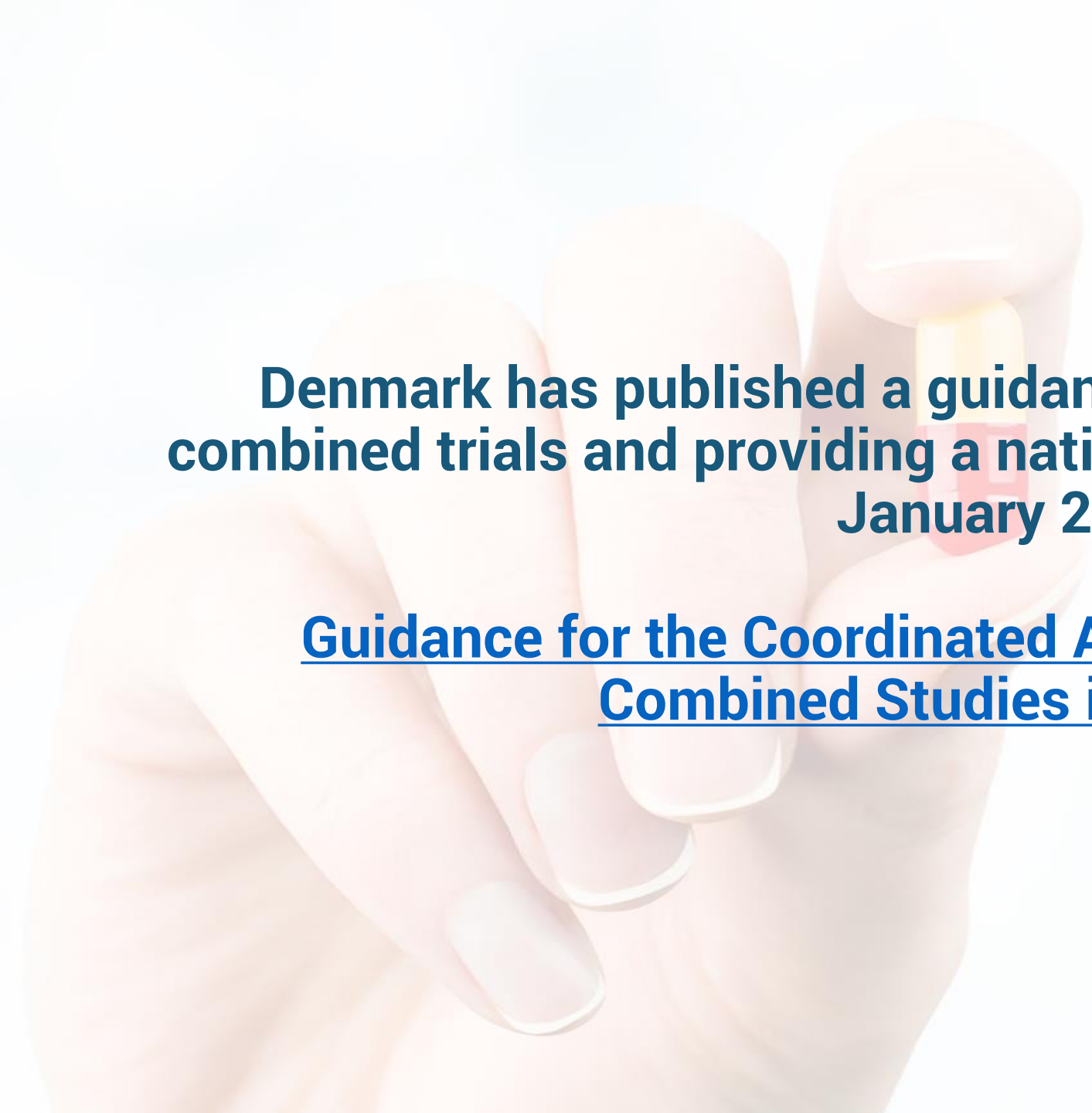
Proposals for solutions that could address the issues identified, taking into account also the mapping of landscape and ongoing work

The outcome of the analysis phase will be a document describing the three analysis elements and the proposed solutions.

European Commission

Combine Project: analysing the regulatory landscape for combined studies on the IVDR/MDR/CTR interface

High-level timeline



Denmark has published a guidance specific to IVDR/CTR combined trials and providing a national coordinated process in January 24:

Guidance for the Coordinated Application Process for Combined Studies in Denmark

EMA proposed language for SmPC section 4.2

- *"…should be assessed by a CE marked IVD with the corresponding intended purpose. If the CE-marked IVD is not available, an alternative validated test should be used."*

EMA Q&A, released Dec. 6, 2023

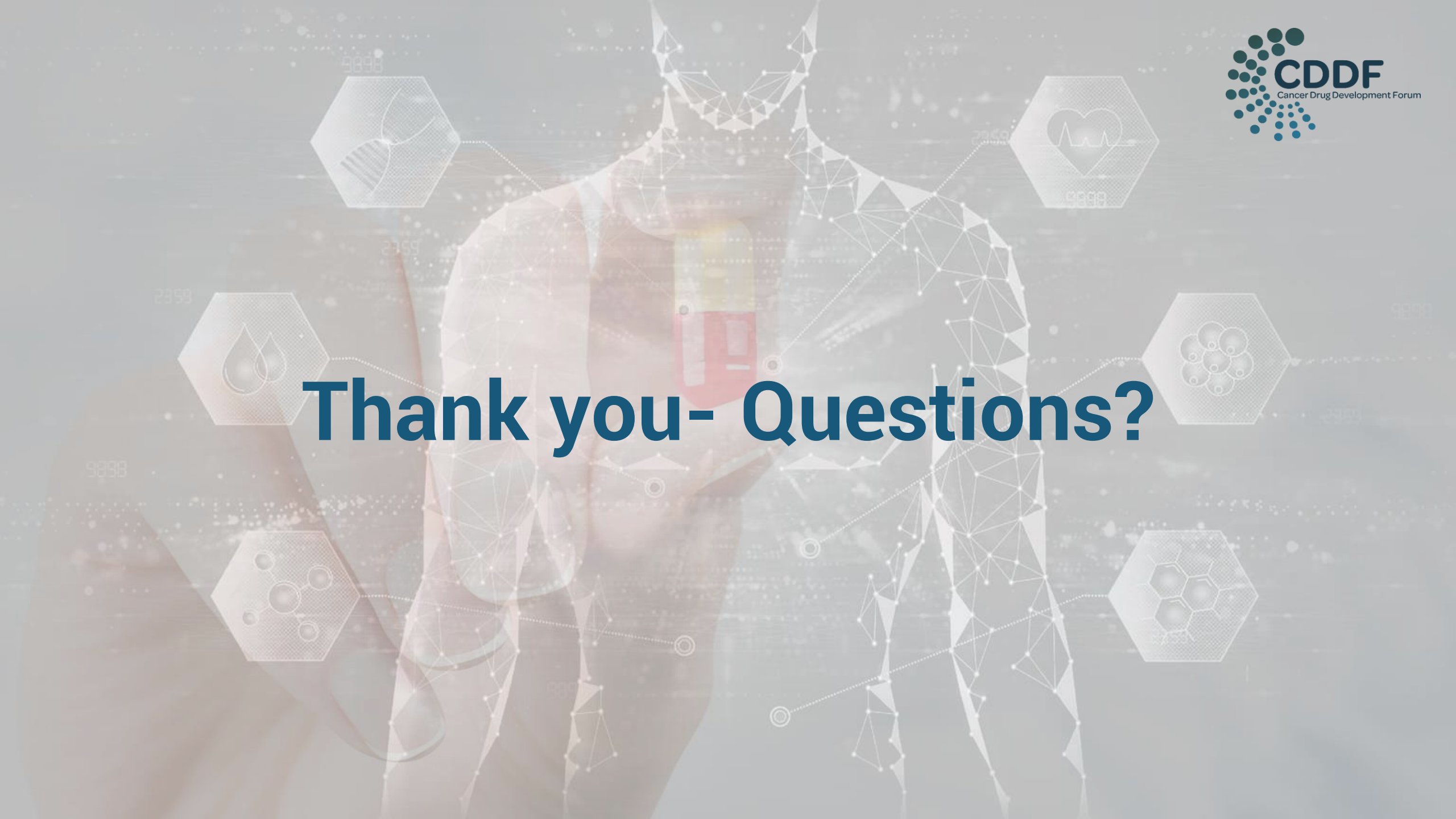
Conclusion: Reduce complexity

Biomarkers are widely used at every stage of drug discovery, drug development and in clinical care.

The IVDR increases complexity for
- clinical trials using IVDs (medical treatment decisions)
- and for CDx drug approvals.
How to cope with this?

- Close collaboration between all stakeholders is required
- Focus on simplification: e.g. ensure harmonised approval process for performance studies
- Focus on improved guidance for Health Authorities, Pharma & Academia

Our common goal as outlined in the IVDR:
High standards of quality, safety and reliability to safeguard patients.



Thank you- Questions?