How to visualize the complexity and diversity of biomarker implementation in Europe

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ELBS, WG regulatory
10-July-2025

ELBS WG regulatory

Main objective:

- The regulatory WG pursues the overarching goal of driving implementation and the introduction of liquid biopsy assays into routine clinical practice.

27th November 2024, Barcelona - ELBS Workshop: THE FUTURE OF LIQUID BIOPSY ADOPTION IN EUROPE

Action items

- Write a position paper to increase knowledge and awareness about the current hurdles and gaps in the biomarker implementation process.
- Install expert review teams, to provide recommendations for guidelines.
- Seek dialogue with and ask advice from the EMA; formulate a best-practice regulatory framework for EU biomarker regulatory acceptance and implementation.
- Seek endorsement by (medical professional) societies (e.g. ESMO and others).
- Seek dialogue with and ask advice from European / EU member state national regulatory authorities; formulate a best practice regulatory framework for national biomarker regulatory acceptance and implementation.

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Recap of ‘showstoppers’ European biomarker implementation
The example: drug development and approval

- **1**. Drug discovery
- **2**. Pre-clinical development
- **3**. Formulation
- **4**. Clinical research: phase 1, 2, 3
- **5**. Evaluation and approval
- **6**. Adoption

Treatment of a specific condition

Outcome measures: DFS/PFS/OS

Evaluation, Approval: EMA/CBG/cieBOM/governm

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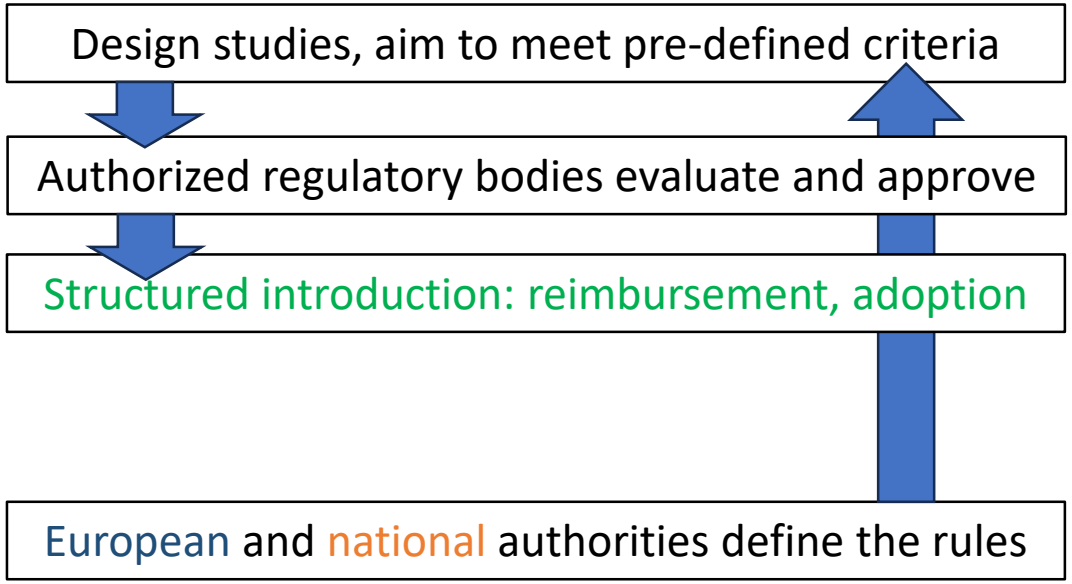
‘Solidarity’

‘healthcare for all’ versus ‘best care for some’



Path to reimbursement of novel drugs

interaction procedures EU-level and EU member state-level

EU member state procedures

EU-procedures

National level ⟷ *European level*

Path to reimbursement of novel drugs
(according to ChatGPT)

					
Criteria	**Paskwil (NL)**	**NICE (UK)**	**IQWiG (DE)**	**EMA (EU-wide)**	**FDA (US)**
Focus	Innovation & Public Health	Cost-Effectiveness	Added Benefit	Safety, Efficacy, Quality	Safety & Efficacy
Cost Threshold	Considered	£20,000–£30,000 per QALY	Negotiated	Not assessed	Not assessed
Unmet Need	High Priority	Prioritized	Important but secondary	Central for special cases	Central for Accelerated Approval
Comparative Evidence	Encouraged	Strongly emphasized	Required	Encouraged	Not mandatory
Outcome	Reimbursement Decision	Reimbursement Decision	Reimbursement Decision	Marketing Authorization	Marketing Authorization

The comparison: drugs *versus* biomarkers

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Biomarker discovery. **1**

Assay development (analytical). **2**

Test characteristics (clinical). **3**

Clinical research: prosp/interv. **4**

Evaluation and approval. **5**

Adoption. **6**

a.o. determine prognosis; treatment response

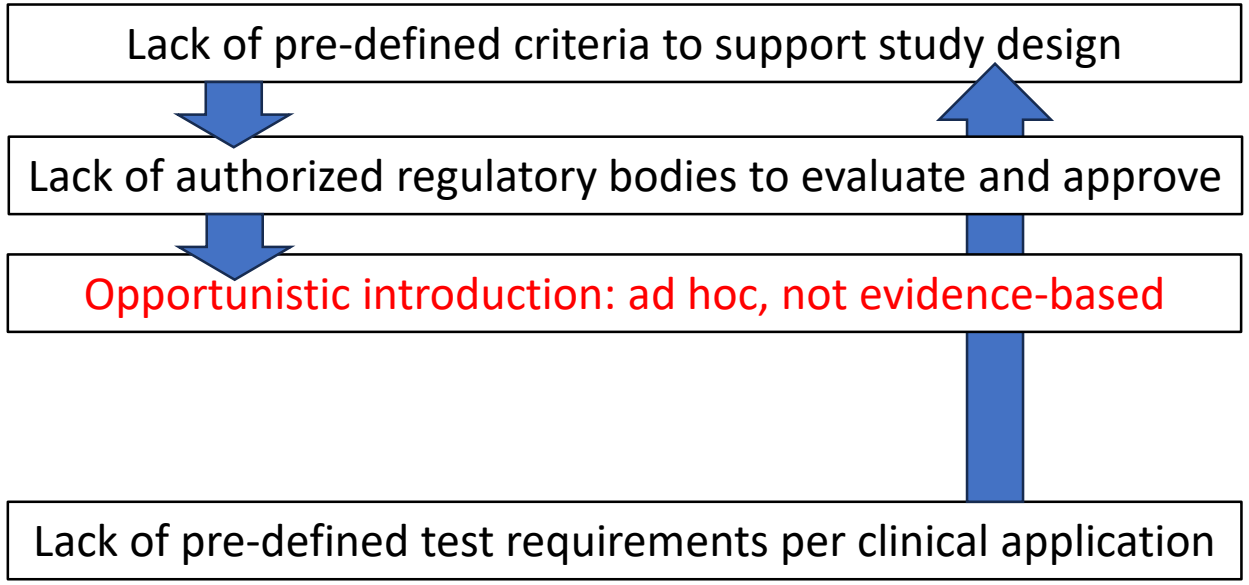
Outcome measure: sens/spec/PPV/NPV/..

Evaluation, Approval: …?/…?/…?/…?

The example: development and approval of prognostic and response monitoring biomarkers

‘Anarchism’

‘Apply where you can’ versus ‘Apply when you should’



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Who can define test requirements for prognostic and response monitoring biomarkers?

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Who can define test requirements per clinical application?

Who can define test requirements for prognostic and response monitoring biomarkers?

ELBS

- Public – private ctDNA expertise
- European voice
  - Prognosis: a.o. GUIDE.MRD
  - Monitoring: a.o. ctDNA-RECIST

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to provide recommendations for guidelines?

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- GDPR
- IVDR
- EMA?

Who can evaluate and approve biomarkers per clinical application?

European level

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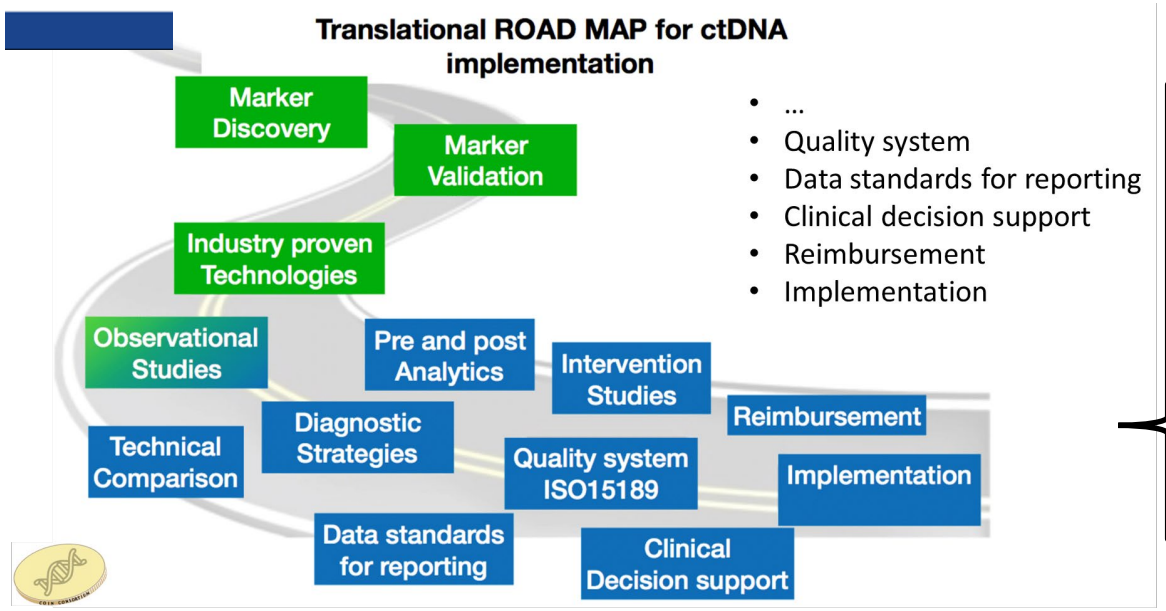
- EMA?

Seek dialogue with and ask advice from the EMA;
formulate a best-practice regulatory framework for
EU biomarker regulatory acceptance and implementation?

What is the regulatory framework for adoption of prognostic and response monitoring biomarkers

EU member state procedures



COIN: Circulating tumor DNA On the road to Implementation in the Netherlands (www.cfdna.nl/coin-2021-new/)

EU-procedures

ELBS

- GDPR
- IVDR
- EMA?

National level ⟷ *European level*

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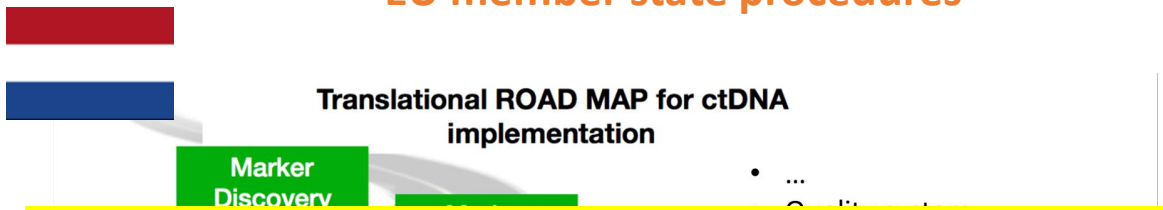

EU-procedures

- Seek endorsement by (medical professional) societies
- Seek dialogue with and ask advice from European national regulatory authorities
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National level ⟷ *European level*

Key questions for biomarker implementation

- Is it safe?
  - (pre)analytical test performance
  - clinical test performance
- Is it useful?
  - clinical utility of a test
- Is it affordable, accessible, available?
  - regulatory path to reimbursement
  - test adoption in routine clinical practice

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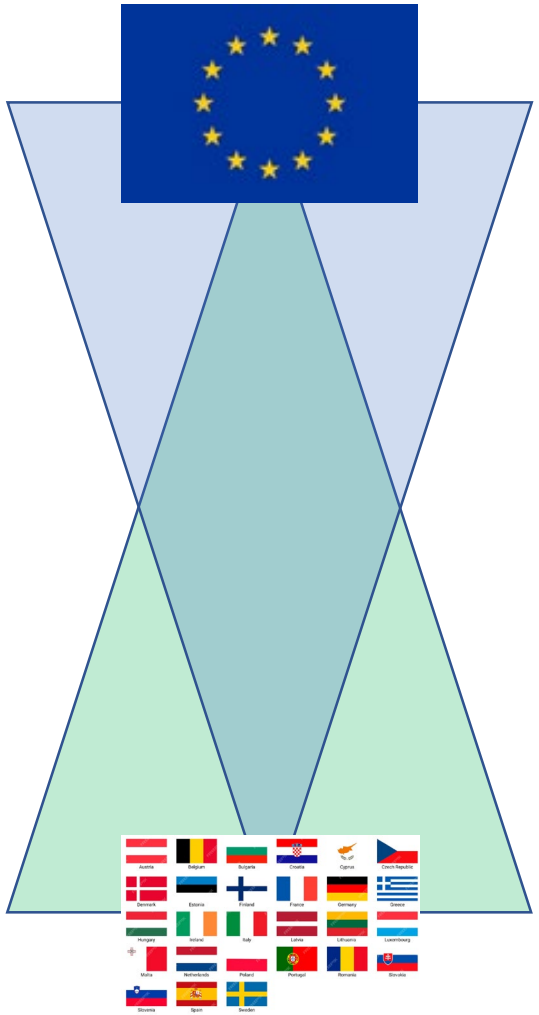

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"How to visualize the complexity and diversity of biomarker implementation in Europe"

Position paper – biomarker implementation

Steps to take:

- Generate Table to visualize complexity and diversity biomarker implementation
  - Proposed content: coming up next
  - Collect your initial feedback ‘now’
  - Collect your input in September – incorporate in manuscript

Position paper – biomarker implementation

Problem: unequal access to innovative diagnostics

- US cancer patients ‘have access’ to ctDNA testing, EU cancer patients ‘don’t’ – WHY NOT?
- Unregulated integration of ctDNA testing aggravates inequity

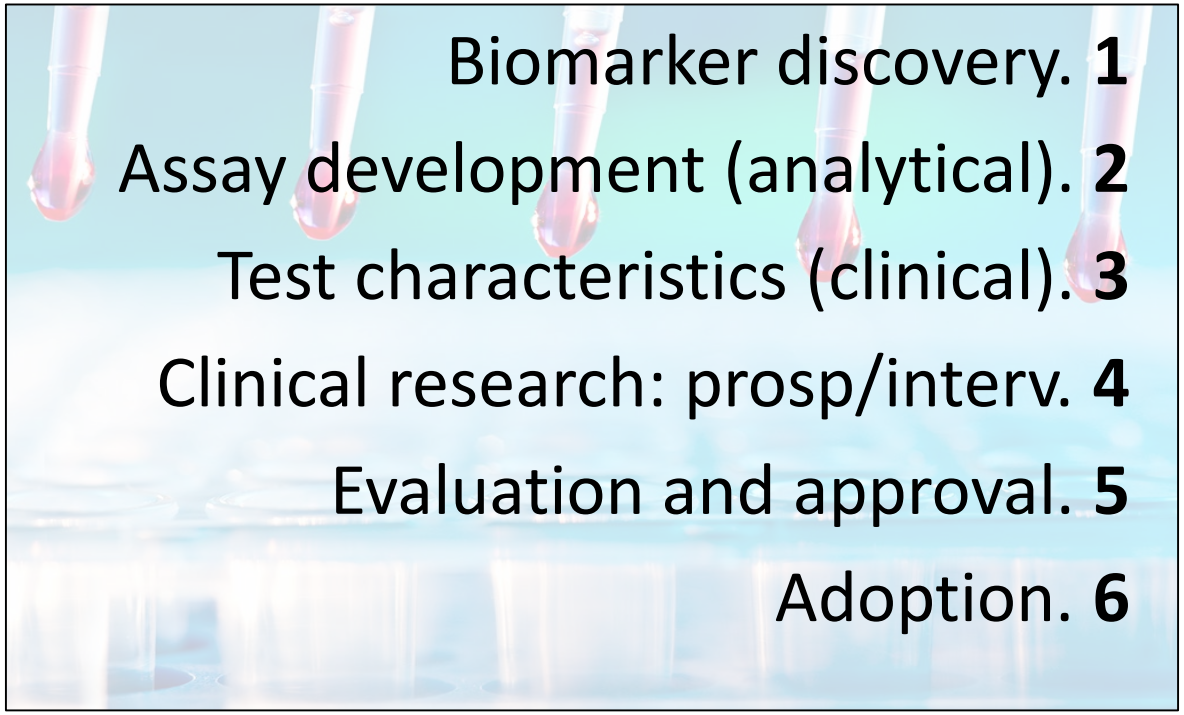
Goal:
Highlight the current trajectory—and existing gaps—in biomarker implementation across Europe

Methods:

- Identify key barriers hindering biomarker adoption in Europe / the EU
- Conduct a survey to assess the implementation status across member countries
- Analyze survey results to pinpoint critical factors for successful biomarker integration

WG regulatory - survey

- Participant details
- General liquid biopsy information
- (Pre)analytical performance
- Clinical performance
- Approval
- Adoption



General liquid biopsy information

- Application of liquid biopsy
  - Tumor types
  - Clinical applications
  - Use in clinical practice
- Performance evaluation
  - Performance criteria for use
  - Accreditation requirements
- Reimbursement
  - Hospital budget
  - Cost covered by government / health insurance companies

(Pre)analytical performance

- How to determine (pre)analytical performance
  - Standardized preanalytical requirements
  - Predefined analytical performance criteria
- When is a test good enough
  - Assay performance validation
    - Technical performance
    - Reference standards
    - Clinical applicability

Clinical performance

- How to assess clinical utility
  - Clinical performance criteria
- When did you show sufficient clinical utility
  - Type of study
    - RCT
    - RWD
  - Type of data
    - Accuracy
    - Survival
    - Cost-effectiveness
- Health technology assessment
  - Necessity for cost-effectiveness

Approval

- When can an assay be used in clinical practice
  - Which performance criteria must an assay meet to get approval
  - How is approval granted
  - Who is entitled to approve
- Reimbursement in clinical practice
  - Does approval lead to reimbursement

Adoption

- Who can use an approved assay
  - Is adoption regulated
  - Is equal access to biomarkers ensured
- Reimbursement in clinical practice
  - Is reimbursement a requirement for adoption

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