IMDRF International Medical Device Regulators Forum

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In vitro diagnostic perspective and examples of real-world data applications

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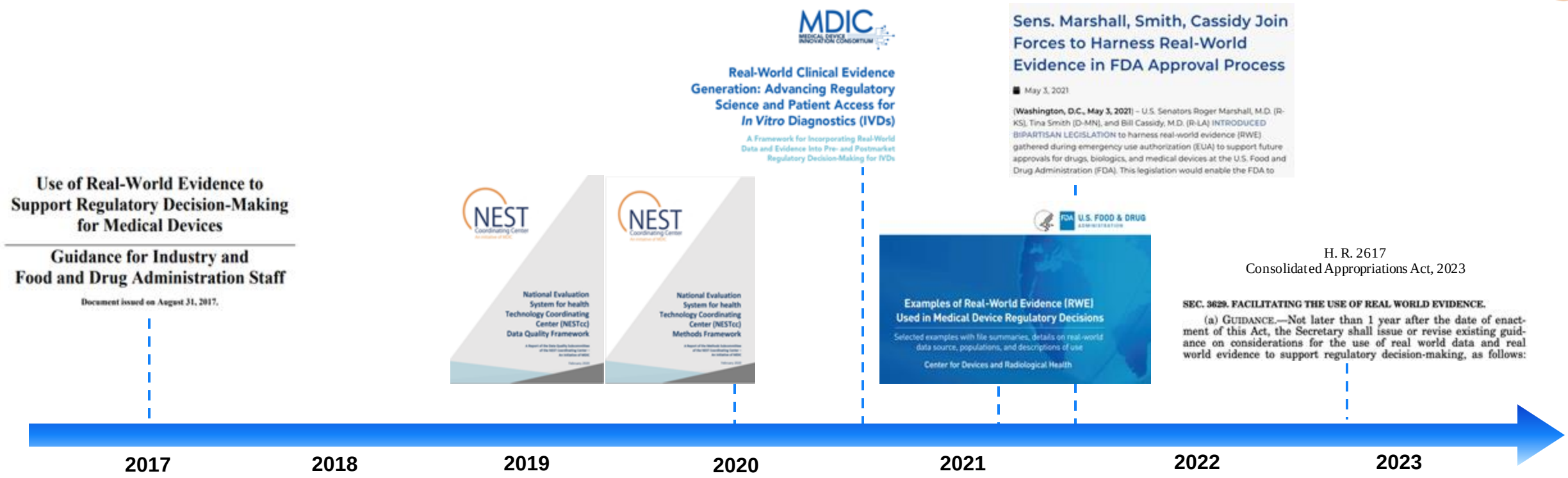
Current regulatory landscape* in the United States



- Growing interest and acceptance in using real-world evidence (RWE) for regulatory decisions for IVDs
- The use of RWE spans the "total product life cycle" (TPLC), from pre-market to post-market decisions
- *"By unleashing the power of RWE, we can accelerate medical product development and bring new innovations and advances faster and more efficiently to the patients who need them, without compromising patient safety"* – J. Shuren, D. Caños (FDA)

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*Note: Examples are non-exhaustive; many parallel guidances were also released for the pharma industry, on topics of data quality, evidence acceptability, etc.

Potential uses of RWD throughout the product lifecycle

Pre-market | Post-market

Analytical Studies

Clinical Performance

Clinical Utility

LOW ⟷ HIGH

E.g.,
Sample collection studies
Stability testing
Precision studies

E.g.,
Converting EUA
Claim expansion
Measurement ranges

E.g.,
Clinical outcomes
Clinical pathways
Economic value

De novo requests

510(k) submissions

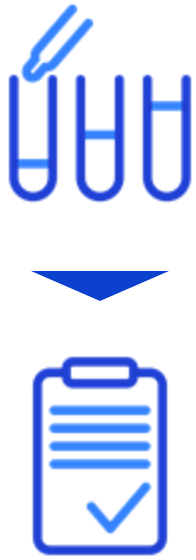
"Assay A": de novo classification request

Objective

- Seeking full market clearance for "Assay A" from its current Emergency Use Authorization (EUA) in the United States
- Aiming to fully leverage already available data to convert to full approval

Approach

- Leveraged real-world data to complement a clinical study
- Leveraged public-private partnerships
  - Pre-sub through the Medical Device Innovation Consortium (MDIC) "Open Hand" pilot program
  - Registered the study in the ISPOR RWE Registry to increase transparency



Methods

- A retrospective RWD study mimicking inclusion/ exclusion criteria and design of the clinical study, aiming to demonstrate real-world clinical performance
- **RWD source:** Data from an academic collaborator: lab test data + patient chart review
- **Data quality:** Certain key variables extracted manually, then additionally validated

Conclusions

The RWD study showed almost identical assay performance compared to the clinical study, suggesting that data pooling is possible

Status Summary

Submission almost completed; a joint manuscript by Roche, the FDA, the MDIC, and other sponsors is in preparation

"Assay B": claim expansion in a vulnerable population

Objective

- Demonstrating clinical performance of a test already established on the market in a different patient population
- Seeking claim expansion into a a high-risk, vulnerable patient population, for whom conducting large clinical studies is difficult

Approach

- A complementary approach was proposed, using RWD as primary evidence source, additionally validated by a smaller prospective clinical study
- Also leveraged public-private partnerships

Methods

- A retrospective RWD study to derive and validate "Assay B" cutoff in the new patient population
- **RWD source:** EMR data from Europe for the new population, containing all necessary elements
- **Data quality:** Thorough evaluation of data completeness and plausibility, performed by the partnering institution

Conclusions

The RWD study will determine the assay cutoff, and further cutoff validation is planned through the clinical study

Status Summary

FDA pre-sub feedback was encouraging; proposed approach was deemed acceptable, enabling us to move forward

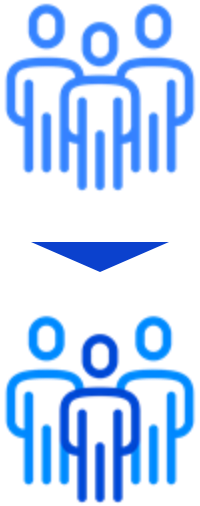
"Assay C": claim expansion using the totality of evidence

Objective

- "Assay C" received FDA 510(k) clearance in the symptomatic population in 2022
- Seeking to support its claim expansion to an asymptomatic patient population

Approach

- Proposed a totality of evidence approach, receiving constructive feedback from the FDA
- No additional studies - only further analysis of available data
- Partnered with external collaborators



Totality of evidence

Data collected under current EUA	RWD from surveillance program	Published literature

Methods

Surveillance program:

- **RWD source:** Surveillance testing program of a specific patient group
- **Data quality:** High completeness due to prospective collection and medical adjudication
- **Additional analysis** of the surveillance program data to address FDA questions

Literature review:

- Systematic literature review in the asymptomatic population

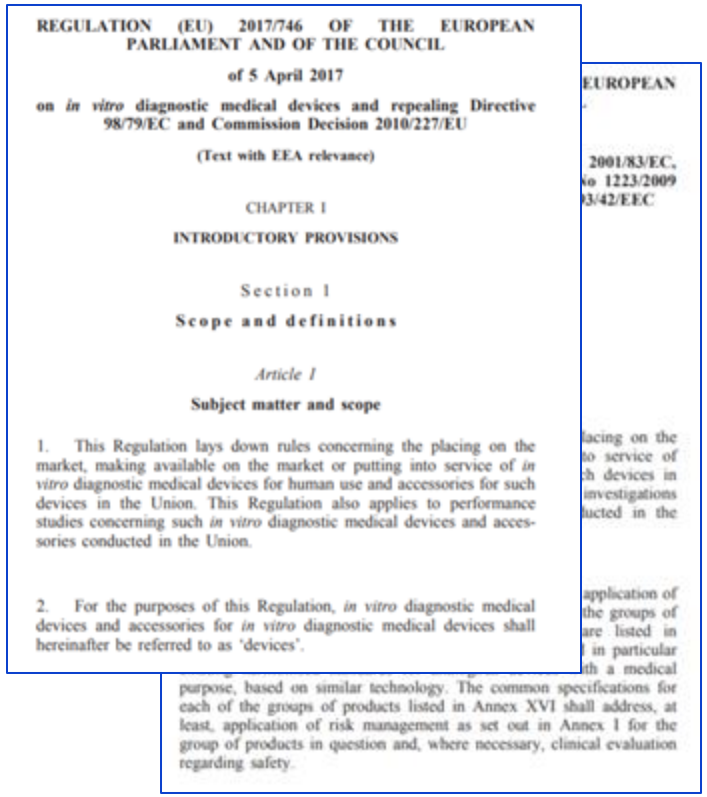
Conclusions

Assay results showed nearly 100% agreement with medical adjudication

Status Summary

FDA pre-sub feedback was encouraging; proposed approach was deemed acceptable, enabling us to move forward

IVDR perspective on RWE is opening new possibilities



REGULATION (EU) 2017/746 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 5 April 2017

on *in vitro* diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU

(Text with EEA relevance)

CHAPTER I

INTRODUCTORY PROVISIONS

Section 1

Scope and definitions

Article 1

Subject matter and scope

1. This Regulation lays down rules concerning the placing on the market, making available on the market or putting into service of *in vitro* diagnostic medical devices for human use and accessories for such devices in the Union. This Regulation also applies to performance studies concerning such *in vitro* diagnostic medical devices and accessories conducted in the Union.

2. For the purposes of this Regulation, *in vitro* diagnostic medical devices and accessories for *in vitro* diagnostic medical devices shall hereinafter be referred to as 'devices'.

- The EU In Vitro Diagnostic Regulation (IVDR) allows for a wide selection of evidence types, permitting - under due justification - the use of a multitude of data sources, including RWD/E

- IVDR requirements open multiple avenues for the use of RWD:
  - Emphasis on traceability based on unique device identification (UDI) enables design of product-specific studies
  - Strengthening of post-market surveillance requirements encourages the use of retrospectively collected data

Key takeaways

RWD is a valid source of evidence to support regulatory submissions - after application of appropriate and rigorous scientific methods

Together we can unleash the potential of RWD for speeding up evidence generation, and bringing innovation to patients without compromising safety

External collaboration is crucial in this endeavor, including public-private initiatives like the MDIC, NESTcc, and SHIELD; academic collaborations; and industry partnerships

THANK YOU

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