REAL WORLD EVIDENCE

RWE4Decisions Symposium

Real-World Evidence over the Medicine's Lifecycle to Inform HTA/Payer Decisions

23 November 2023

BIP Meeting Center, Brussels

www.rwe4decisions.com

#RWE4Decisions

REAL WORLD EVIDENCE
RWE4Decisions

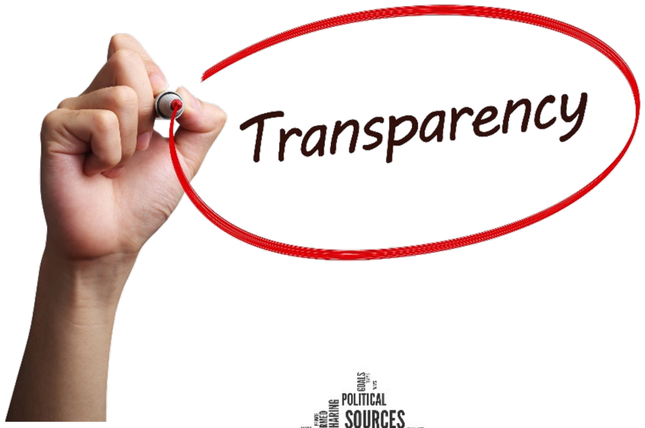
Principles

Payer-Led Multi-Stakeholder Learning Network

Highly innovative technologies often have immature clinical evidence (and high prices)

Potential for Real World Evidence (RWE)
- to fill gaps in clinical development, and/or
- resolve uncertainties post-launch?

Can requirements be aligned across stakeholders and health jurisdictions/payers?



Welcome by the co-moderators

Hans-Georg Eichler

Consulting physician,
Association of Austrian Social
Insurance Institutions

Karen Facey

Senior Adviser HTA, FIPRA
RWE4Decisions Facilitator

Keynote address by the Spanish EU Presidency

Enrique Terol García

Coordinating Advisor on Health,
Permanent Representation of
Spain to the European Union

Data policies and patient access - EU Spanish Presidency priorities

RWE4Decisions Symposium

REAL-WORLD EVIDENCE OVER THE MEDICINE'S LIFECYCLE TO INFORM HTA/PAYER DECISIONS

23 NOVEMBER 2023
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Priorities in health of the Spanish Presidency of the Council

Enrique Terol
Health Counsellor
Permanent Representation of Spain

PRESIDENCIA ESPAÑOLA CONSEJO DE LA UNIÓN EUROPEA

Priorities in Public Health

Political Priorities

Prevention and healthy lifestyles

- Childhood obesity
- Healthy Cities
- Vaccination throughout life
- Chronicity
- Response to addictions

Strengthening the capacities of health systems

- **Digital health in the EU.**
- One Health:
  - health and environment plans.
  - further progress in the fight against AMR.
- Open Strategic Autonomy in the health sector.
  - Strengthening and ensuring supply chains.
- Support the ongoing activities of working groups of EU bodies (EMA, eHealth network, etc.)

Support & development of EU health strategies

- Aligning EU action with the Targets of Sustainable Development Goal 3.
  - HIV and its associated stigma.
  - Mental health (Council Conclusions)
- Cancer
- Rare Diseases & European Reference Networks
- Organ donation & SOHO

Legislative actions

- EMA fees Regulation
- European Health Data Space (EHDS)
- Regulation on blood, tissues and cells (SoHO)
- Pharmaceutical legislative package
- Cosmetics Regulation

First reading agreement with EP September 2023

General approach agreement

General approach agreement
1st reading agreement with EP Dec 2023

Presentation of impact assessment

Presentation

Multilateral and non legislative

- Treaty on pandemics
- COP10 on tobacco
- Council conclusions on mental Health

Preparation of UN assembly May 2024

Agreements Nov 2023

Adoption EPSCO 30 Nov

Conference on Personalised Digital Healthcare

Dates:

September 27: Personalized Digital healthcare + eHN Semantic SG
September 28: Personalized Digital healthcare + eHN Technical SG
September 29: joint session at the national conference

Venue:

León, Spain

(320 km from Madrid)

Expenses:

Transportation: Spain / EU Commission (*)

Airplane ticket to Madrid + speed train from Madrid to León
speed train from León to Madrid + Airplane ticket from Madrid

Accommodation & meals & cultural activities: Spain

Up to 2 persons per MS for September 27-29:
1 representative for the eHN Semantic SG
+ 1 representative for the eHN Technical SG

Regulation of the European Health Data Space

- Ambitius initiative
- First in its approach and dimensión
- Addressing three key different environments
  - ✓ Patients rights and protection
  - ✓ Healthcare systems organisation and provision of care
  - ✓ IT dimension: hardware , software, specifications etc.

Understanding the European Health Data Space Regulation: Key Characteristics

- Unlocking the Potential of Health Data in Europe

- The European Health Data Space (EHDS) Regulation is a pivotal initiative aimed at
  - fostering collaboration,
  - innovation, and
  - data-driven healthcare across the European Union.

Regulation of the European Health Data Space

- Primary Use of Health data
- Secondary Use of Health data
- Governance
- Infrastructure development
- Standardisation – common criteria
- Electronic Health Records (concept, definitions and standards)

Actors

1. Data recipients : citizen & patients

1. Data holders: health data providers, public Health databases, Patient registers, research datasets etc.

2. Data controllers and processors

3. Nacional Data Authorities

4. Data access bodies

Background

Overview of the European Health Data Space:

- Fragmententation
- lack of common standards and data validation systems, lack of interoperability

Need for a Unified Framework:

- Challenges in sharing health data across borders
- Importance of Data Interoperability: Enhancing healthcare outcomes through seamless data exchange

Objectives of EHDS Regulation

- Promoting Interoperability: Ensuring the compatibility of health data systems
- Facilitating Cross-Border Data Exchange: Breaking down silos for improved healthcare coordination
- Empowering Patients: Granting individuals greater control over their health data
- Driving Innovation: Encouraging research and development in healthcare

Legal Framework

Article 114 TFEU aims at improving the functioning of the internal market through measures for the approximation of national rules.

Article 16 of the TFEU protection of individuals with regard to the processing of personal data

Alignment with GDPR: Ensuring data protection and privacy

Respect of Article 168 – 7 respect the responsibilities of the Member States for the definition of their health policy and for the organisation and delivery of health services and medical care.

Governance Structure: Establishing regulatory bodies for oversight and enforcement

Scope of Health Data

- Definition of Health Data: Understanding the types of data covered
- Inclusion of Real-World Data: Expanding the scope beyond traditional clinical data
- Balancing Access and Privacy: Ensuring responsible use of health information

Technical Infrastructure

- European Health Data Space Gateway: Creating a secure and standardized gateway for data exchange
- Health Data Spaces: Promoting the establishment of dedicated spaces for specific health-related purposes
- Interoperability Standards: Adopting common technical standards for seamless data sharing
- myHealth@EU
- HealthData@EU

Cross-Border Collaboration

- Cross-Border Health Data Exchange: Encouraging collaboration between Member States
- Common Data Sets: Standardizing data formats to enhance compatibility
- Use Cases: Highlighting examples of cross-border projects and collaborations

Patient Empowerment

- Digital Health Literacy: Promoting understanding and engagement among patients
- Patient Consent and Control: Opt-out & Opt-in Empowering individuals to manage their health data
- Patient Portals: Providing access to personal health records and information

Research and Innovation

- Research Opportunities: Unlocking the potential of large-scale health data for scientific discovery
- Public health, epidemiology, healthcare management and health outcomes new treatments, post commercial studies
- Innovation Hubs: Supporting the development of new technologies and solutions
- Data-Driven Healthcare: Transforming healthcare delivery through evidence-based decision-making

Challenges and Concerns

- Data Security and Privacy: Addressing concerns related to the protection of sensitive health information
- Ethical Considerations: Balancing the benefits of data use with ethical considerations
- Legal Harmonization: Overcoming legal and regulatory differences among Member States
- Implementation: technical structures and systems

Key Milestones

- Entry into force
- Transitional periods per data sets characteristics and purposes
- Member State Responsibilities: Roles and responsibilities in implementing the regulation
- Monitoring and Evaluation: Assessing the impact and effectiveness of the EHDS Regulation

THANK YOU!

The Policy Context for Real-World Evidence

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The Policy Context for Real-World Evidence

Marco Marsella

Director of Digital, EU4Health and Health Systems Modernisation, DG SANTE, European Commission

The role of Real-World Evidence for Sustainable Healthcare Systems

Marco Marsella
Director SANTE.C – Digital, EU4Health and Health Systems Modernisaton

RWE4Decisions Symposium, 23 November 2023

European Health Data Space (EHDS)

- The **EHDS legislative proposal (under negotiation) aims at**
  - Empowering individuals to take control of their health data
  - Enable the Union to fully exploit the potential to use and reuse health data
- The EHDS framework proposes a set of **rules, common standards and practices, infrastructures and a governance framework** that aims at providing a consistent, trustworthy, and efficient set-up for the use and reuse of health data for health, research, innovation, policy-making and regulatory purposes.
- Many of the data categories the proposed legislation **will apply to are real-world data** such as electronic health records, administrative data, genomic and other omics data, data from medical devices, registries, among others.

HealthData@EU infrastructure pilot project

HealthData@EUpilot

17 partners, 9 countries

2 years

5 million euros of European fundings

Create and test a beta version of the European Health Data Space

Build a network of data platforms on a European scale…

…tested by concrete cross-border use cases generating real-world evidence

HEALTH DATA HUB

Bundesinstitut für Arzneimittel und Medizinprodukte
DANISH HEALTH DATA AUTHORITY
BBMRI-ERIC
CROATIAN INSTITUTE OF PUBLIC HEALTH
eeszt elektronikus egészségügyi szolgáltatási tér
EBRAINS
EUROPEAN MEDICINES AGENCY SCIENCE MEDICINES HEALTH
ecdc
IACS Instituto Aragonés de Ciencias de la Salud
elixir
FINDATA Social and Health Data Permit Authority
EUPHA EUROPEAN PUBLIC HEALTH ASSOCIATION
GOBIERNO DE ESPAÑA MINISTERIO DE SANIDAD
orphanet
The Norwegian Directorate of eHealth
sciensano

European Commission

RWD / RWE - towards a common language

- Strong engagement of regulatory agencies across the globe to **address the gaps due to a lack of RWD / RWE standardisation**
- **The Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)** leads an international level process to address these questions
- EMA, in collaboration with the Member States, supports the **European Commission's membership in ICH** as well as the development and implementation of ICH guidelines

European Commission

RWD / RWE - Medicinal products

- The **COM proposal reviewing the general pharmaceutical legislation, recognises new sources of evidence including RWD** as valuable for regulatory decision-making

- **RWE already now has an impact** on regulatory decision making (pre-authorisation, pharmacovigilance)

- **Methodological challenges remain** before RWE can become a routine part of decision making across all parts of the development of medicines development

- The **joint HMA/EMA Big Data Steering Group** is contributing to increase the utility of big data (incl. RWD), incl. via **DARWIN EU**

- Close cooperation among Commission services, the **European Medicines Agency** and **National Competent Authorities**

Medical devices Regulations

- **New regulatory framework with stricter requirements in terms of clinical evaluation of medical devices (MD)**:
  - Clinical evidence to be continuously updated throughout the lifetime of the product for all risk classes of devices
  - Clinical investigation mandatory for higher risk devices
- **Possible sources of clinical data for clinical evaluation** vary depending on the risk class of the device and its development stage
- **Why RWD is critical for the clinical evaluation of medical devices?**
  - To complement evidence generated from clinical investigation data
  - To meet MDR requirements for ongoing clinical evaluation

MD initiatives with RWD / RWE relevance

- **Policy initiatives**
  - **MDCG* task force on orphan devices**: guidance on what constitutes acceptable clinical evidence gap and how to address them with RWD
  - **MDCG task force on certificates with conditions**: guidance to notified bodies on the issuance of certificates with conditions incl. follow-up of conditions to generate RWE
- **Research initatives**
  - EU funded CORE-MD research project (2021-2024) with the objective to review methods for medical device evaluation incl. methods to generate and combine RWD
  - new call for proposals under Horizon Europe (deadline April 2024) on the development of a methodological framework for MD evaluation incl. the use of registries and other sources of RWD at pre- and post-market phase

* The Medical Device Coordination Group (MDCG) is an expert committee representing the competent authorities of the MS. It assists the EC and the MS in ensuring a harmonised implementation of the medical devices Regulations.

HTA Regulation - Implementation timeline

Adoption

December 2021

Entry into force

January 2022

Date of Application

January 2025

Joint Clinical Assessment Full Scope

January 2030

Preparatory phase

Implementation phase

- **Setting up the Coordination Group/HTACG (EC)**
- **Setting up the Stakeholder Network (EC)**
- **Drafting implementing and delegated acts (EC)**
- **Drafting guidance documents (CG)**

Joint Scientific Consultations (JSC)
+
Stepwise build-up of Joint Clinical Assessments (JCA) scope for medicines:

- ***From Jan. 2025****: cancer drugs, ATMPs*
  (from date of application)
- ***From Jan. 2028****: orphan drugs*
  (3 years after date of application)

eunethta
EUROPEAN NETWORK FOR HEALTH TECHNOLOGY ASSESSMENT

Service contract EUnetHTA21

European Commission

RWE - HTA clinical domains

- Activities under the **HTA Regulation are restricted to the HTA clinical domains**, whereas the non-clinical domains remain within the responsibility of the MS
- The views on RWD / RWE methods / tools vary across the HTA community. A major concern is the **quality of data to assure high levels of evidence**
- To implement the regulation, the **HTA Coordination Group and its Subgroups will develop methodological guidance**
- **High degree of interdependencies:** The HTA Regulation will be impacted by RWD / RWE developments in the fields of medicinal products, medical devices and the EHDS

RWE - Economic evaluation

- Economic evaluation remains within the responsibility of the Member States
- The Commission is facilitating cooperation in the network of the National Competent Authorities on Pricing and Reimbursement and Public Healthcare Payers (NCAPR)
- Regular NCAPR discussions on the challenges and opportunities of RWE

European Commission

Conclusions – Concerted efforts needed to make health systems fit for RWD / RWE

Continue work on methodologies / tools and data, e.g.,

- Support **standardised RWD / RWE data collection**
- Support the **development of RWD quality standards and validation processes**
- Support the establishment **of representative databases for RWD use**
- Support **the development of evidence synthesis methods** (e.g. meta-analytical techniques, AI)
- Support **case studies demonstrating how RWD / RWE can be used** (e.g. for clinical decision-making, regulatory decision-making, HTA, managed entry agreements)
- Support guidance on the **level of evidence needed at different stages in a health technology's life cycle** (R&D, pre-clinical, clinical, authorisation, post-market authorisation phases)

Ensure involvement of relevant stakeholders

Thank you

European Commission

The Policy Context for Real-World Evidence

Patrice Verpillat

Head of Real-World Evidence Workstream, European Medicines Agency

Scaling-up Real-World Evidence generation in Europe – DARWIN EU

RWE4Decisions Symposium – Brussels

Presented by Patrice Verpillat on 23 November 2023
Data Analytics and Methods Taskforce, Real World Evidence Workstream

An agency of the European Union

Disclaimer

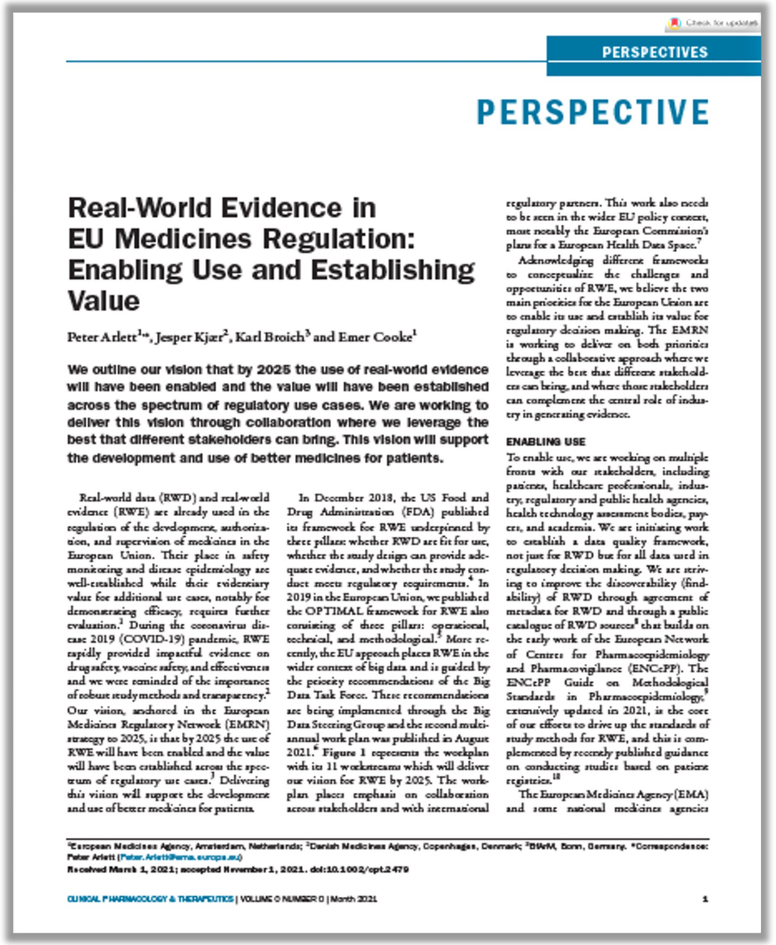
The presenter does not have any conflict of interest

The views expressed in this presentation are personal views and may not be understood or quoted as being made on behalf of, or reflecting the position of the European Medicines Agency or one of its committees or working parties

Clinical evidence 2025: Real world evidence

Enable the Use & Establish the Value of RWE

- Enable data access (including via EHDS)
- Build processes
- Set standards
- Validate methods
- Train/share knowledge & Manage change
- Establish value across various use cases
- Internationalise (build on ISPE-ISPOR, ICMRA, ICH)



PERSPECTIVES

PERSPECTIVE

Real-World Evidence in EU Medicines Regulation: Enabling Use and Establishing Value

Peter Arlett[1]*, Jesper Kjær[2], Karl Broich[3] and Emer Cooke[1]

We outline our vision that by 2025 the use of real-world evidence will have been enabled and the value will have been established across the spectrum of regulatory use cases. We are working to deliver this vision through collaboration where we leverage the best that different stakeholders can bring. This vision will support the development and use of better medicines for patients.

Real-world data (RWD) and real-world evidence (RWE) are already used in the regulation of the development, authorization, and supervision of medicines in the European Union. Their place in safety monitoring and disease epidemiology are well-established while their evidentiary value for additional use cases, notably for demonstrating efficacy, requires further evaluation.[1] During the coronavirus disease 2019 (COVID-19) pandemic, RWE rapidly provided impactful evidence on drug safety, vaccine safety, and effectiveness and we were reminded of the importance of robust study methods and transparency.[2] Our vision, anchored in the European Medicines Regulatory Network (EMRN) strategy to 2025, is that by 2025 the use of RWE will have been enabled and the value will have been established across the spectrum of regulatory use cases.[3] Delivering this vision will support the development and use of better medicines for patients.

In December 2018, the US Food and Drug Administration (FDA) published its framework for RWE underpinned by three pillars: whether RWD are fit for use, whether the study design can provide adequate evidence, and whether the study conduct meets regulatory requirements.[4] In 2019 in the European Union, we published the OPTIMAL framework for RWE also consisting of three pillars: operational, technical, and methodological.[5] More recently, the EU approach places RWE in the wider context of big data and is guided by the priority recommendations of the Big Data Task Force. These recommendations are being implemented through the Big Data Steering Group and the second multi-annual work plan was published in August 2021.[6] Figure 1 represents the workplan with its 11 workstreams which will deliver our vision for RWE by 2025. The workplan places emphasis on collaboration across stakeholders and with international regulatory partners. This work also needs to be seen in the wider EU policy context, most notably the European Commission's plans for a European Health Data Space.[7]

Acknowledging different frameworks to conceptualize the challenges and opportunities of RWE, we believe the two main priorities for the European Union are to enable its use and establish its value for regulatory decision making. The EMRN is working to deliver on both priorities through a collaborative approach where we leverage the best that different stakeholders can bring, and where those stakeholders can complement the central role of industry in generating evidence.

ENABLING USE

To enable use, we are working on multiple fronts with our stakeholders, including patients, healthcare professionals, industry, regulatory and public health agencies, health technology assessment bodies, payers, and academia. We are initiating work to establish a data quality framework, not just for RWD but for all data used in regulatory decision making. We are striving to improve the discoverability (findability) of RWD through agreement of metadata for RWD and through a public catalogue of RWD sources[8] that builds on the early work of the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP). The ENCePP Guide on Methodological Standards in Pharmacoepidemiology,[9] extensively updated in 2021, is the core of our efforts to drive up the standards of study methods for RWE, and this is complemented by recently published guidance on conducting studies based on patient registries.[10]

The European Medicines Agency (EMA) and some national medicines agencies

[1]European Medicines Agency, Amsterdam, Netherlands; [2]Danish Medicines Agency, Copenhagen, Denmark; [3]BfArM, Bonn, Germany. *Correspondence: Peter Arlett (Peter.Arlett@ema.europa.eu)

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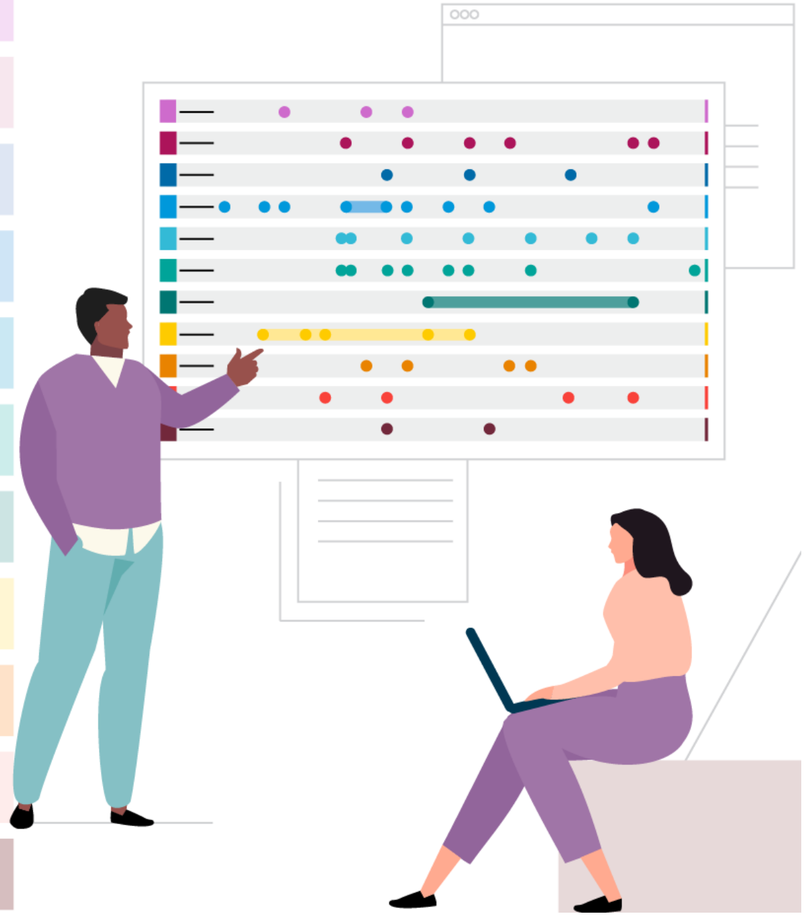
Big Data Steering Group workplan 2022-2025

Framework - to enable use of data and facilitate its integration into regulatory decision making

- DARWIN EU
- Data quality & representativeness
- Data discoverability
- EU Network skills
- EU Network processes
- Network capability to analyse
- Delivery of expert advice
- Governance framework
- International initiatives
- Stakeholder engagement
- Veterinary recommendations



3 main pathways for generating RWE

EMA studies using in-house databases

- **Primary care** health records from the **France**, **Germany, UK, Italy, Spain** and **Romania**

Studies procured through EMA FWCs

- New framework contract (FWC) since September 2021: services of **8 research organisations** and academic institutions
- Access to **wide network of data sources**: 59 data sources from 21 EU countries
- Ability to leverage external **scientific expertise**

DARWIN EU

DARWIN EU®

- Coordination Centre launched February 2022
- Onboarded first **10 data partners in 2022.** Additional 10 data partners to **be added each year** for 2023 and 2024
- **Multiple studies** finalised assessing different pilot use cases for regulatory purpose and beyond

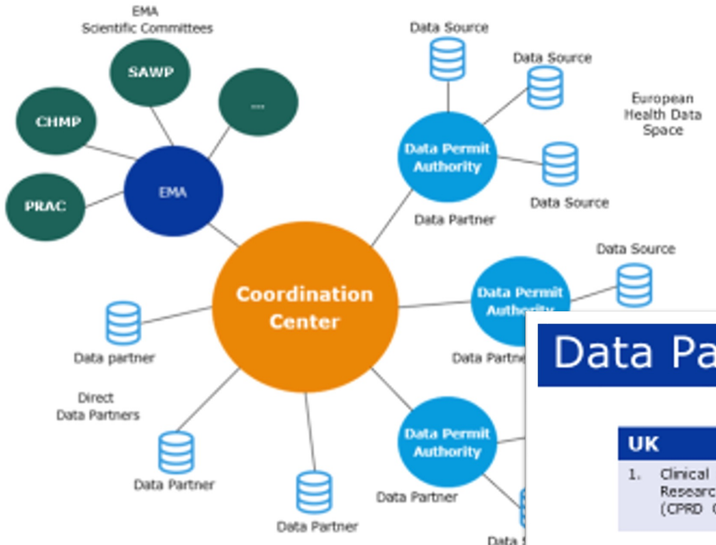
Data Analysis and Real-World Interrogation Network

EUROPEAN MEDICINES AGENCY

DARWIN EU® is a federated **network** of **data**, **expertise** and **services** that supports better decision-making throughout the product lifecycle by generating reliable **evidence from real-world healthcare data**

FEDERATED NETWORK PRINCIPLES

- Data stays **local**
- **Use of Common Data Model** (where applicable) to perform studies in a timely manner and increase consistency of results



Data Partners – Phase I

EUROPEAN MEDICINES AGENCY

UK
1. Clinical Practice Research Datalink (CPRD GOLD)

Belgium
2. IQVIA Belgium Longitudinal Patient Data

France
3. Bordeaux University Hospital

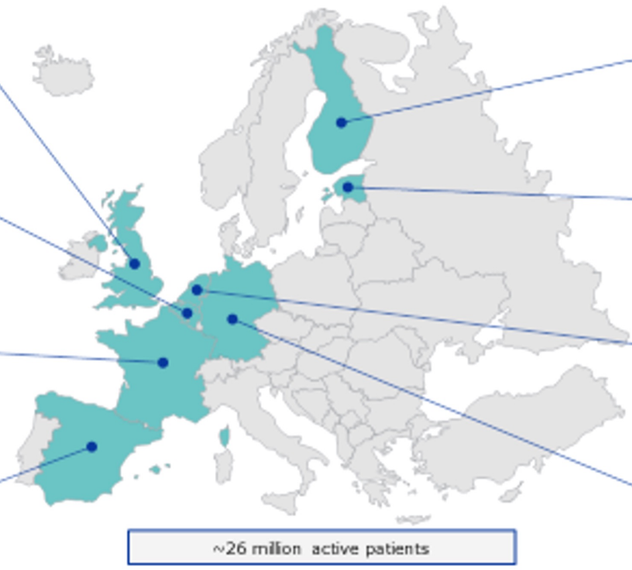
Spain
4. IDIAPJGol
5. Parc Salut Mar Barcelona, Hospital del Mar (IMIM)

Finland
6. Auria Clinical Informatics at Hospital District of Southwest Finland (HDSF)

Estonia
7. University of Tartu (Biobank)

Netherlands
8. Integrated Primary Care Information
9. Netherlands Comprehensive Cancer Organisation

Germany
10. IQVIA Germany Disease Analyser



Use cases: How RWE can support decision-making?

1 Understand the clinical context

- Disease epidemiology
- Clinical management
- Drug utilisation

2 Support the planning and validity

- Design and feasibility of studies
- Representativeness and validity of completed studies

3 Investigate associations and impact

- Effectiveness and safety studies
- Impact of regulatory actions

DARWIN EU® timelines

✓ PHASE I Establishment – 1st year | PHASE II Establishment – 2nd year | PHASE III Operation – 1st year | Operation 2nd year | Operation 3rd year

Phase I – February 2022

- Start running pilot studies to support EMA committees – **First benefits delivered**
- Consultation of stakeholders

Phase II - 2023

- Support the majority of Committees in their decision-making with reliable RWE
- Expand to other stakeholders

Phase III - 2024

Up-scale delivery and **capacity to routinely support scientific evaluations** of EMA's committees by delivering studies and maintaining data sources

Operation - 2025/2026

- DARWIN EU fully operational and evolves to meet the needs of the EU Regulatory Network
- **Integration with the EHDS**

	Phase I	Phase II	Phase III	Operation 2	Operation 3
Total number of studies	4	16	72	145	145

Examples of ongoing/recently completed DARWIN EU studies

Background all-cause **mortality rates in patients with severe asthma aged ≥12 years** old [EUPAS103936]

CHMP
Complex

EHDS natural history & risk factors for coagulopathy and COVID-19

EC / EHDS
Complex

Effectiveness of **COVID-19** vaccines against severe COVID-19 and post-acute outcomes of SARS-CoV-2 infection

ECDC - VMP
Complex

Drug utilisation study on co-prescribing of **endothelin receptor antagonists** (ERAs) and **phosphodiesterate-5 inhibitors** (PDE-5is) in pulmonary arterial hypertension. [EUPAS106052]

CHMP
OTS

Multiple myeloma: patient characterisation, treatments and survival [EUPAS105033]

HTA / Payers
OTS

Drug utilisation study of **medicines with prokinetic properties** in children and adults diagnosed with gastroparesis

NCA
OTS

Naloxone use in treatment of opioid overdose [EUPAS105644]

CHMP
OTS

Drug utilisation study of prescription **opioids** [EUPAS105641]

PRAC
OTS

OTS = off-the-shelf study

DARWIN EU supporting HTA/Payer decision-making

Workshop October 2022

- Need to address concerns that may be an obstacle to use RWD for decision making, e.g. quality of RWD => EU Data Quality Framework (EU DQF)
  - Further deep-dives to be developed with RWD deep-dive under preparation
- Which research questions can be addressed will depend on available RWD
  - RWD will increase in volume and variety as network of DPs of DARWIN EU grows
- Focus first on the potentially most feasible studies
- Transparency on how DARWIN EU operates will be helpful
  - All protocols and reports of DARWIN EU studies published in EU PAS register => Public release of EMA-HMA catalogues of real-world data sources & non interventional studies planned for Q1 2024

Workshop outcomes

On topics to be addressed by studies

- **Effectiveness of medicines** is key to support HTA/Payer decision making
  - To bridge the gap in situations where authorization is based on limited evidence
- **Natural disease history**
  - Provide a better understanding of standard of care, sequence of treatments…
  - External validation of patient population targeted in clinical trials

Two pilot studies agreed

- **Effectiveness study** to assess overall survival of patients with non-small cell lung cancer treated with selected immunotherapies as first line
  - **Study protocol under development**
- **Natural history of multiple myeloma** to characterise MM patients, including treatments (sequences) received and overall survival
  - **Study completed; report under development**

Further information

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The Policy Context for Real-World Evidence

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RWE4Decisions 2023

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RWE4Decisions REAL WORLD EVIDENCE Symposium

REAL-WORLD EVIDENCE OVER THE MEDICINE'S LIFECYCLE TO INFORM HTA/PAYER DECISIONS

23 NOVEMBER 2023
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Key takeaways from RWE4Decisions 2022 Symposium

1. **Continue to build trust among stakeholders**
2. Link with **Payer networks** to support shared learnings and identification of RWE needs
3. Continue engagement with **European Medicines Agency (EMA)**
4. Work with **clinicians** to understand how to support a learning health system
5. Go beyond “**patient** centricity” to co-creation

RWE4Decisions REAL WORLD EVIDENCE 2023 STEERING GROUP

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Antonella Cardone

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Chris Sotirelis

Patient Advocate for Thalassemia

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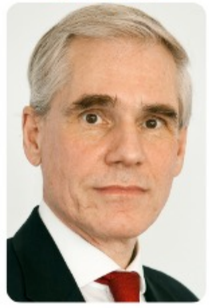

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Pfizer

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The RWE4Decisions multi-stakeholder community

INAMI-RIZIV

Secretariat: FIPRA

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UZ Leuven, ECO, EORTC, EBMT, Canadian Registry

Patients/Foundations

EURORDIS, ECO, ECPC AfM-Téléthon, SMA UK

Regulators

European Medicines Agency (EMA)

HTA bodies, Payers and Health Ministries

AITHA, Austrian Social Insurance Association; INAMI-RIZIV, KCE; CADTH; Danish Medicines Council, Amgros; NICE; FIMEA; HAS; G-BA, AOK; NCPE; AIFA; ZIN; NoMA; AOMIT; INFARMED; Health Insurance Institute; Health Ministry; TLV

Analytics experts/Statisticians

Aetion, Flatiron, EFSPI

Academia

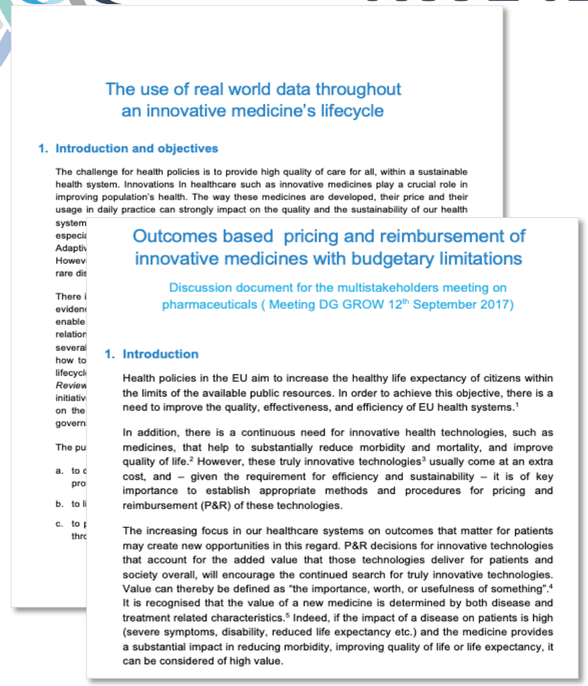
Università Cattolica del Sacro Cuore, University of Edinburgh, Mc Master University, University of Quebec, University Lyon, University of Helsinki

Industry

EUCOPE, AstraZeneca, Boehringer Ingelheim, Novartis, Pfizer, Roche, Takeda

"Learning by Doing"

RWE4Decisions Dialogues leading to Learned Papers



The use of real world data throughout an innovative medicine's lifecycle

1. Introduction and objectives

The challenge for health policies is to provide high quality of care for all, within a sustainable health system. Innovations in healthcare such as innovative medicines play a crucial role in improving population's health. The way these medicines are developed, their price and their usage in daily practice can strongly impact on the quality and the sustainability of our health system

Outcomes based pricing and reimbursement of innovative medicines with budgetary limitations

Discussion document for the multistakeholders meeting on pharmaceuticals (Meeting DG GROW 12th September 2017)

1. Introduction

Health policies in the EU aim to increase the healthy life expectancy of citizens within the limits of the available public resources. In order to achieve this objective, there is a need to improve the quality, effectiveness, and efficiency of EU health systems.[1]

In addition, there is a continuous need for innovative health technologies, such as medicines, that help to substantially reduce morbidity and mortality, and improve quality of life.[2] However, these truly innovative technologies[3] usually come at an extra cost, and – given the requirement for efficiency and sustainability – it is of key importance to establish appropriate methods and procedures for pricing and reimbursement (P&R) of these technologies.

The increasing focus in our healthcare systems on outcomes that matter for patients may create new opportunities in this regard. P&R decisions for innovative technologies that account for the added value that those technologies deliver for patients and society overall, will encourage the continued search for truly innovative technologies. Value can thereby be defined as "the importance, worth, or usefulness of something".[4] It is recognised that the value of a new medicine is determined by both disease and treatment related characteristics.[5] Indeed, if the impact of a disease on patients is high (severe symptoms, disability, reduced life expectancy etc.) and the medicine provides a substantial impact in reducing morbidity, improving quality of life or life expectancy, it can be considered of high value.

Annemans and Makady *Orphanet Journal of Rare Diseases* (2020) 15:127
https://doi.org/10.1186/s13023-020-01370-3

Orphanet Journal of Rare Diseases

POSITION STATEMENT Open Access

TRUST4RD: tool for reducing uncertainties in the evidence generation for specialised treatments for rare diseases

Lieven Annemans[1*] and Amr Makady[2]

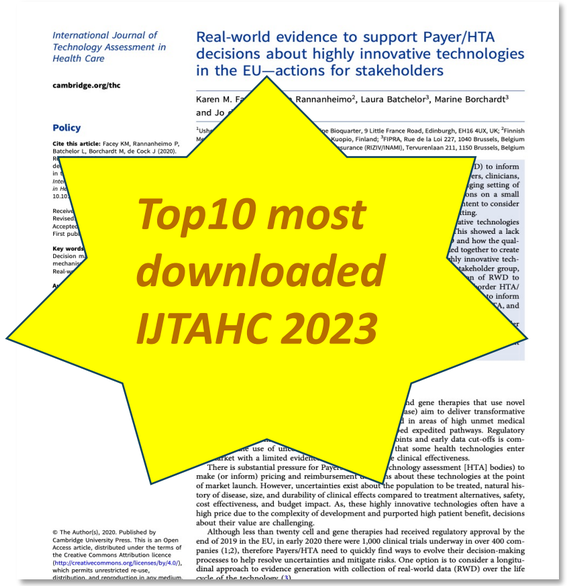
Abstract

Background: Many treatments developed for rare diseases will have an Orphan Medicinal Product (OMP) designation, indicating that they are likely to deliver benefit in an area of high unmet need. Their approval may be based on a small or uncontrolled trial, as randomised controlled trials (RCTs) of sufficient size are often difficult to conduct, or repeat, as a result of the rarity of the condition, sparsity of patients, or for ethical reasons. Furthermore, many products are given a conditional marketing authorisation, requiring additional evidence to be collected after product launch. This is even more challenging with the advent of advanced therapeutic medicinal products, which use novel scientific approaches like gene or somatic cell therapy.

Issue: Given the high unmet need associated with these products, there is pressure for Health Technology Assessment (HTA)/reimbursement bodies to enable rapid access to effective treatments. However, there is often only limited evidence available for assessment.

Methods: TRUST4RD proposes an approach to identify uncertainties of most concern for decision-makers by developing an iterative and informed dialogue amongst stakeholders (including manufacturers, clinicians, patients, regulatory- and HTA agencies and payers), so that potential approaches to resolution can be discussed. As evidence is generated, uncertainties are reviewed and prioritised, and evidence-generation plans revised or clarified accordingly. The aim is to develop – both pre- and post HTA submission – a better understanding of evidence requirements versus evidence-generation trade-offs as an evidence base grows and the potential value of a product becomes clearer.

Conclusion: TRUST4RD presents guidance on defining uncertainties and evidence gaps in the assessment of value and value for money of specialised treatments for rare diseases. It also provides guidance on the potential of Real World Evidence (RWE) to help address such uncertainties, including the typology of evidence uncertainties, the importance of different uncertainties and the data sources available to address them before and after HTA submission. In making use of the guidance, authorisation and reimbursement discussions on such treatments can be embedded in an evidence-rich context, thereby ensuring value to all parties, particularly to patients.



International Journal of Technology Assessment in Health Care

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Real-world evidence to support Payer/HTA decisions about highly innovative technologies in the EU—actions for stakeholders

Karen M. Fa… Rannanheimo[2], Laura Batchelor[3], Marine Borchardt[3] and Jo…

Policy

Cite this article: Facey KM, Rannanheimo P, Batchelor L, Borchardt M, de Cock J (2020).

There is substantial pressure for Payer… chnology assessment [HTA] bodies) to make (or inform) pricing and reimbursement … about these technologies at the point of market launch. However, uncertainties exist about the population to be treated, natural history of disease, size, and durability of clinical effects compared to treatment alternatives, safety, cost effectiveness, and budget impact. As, these highly innovative technologies often have a high price due to the complexity of development and purported high patient benefit, decisions about their value are challenging.

Although less than twenty cell and gene therapies had received regulatory approval by the end of 2019 in the EU, in early 2020 there were 1,000 clinical trials underway in over 400 companies (1,2), therefore Payers/HTA need to quickly find ways to evolve their decision-making processes to help resolve uncertainties and mitigate risks. One option is to consider a longitudinal approach to evidence generation with collection of real-world data (RWD) over the life

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Can we use existing guidance to support the development of robust real-world evidence for health technology assessment/payer decision-making?

Commentary

Cite this article: Capkun G, Corry S, Dowling O, Asad Zadeh Vosta Kolaei F, Takyar S, Furtado C, Jönsson P, Kleinermans D, Lambert L, Schiel A, Facey K (2022). Can we use existing guidance to support the development of robust real-world evidence for health technology assessment/payer decision-making? *International Journal of Technology Assessment in Health Care*, **38**(1), e79, 1–11
https://doi.org/10.1017/S0266462322000605

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Key words:
real-world data; real-world evidence; guidance; health technology assessment; payers

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G.C., S.C., O.D., F.A.Z.V.K., and S.T.: Joint first authorship.

Gorana Capkun[1*], Sorcha Corry[2], Oonagh Dowling[1], Fatemeh Asad Zadeh Vosta Kolaei[3], Shweta Takyar[4], Cláudia Furtado[3], Páll Jónsson[5], Diane Kleinermans[3], Laurie Lambert[6], Anja Schiel[7] and Karen Facey[8]

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Abstract

Advances in the digitization of health systems and expedited regulatory approvals of innovative treatments have led to increased potential for the use of real-world data (RWD) to generate real-world evidence (RWE) to complement evidence from clinical trials. However, health technology assessment (HTA) bodies and payers have concerns about the ability to generate RWE of sufficient quality to be pivotal evidence of relative treatment effectiveness. Consequently, there is a growing need for HTA bodies and payers to develop guidance for the industry and other stakeholders about the use of RWD/RWE to support access, reimbursement, and pricing. We therefore sought to (i) understand barriers to the use of RWD/RWE by HTA bodies and payers; (ii) review potential solutions in the form of published guidance; and (iii) review findings with selected HTA/payer bodies. Four themes considered key to shaping the generation of robust RWE for HTA bodies and payers were identified as: (i) data (availability, governance, and quality); (ii) methodology (design and analytics); (iii) trust (transparency and reproducibility); and (iv) policy and partnerships. A range of guidance documents were found from trusted sources that could address these themes. These were discussed with HTA experts. This commentary summarizes the potential guidance solutions available to help resolve issues faced by HTA decision-makers in the adoption of RWD/RWE. It shows that there is alignment among stakeholders about the areas that need improvement in the development of RWE and that the key priority to move forward is better collaboration to make data usable for multiple purposes.

Introduction

Real-world data (RWD) has been used for decades by regulators for pharmacovigilance purposes and by HTA for contextualization of evidence to a specific health system setting, to extrapolate outcomes and input to economic modeling. With the advancement of digitization in health systems and expedited regulatory approvals of innovative treatments, there is greater potential for the use of RWD to generate real-world evidence (RWE) to complement evidence from clinical trials. However, many health technology assessment (HTA) bodies and payers have voiced concerns about the ability to develop RWE of sufficient quality to be pivotal evidence of relative treatment effectiveness, and argue that randomized controlled trials (RCTs) should remain the key evidence base (1).

HTA is based on an evidence-based medicine paradigm, with a foundation of critical review of

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2016/2017	2018	2020	2022
Use of RWD throughout medicine's lifecycle Outcomes based pricing & reimbursement of medicines with budgetary limitations	TRUST4RD Tool for Reducing Uncertainties in evidence generation for Specialised Treatments for Rare Diseases	RWE4Decisions recommended actions for stakeholders to support payer/HTA decisions about highly innovative technologies	Can we use existing guidance to support development of robust RWE for HTA/payer decision-making?

More key takeaways from 2022

6 Importance of **HTA Regulation implementation**

7 **Define priorities for use of RWD by Payers**

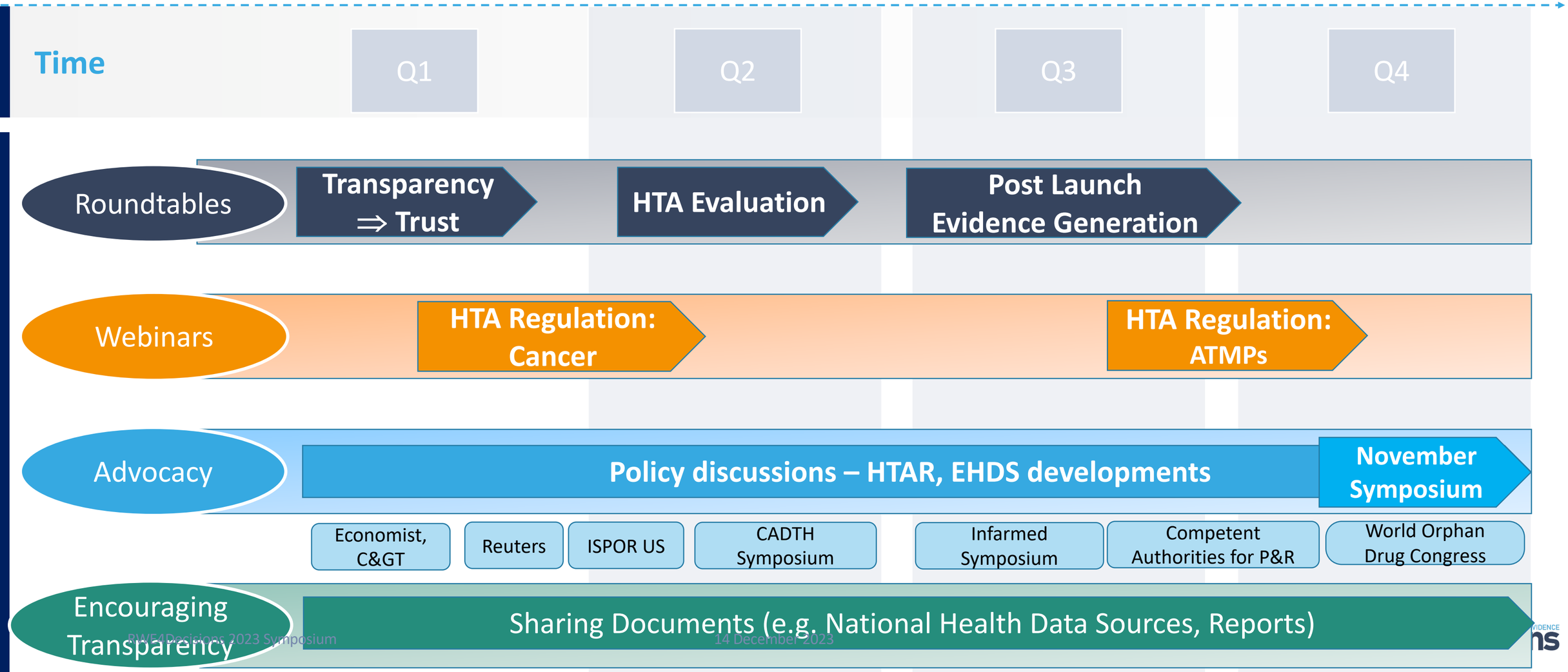
8 **Discuss cross border data strategies for RWD collection** - EHDS, EU-wide disease registries to meet payers needs, cross border collaboration etc

9 Share experiences of implementation of **Outcomes-Based Managed Entry Agreements/ Post Launch Evidence Generation (PLEG)**

10 **Coordinate and share learnings**

RWE4Decisions 2023

A variety of ways of learning across the multi-stakeholder network



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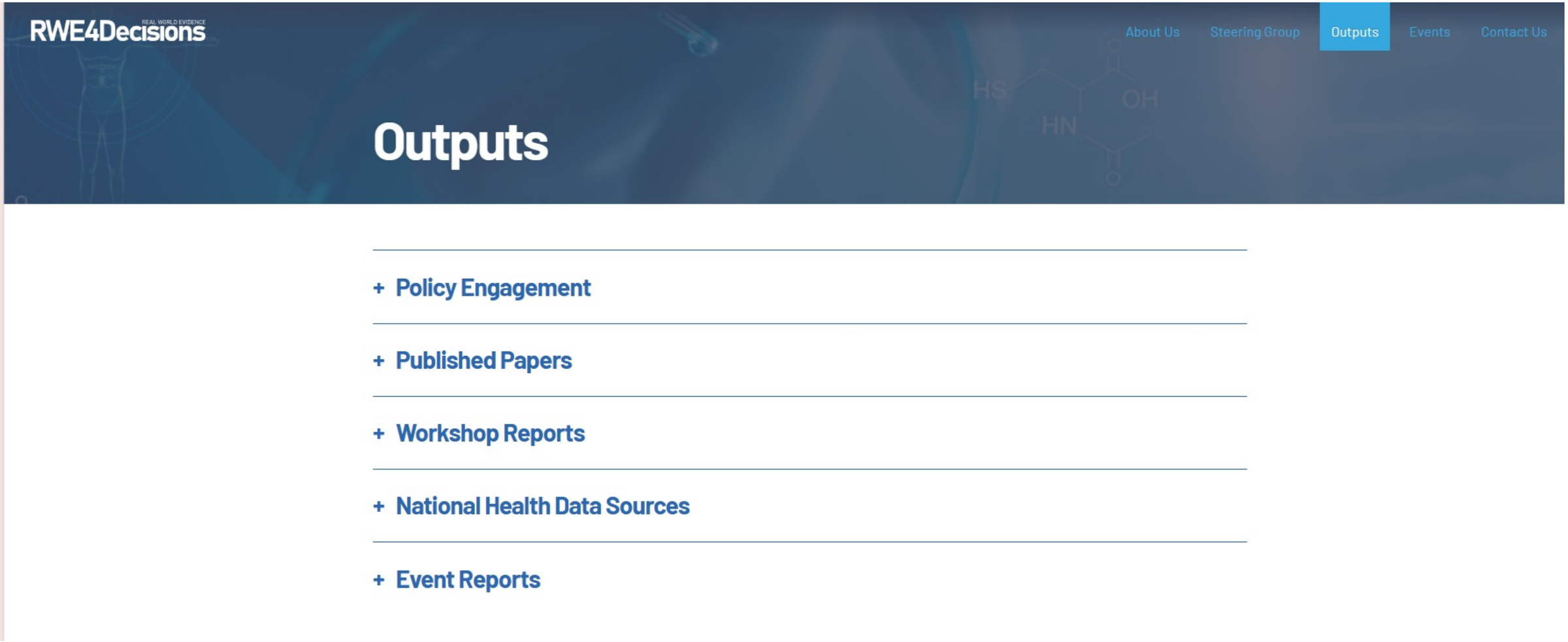

IQWiG

IQWiG Reports – Commission No. A19-43

Concepts for the generation of routine practice data and their analysis for the benefit assessment of drugs according to §35a Social Code Book V

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ASSESS
HEALTH TECHNOLOGIES

METHODOLOGICAL GUIDE

Real-world studies for the assessment of medicinal products and medical devices

REPORT January 2022

Generating Evidence from Real-World Data in Health Technology Assessment

Methodological guideline

NICE National Institute for Health and Care Excellence

NICE real-world evidence framework

cadth Canada's Drug and Health Technology Agency

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

1 17 April 2023
2 EMA/CHMP/564424/2021
3 Committee for Medicinal Products for Human Use (CHMP)

4 Reflection paper on establishing efficacy based on single-5 arm trials submitted as pivotal evidence in a marketing 6 authorisation

7 Considerations on evidence from single-arm trials

8 Draft

Draft agreed by Drafting Group on single-arm trials	27 January 2023
Adopted by CHMP for release for consultation	17 April 2023
Start of public consultation	21 April 2023
End of consultation (deadline for comments)	30 September 2023

9

Comments should be provided using this template. The completed comments form should be sent to RP-SATs@ema.europa.eu

10

Keywords	Single-arm trials, non-randomised trials, regulatory decision making

11

Real-world data and real-world evidence in regulatory decision making

CIOMS Working Group report
Draft, 6 June 2026

This report was posted for comment on 6 June 2023 at: https://cioms.ch/working-groups/real-world-data-and-real-world-evidence-in-regulatory-decision-making/.

The CIOMS Working Group (WG) XIII welcomes your input to the report, or any parts of it. A list of WG XIII members can be found on the CIOMS website. A detailed list will be appended to the final report.

Please note that the layout will be improved in the final version, and best efforts will be made to correct remaining typographical and/or grammatical errors, as well those pertaining to references.

Permissions are being sought to reproduce some of the illustrative materials included in this report. We welcome responses from organisations that own any of these materials and have not yet been contacted in this regard.

Please submit your comments using the form posted on the CIOMS website at https://cioms.ch/working-groups/real-world-data-and-real-world-evidence-in-regulatory-decision-making/.
The timeline for submission of comments is 14 July 2023.

Thank you.

CADTH Methods and Guidelines

Guidance for Reporting Real-World Evidence

May 2023

To conclude, in itself, RWD does not define a type of clinical study design and RWE can be produced with varying certainty of results for a given research question. Therefore, the certainty of results that is produced, especially the level of internal validity, is mainly determined by the study design of a given clinical study based on the use of RWD. Especially because most clinical studies using RWD are currently not RCTs, controlling for confounding bias is one of the main issues when estimating treatment effectiveness. Indeed, the lack of randomisation requires the proper use of methods to control for confounding bias (see Section 4.2), which rely on assumptions (e.g., the assumption of exhaustivity on confounders and effect modifiers) that are, in part, unverifiable.

Practical Guideline (Requirement for JCA reporting)

RWD is not a design *per se*; thus, the design of a clinical study should be described and classified according to the principles already described in this guideline.

RoB should be assessed according to the principles already described in this guideline.

Specific points of attentions

For a given clinical study, it should be reported if RWD are the sole source of data, or a primary source of data complemented by a secondary source specifically collected for research purposes (and, if so, to which specific design it corresponds).

Given the at least partial use of data that were not initially structured for clinical research, the validity and reliability of RWD for adequately answering a given research question is of particular importance, especially the potential use of proxy variables, the risk of attrition bias, and the adequate measurement of endpoints.

Effective RWD collection post-launch
RWE4Decisions 2021 updated during 2023

Horizon Scanning to anticipate need for PLEG
Rx/indications, types (e.g. gene Txs) conditions?

0 Early and iterative dialogues/scientific advice/joint scientific consultations

1 Identify the decision-relevant uncertainties (real-life effectiveness, sub-populations, etc) and judge whether they can be resolved by patient relevant outcomes collected in clinical practice

2 Link data collection to pricing and reimbursement agreement, and assess feasibility to collect the data required within a reasonable timeframe

3 Collaborate across jurisdictions, with EMA and stakeholders
And publish data collection plans

Effective RWD collection post-launch

RWE4Decisions 2021 updated during 2023

4 Monitoring processes to ensure onboarding of centres, inclusion of appropriate patients, quality of data collection

5 Investment in data collection infrastructure (national monitoring system, registries etc)

6 Reports published in an easily accessible place that show learnings from accumulated data

Effective RWD collection post-launch

RWE4Decisions 2021 updated during 2023

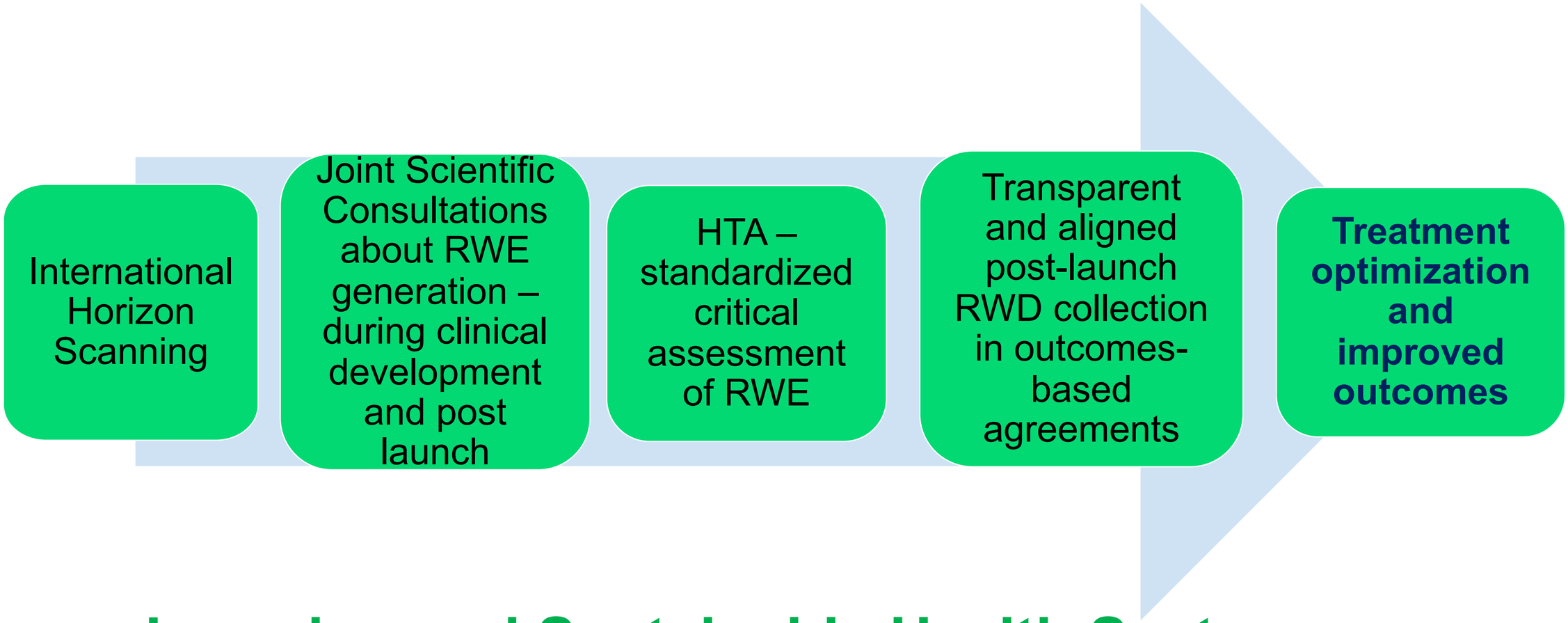
4 Monitoring processes to ensure onboarding of centres, inclusion of appropriate patients, quality of data collection

5 Investment in data collection infrastructure (national monitoring system, registries etc)

6 Reports published in an easily accessible place that show learnings from accumulated data

7 **Align data collection plans, learn from other jurisdictions**

A purposeful approach to RWE generation over the life cycle of high cost, innovative medicines in areas of high unmet need, where data can be collected that demonstrate patient benefit



Learning and Sustainable Health System

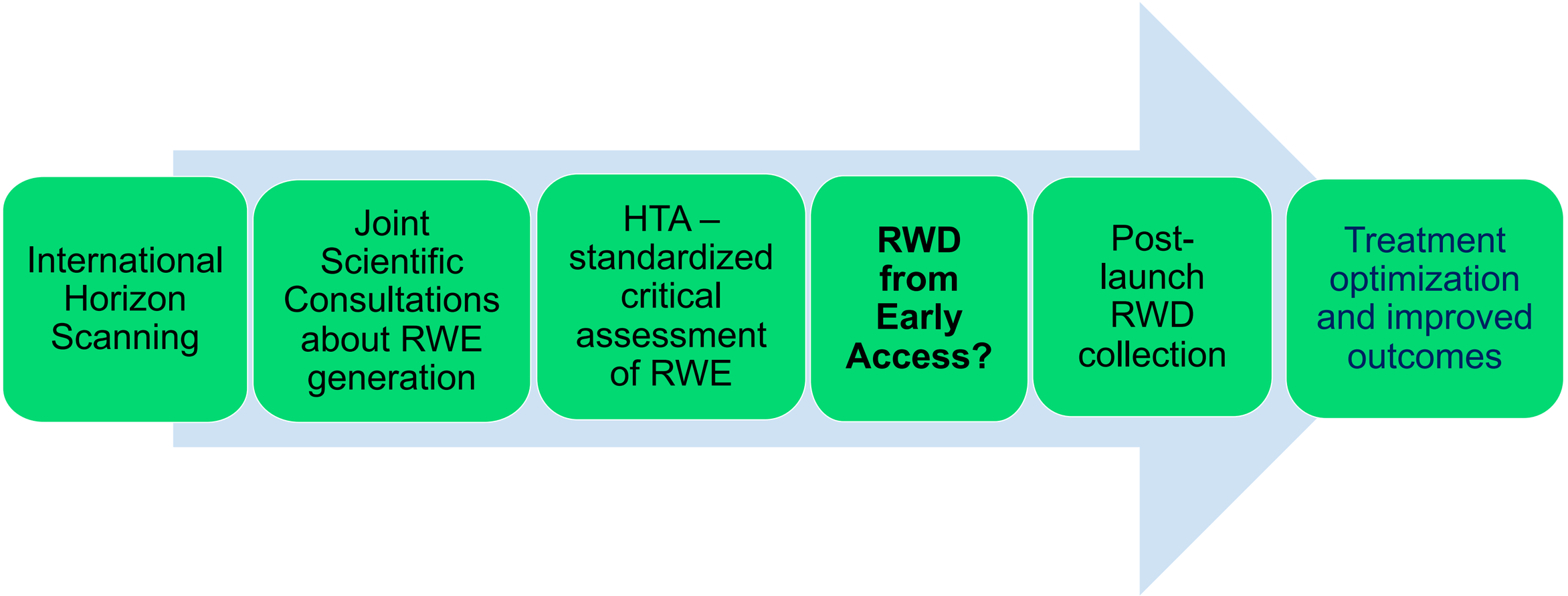
The Potential for Collecting Real-World Data in Early Access to Inform HTA/Payer Decisions

RWE4Decisions Symposium

REAL-WORLD EVIDENCE OVER THE MEDICINE'S LIFECYCLE TO INFORM HTA/PAYER DECISIONS

23 NOVEMBER 2023
BIP MEETING CENTER, BRUSSELS

Covering the entire life cycle of RWE generation Early Access?



The Potential for Collecting Real-World Data in Early Access to Inform HTA/Payer Decisions

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Senior Researcher, Università Cattolica del Sacro Cuore Roma

Review of Early Access schemes in relation to HTA

Entela Xoxi

PharmD, PhD, MSci

Lecturer with Collaboration Agreement for Research Projects

UNIVERSITÀ CATTOLICA del Sacro Cuore Rome - ALTEMS

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ALTA SCUOLA DI ECONOMIA E MANAGEMENT DEI SISTEMI SANITARI

UNIVERSITÀ CATTOLICA del Sacro Cuore

Purposes of Early Access Schemes (EAS)

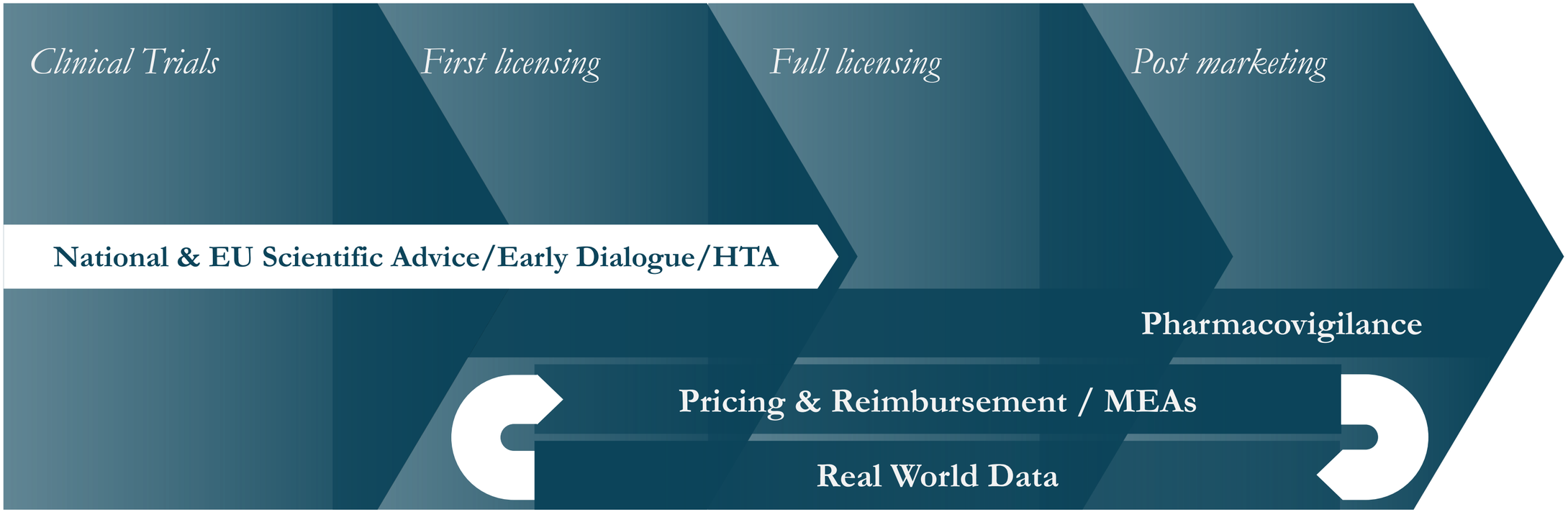
- **To provide access to treatment options in advance of the standard codified pathway for patients with a high unmet therapeutic need, options that are presumed to have a clinically significant impact on patients.**

- **EAS offer a potential advantage not only for patients**, but also for Health Technology Assessment for the purposes of decisions on price, reimbursement and other access conditions, for healthcare system and the pharmaceutical industry.

- **The EAS do not exclude evaluation by regulatory bodies and/or HTAs and payers**. Indeed, these schemes, in addition to offering early access to patients, create an **opportunity to acquire new data** and, possibly, evidence (to complement pivotal clinical trials).

  - Some EAS are in fact associated with data collection programs (real-world) and acquisition of Real-World-Evidence (RWE) in the period between phase II-III and MA, extended in in some cases to the period up to the P&R decision, further supporting the product value proposition.

Progressive authorisation lifecycle



Definitions

01

REGULATORY

02

NATIONAL

HTA/ PAYER

03

CHALLENGES FOR RWD

01

Regulatory

EMA

Provisions to foster patients' early access to new medicines that address public health needs and are eligible for the centralised procedure *such as:*

- Compassionate use program (CUP) or Expanded Access Program (EAP)
  - *Named-patient based compassionate use*
- Accelerate assessment (AA)
  - *PRIME scheme*
- Conditional Marketing Authorisation (CMA)
  - *Exceptional circumstances*

CUP

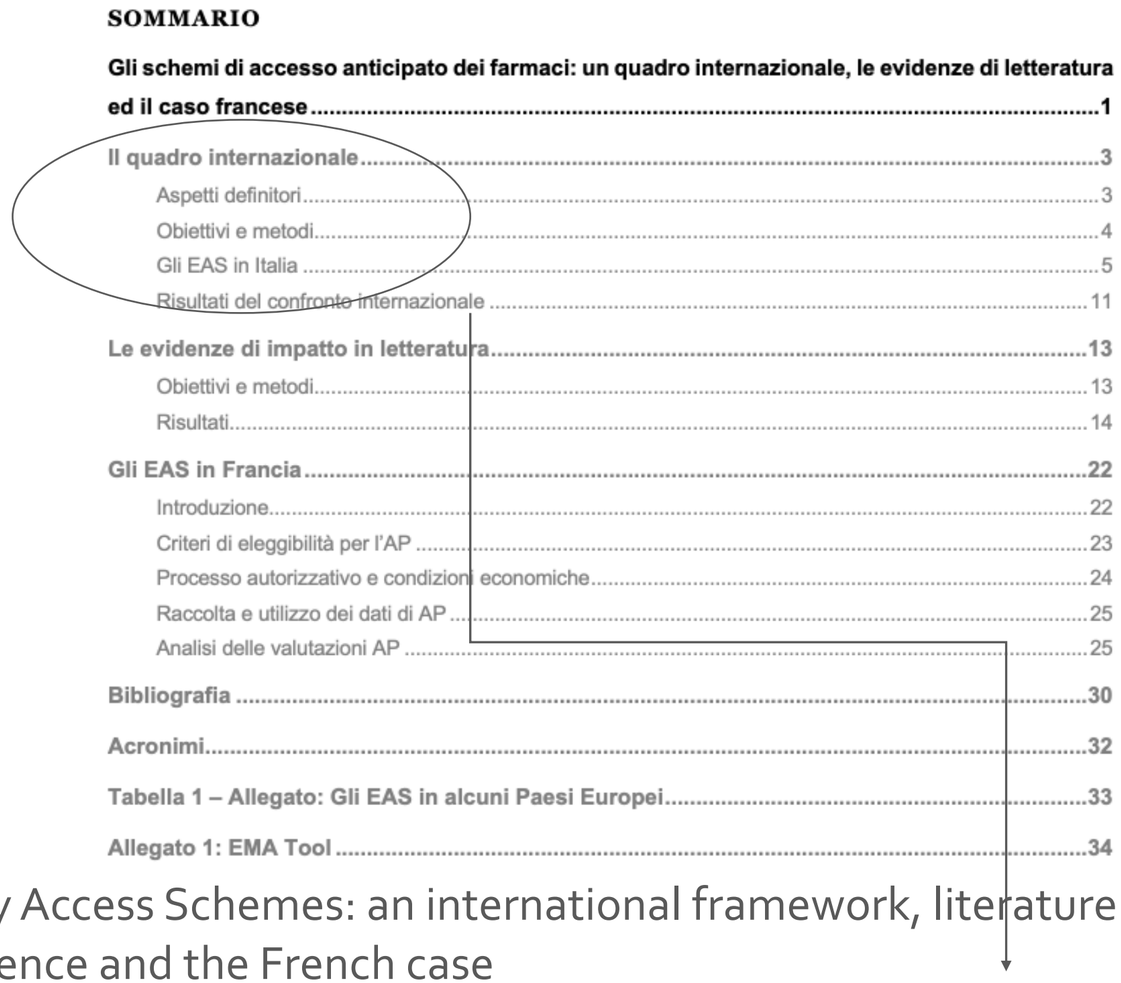
Type of mechanism	Regulatory tool for early access
Medicines eligible	Unauthorised medicinal products: • for chronically, seriously debilitating or life threatening diseases, with no satisfactory treatment authorised in the EU; • targeted at a group of patients rather than an individual; • undergoing centralised marketing-authorisation applications or clinical trials; • falling under the mandatory or optional scope of centralised procedure.
When to apply	CHMP opinion on compassionate use cannot be requested by applicants, they should liaise with national competent authorities
Key features	• Benefits seriously ill patients who cannot be treated satisfactorily or cannot enrol in ongoing clinical trials • CHMP recommendations to Member State to harmonise the conditions of use, distribution and the target population

In general, medicines that are not yet authorised are first made available through clinical trials and patients should always be considered for inclusion in trials **before** being offered CUP.

ISPOR
Italy-Rome Chapter

Early Access Working Group

Report in Italian coming soon

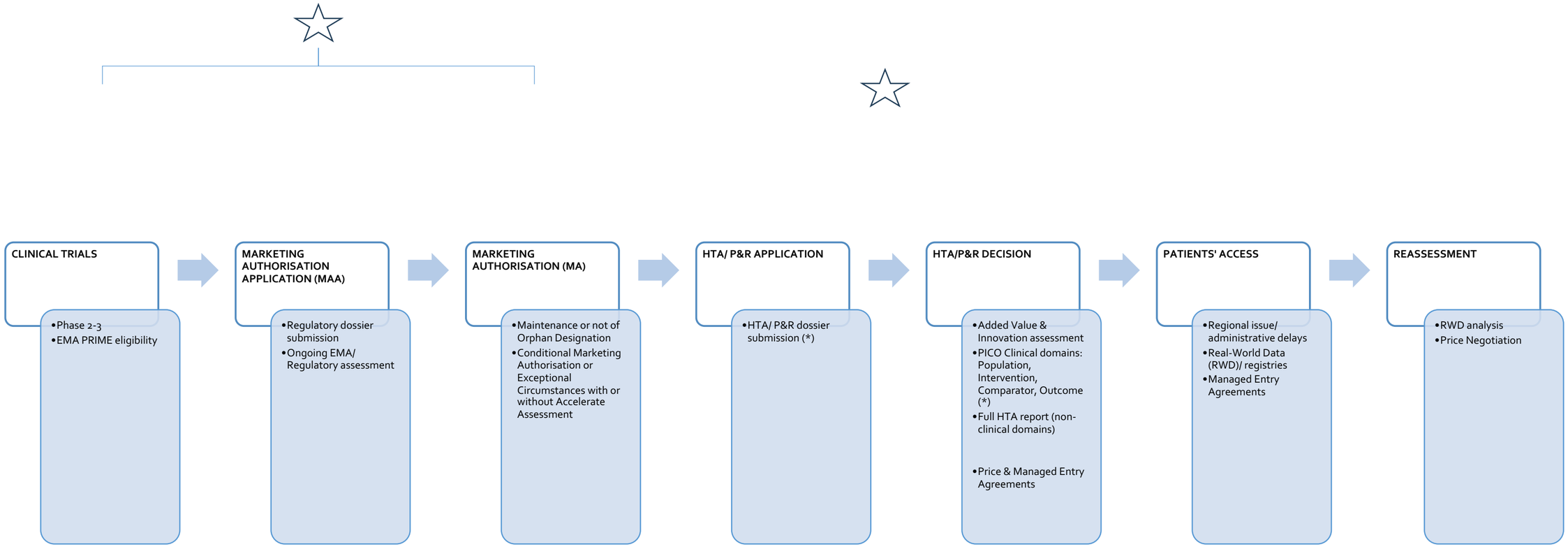


SOMMARIO

Early Access Schemes: an international framework, literature evidence and the French case

- Countries with EAS financed by the public health system (Belgium, France, Italy, Greece, Netherlands, Spain)
- Countries with only CUP, or schemes not financed by the public healthcare system (Austria, Denmark, Germany, UK)

Possible Early Access Schemes



Early access scheme

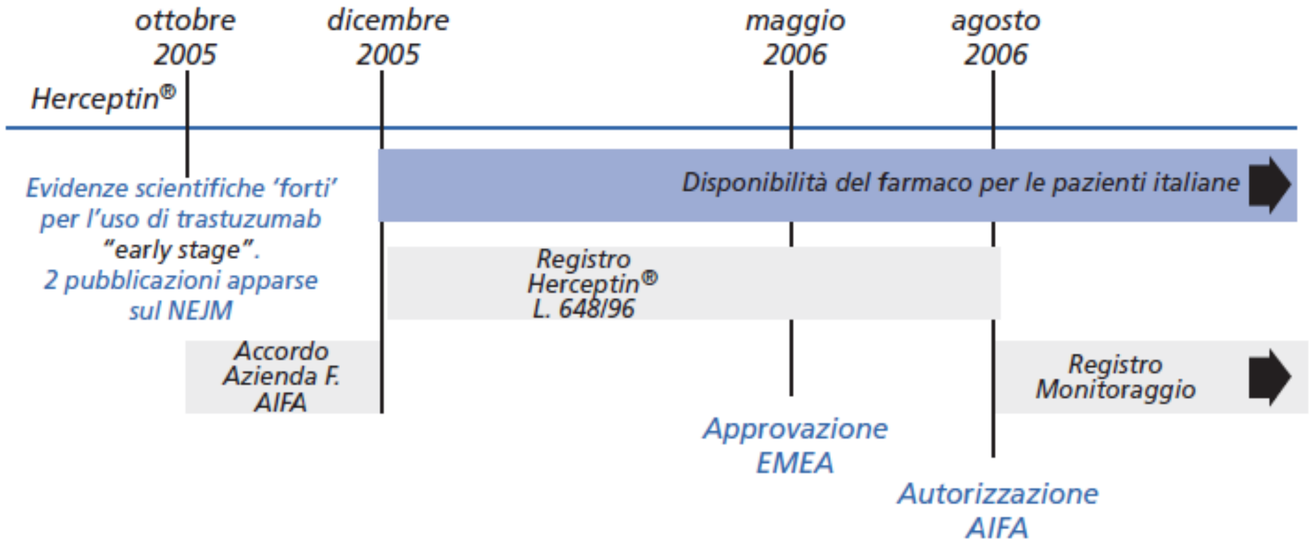
National
HTA/ Payer

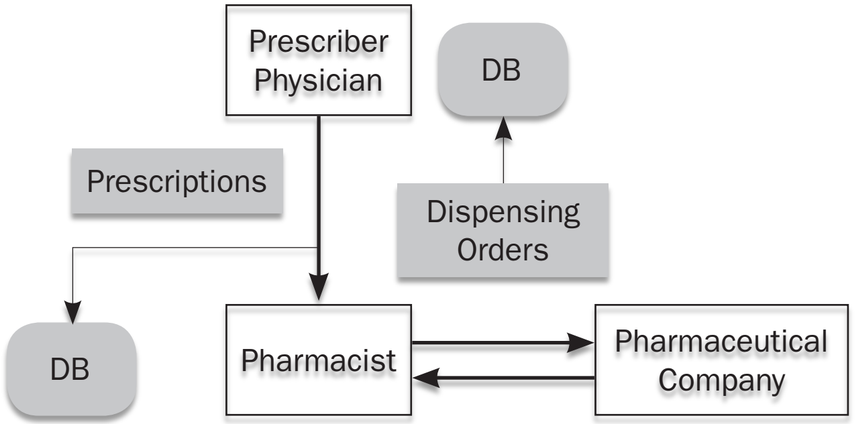
Early access in Italy

Requirements	648/1996 Law[2] (Early access + off-label)	326/2003 Law (National 5% AIFA Fund)	07 Sept. 2017 Ministerial Decree (Compassionate use)	94/1998 Law (former Di Bella Law – off label)
Lack of treatment alternatives	YES	Not detailed	YES	YES
Informed consent	YES	Not detailed	YES	YES
Scientific evidence	Positive results form Ph.2 studies	Rare diseases Not detailed	Positive results form Ph.3 studies, or Ph.2 for life threatening conditions[1]	Positive results form Ph.2 studies
Authorisation	AIFA	AIFA	Ethic Committees Notification to AIFA	Ad-hoc hospital Commission
Medical liability	YES	Not detailed	YES	YES
Monitoring and data trasmission	Clinical & economic monitoring	Not detailed	Limited to safety	Not detailed
Payer	NHS	AIFA	Free supply by Pharma Company	Patient, or NHS in case of hospitalisation

1. In the case of rare diseases or rare tumors, at least Phase I clinical trials, already concluded, that have documented the activity and safety of the medicine (not applicable to ATMPs)
2. Pricing negotiation (AIFA GL 2020)

AIFA registries tool started with an early access





National
HTA/ Payer

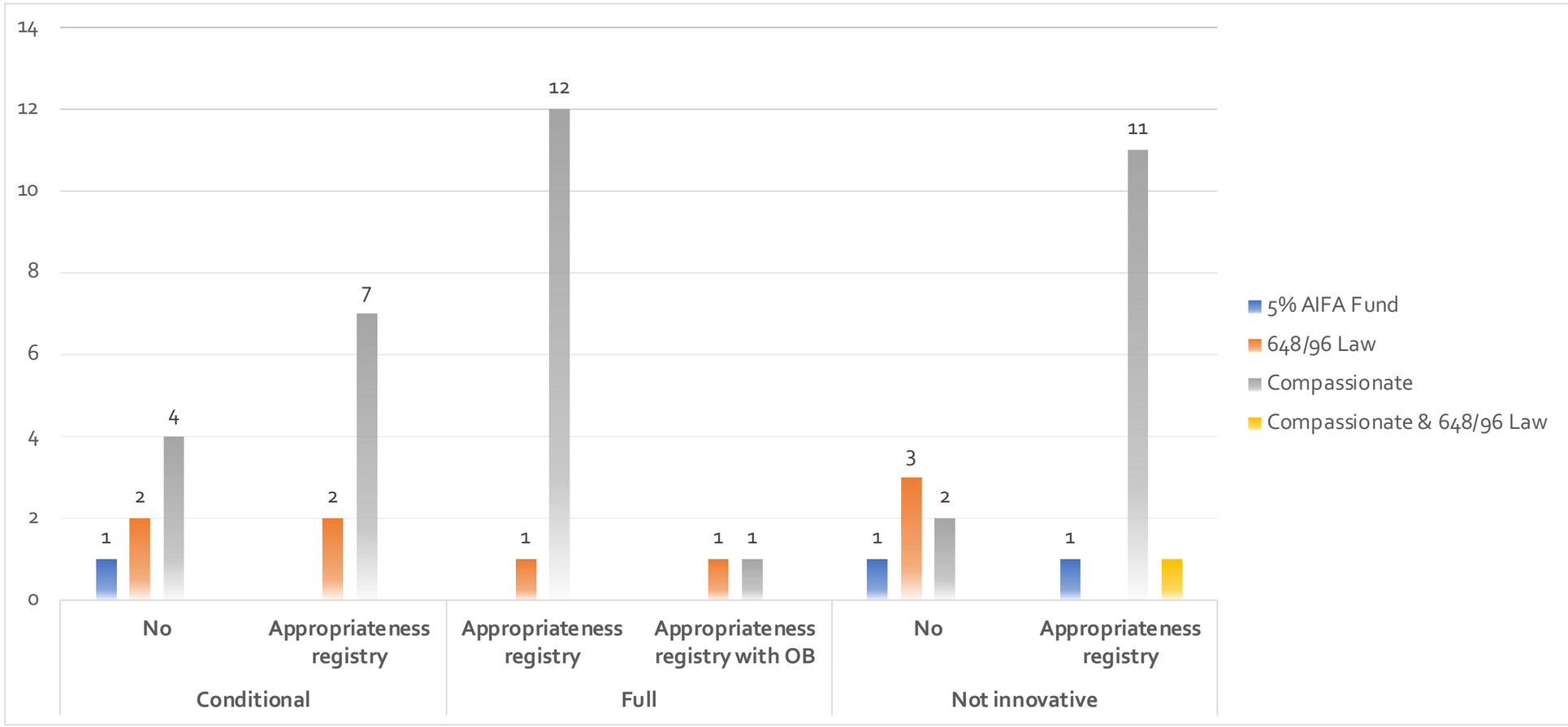
Possible Early Access Schemes and RWD

- CUP (Industry)
- National Early Access Tools with RWD (HTA/Payers)
  - 7 AIFA registries 648/96 Law
  - 1 AIFA registry 5% Fund

Regional/
Hospital

☆ Early access scheme

Impact of recognition of innovation and registries for those drugs with an Early access

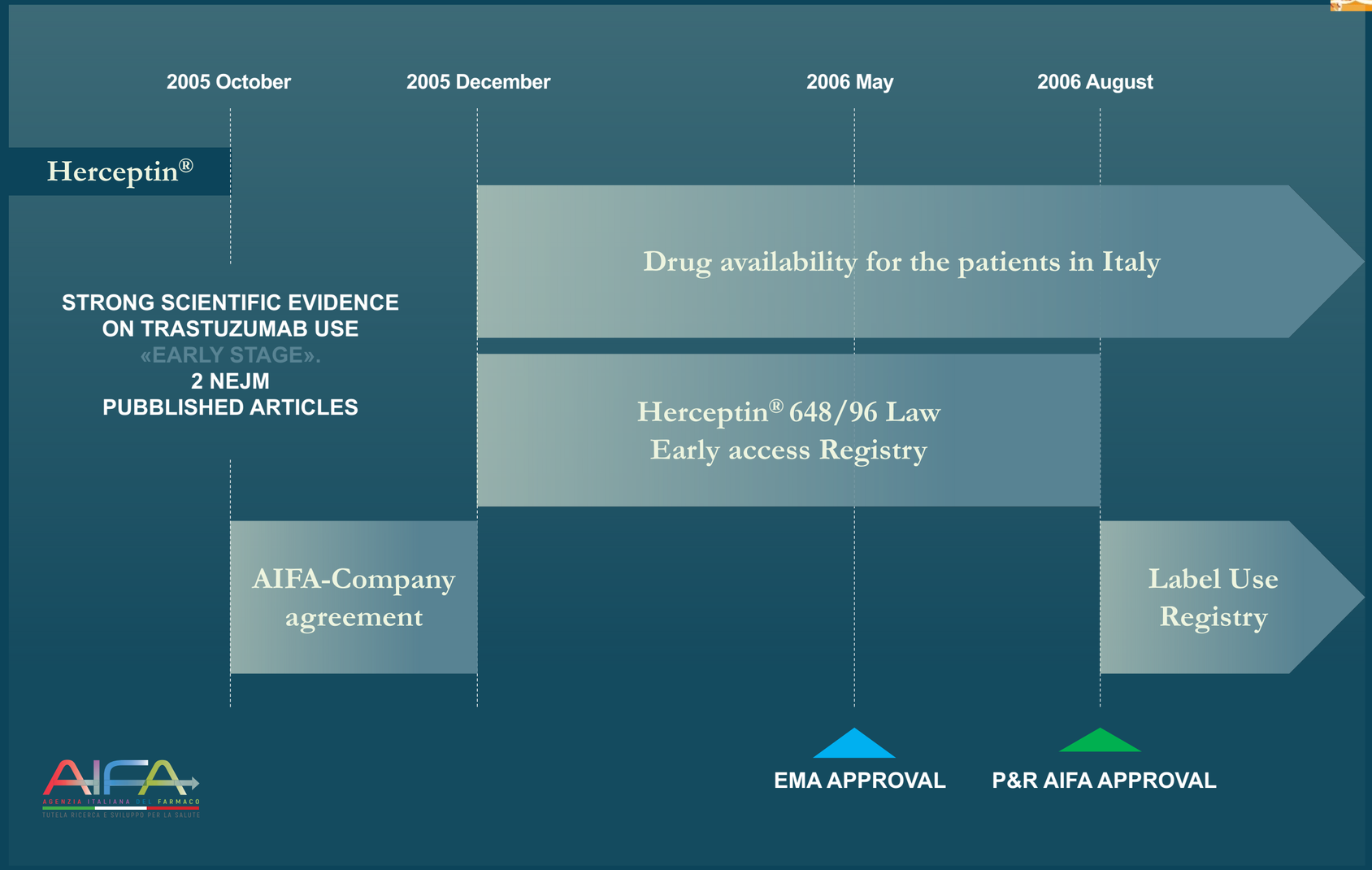


Work in progress on Early access in Italy and impact on the Innovation and HTA decisions: 50 therapeutic indications. Update Nov 2023

Case 1

Registry Trastuzumab in Metastatic Breast Cancer

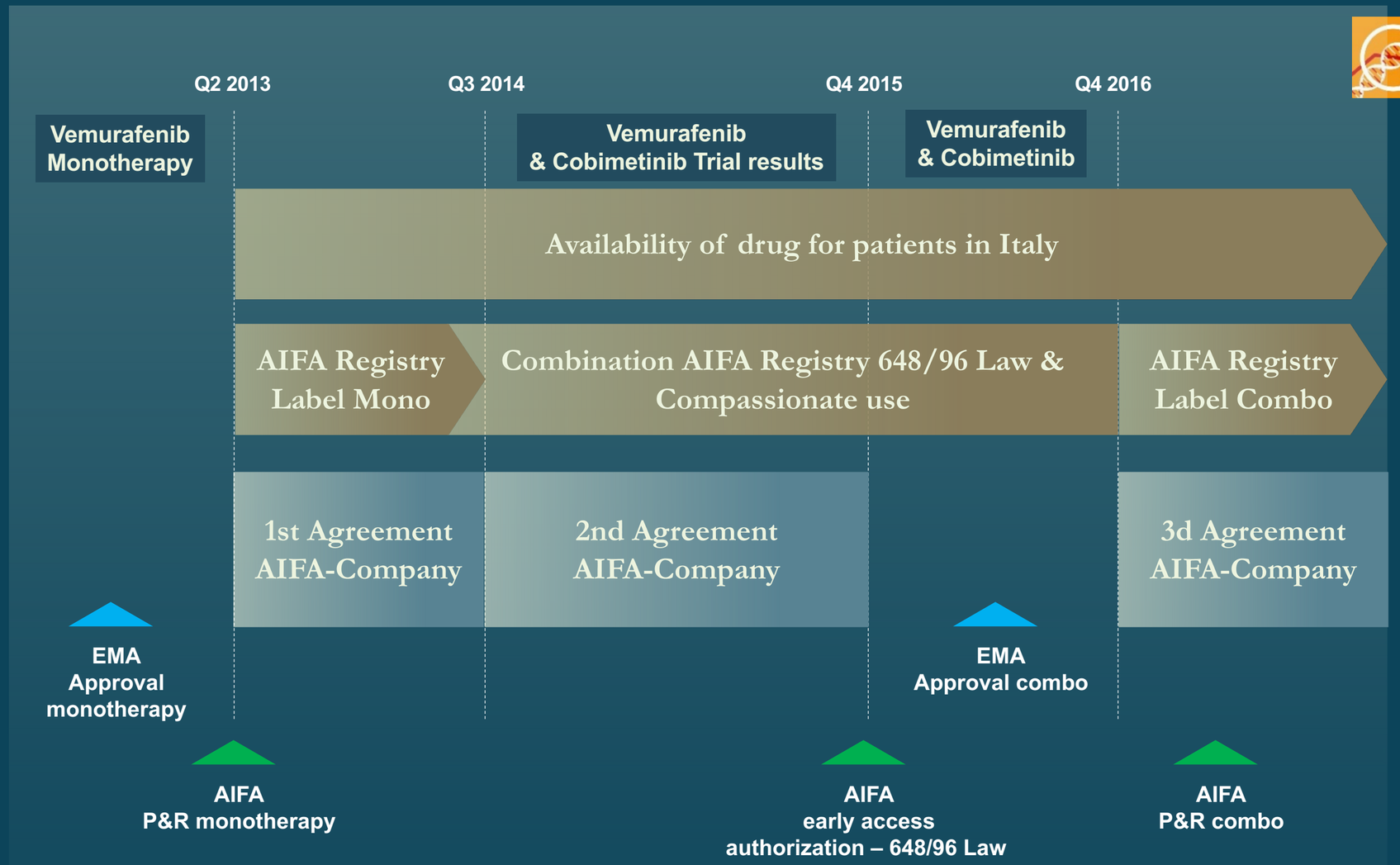
- Early access reimbursed by NHS and mandatory data collection by AIFA Registry
- Dynamism moving from an early access to Patient Access

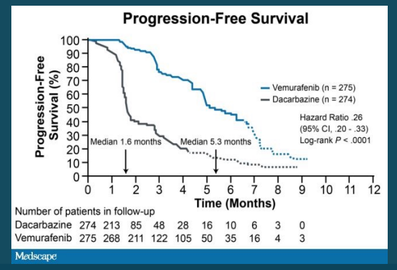


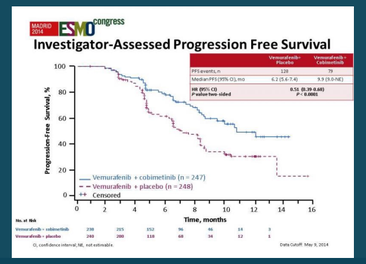
Case 2

Registry BRAF & MEK inhibitor combination

Adaptive Performance-based risk sharing agreements including an early access scheme for the combination therapy







Thank you

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The Potential for Collecting Real-World Data in Early Access to Inform HTA/Payer Decisions

Camille Thomassin

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Early access to medicinal products in France: HTA perspective

Potential for collecting RWD in Early Access to inform HTA/Payer decisions

RWE4Decisions Symposium – 23rd November 2023

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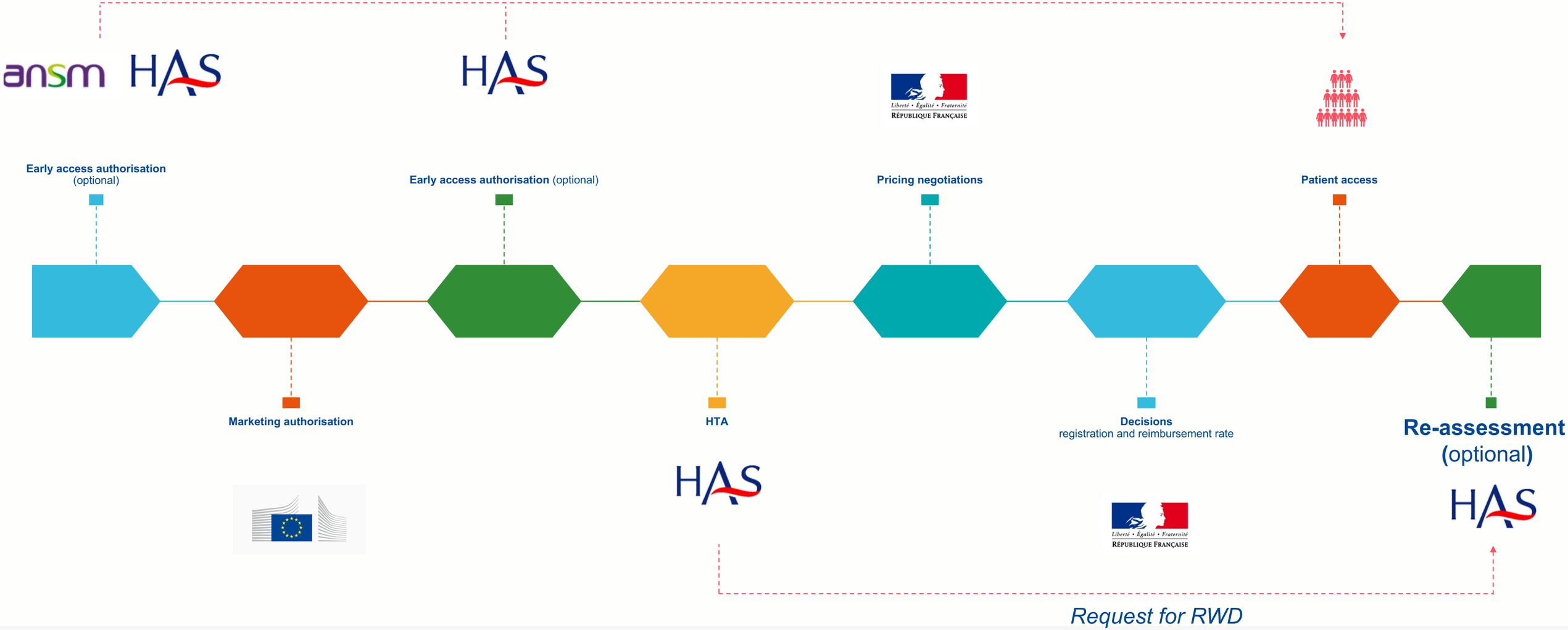
HAS
HAUTE AUTORITÉ DE SANTÉ

Disclosures of Interests

No affiliations. I’m employed by the French National Authority for Health .

Market access pathway in France – *medicinal products*



Focus on early access – *medicinal products*

Authorisation procedure for early access reformed in July 2021.

Allow access and coverage before final decision on reimbursement.

- Can be granted by HAS before MA (MA must be submitted within 2 years) or after MA
- Fast track process : 90 days maximum
- HAS = decision making body

5 eligibility criteria:

- Acceptable preliminary benefit risk ratio
- Serious, rare or debilitating disease
- Responding to unmet need (no treatment or only unsatisfactory treatment available)
- Access to treatment cannot be delayed
- Assumed innovative, notably compared to current standard of care

More information here and here

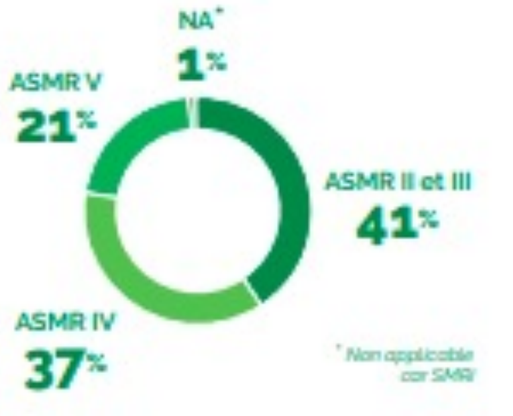
2-year review of EAPs in France

- **98** positive EA initial decisions (oncology is the main therapeutic area).
- **86/98** already evaluated for routine reimbursment (*with at least a minor therapeutic progress recognized for 78% of the dossiers => direct impact on price negociations*).
- Average time between EAA and inscription on the list(s) for routine reimbursment is 9 months.

Haute Autorité de Santé - Accès précoce des médicaments : un bilan positif après deux ans de mise en place du dispositif (has-sante.fr)

Accès précoce des médicaments : un bilan positif après deux ans de mise en place du dispositif

ÉTUDES ET RAPPORTS - Mis en ligne le 23 oct. 2023



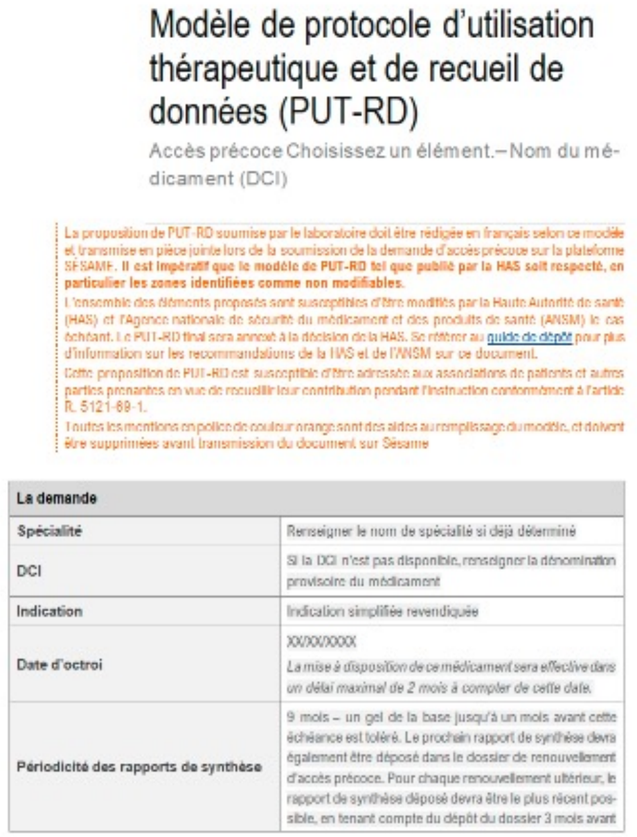
ASMR V = no clinical added value

Requirements on real world data arising from early access

- Mandatory real world data collection for each patient, defined by HAS (+/- ANSM):

Minimum data set with Patient characteristics, Conditions of use; Efficacy, including impact on quality of life/ symptoms/disability using a patient reported outcome measure (PROM), Safety.

- The format of the data to be collected is standardized in the Protocol for temporary use and data collection (PUT-RD).
- Data collected under care routine conditions. Not intended to replace clinical trials.
- Pharma companies are legally responsible for data collection and support the associated costs. Financial compensation for data collection are given to the hospitals (based on a signed agreement).
- Data collection provide input for the assessment of the medicinal product by the HAS for early access authorisation renewal and, eventually, for the assessment for reimbursement (including re-assessment if applicable).



Modèle de protocole d'utilisation thérapeutique et de recueil de données (PUT-RD)

Accès précoce Choisissez un élément.– Nom du médicament (DCI)

La proposition de PUT-RD soumise par le laboratoire doit être rédigée en français selon ce modèle et, transmise en pièce jointe lors de la soumission de la demande d'accès précoce sur la plateforme SESAM**. Il est impératif que le modèle de PUT-RD tel que publié par la HAS soit respecté, en particulier les zones identifiées comme non modifiables.**

L'ensemble des éléments proposés sont susceptibles d'être modifiés par la Haute Autorité de santé (HAS) et l'Agence nationale de sécurité du médicament et des produits de santé (ANSM) le cas échéant. Le PUT-RD final sera annexé à la décision de la HAS. Se référer au guide de dépôt pour plus d'information sur les recommandations de la HAS et de l'ANSM sur ce document.

Cette proposition de PUT-RD est susceptible d'être adressée aux associations de patients et autres parties prenantes en vue de recueillir leur contribution pendant l'instruction conformément à l'article R. 5121-69-1.

Toutes les mentions en police de couleur orange sont des aides au remplissage du modèle, et doivent être supprimées avant transmission du document sur Sésame

La demande	
Spécialité	Renseigner le nom de spécialité si déjà déterminé
DCI	Si la DCI n'est pas disponible, renseigner la dénomination provisoire du médicament
Indication	Indication simplifiée revendiquée
Date d'octroi	XX/XX/XXXX *La mise à disposition de ce médicament sera effective dans un délai maximal de 2 mois à compter de cette date.*
Périodicité des rapports de synthèse	9 mois – un gel de la base jusqu'à un mois avant cette échéance est toléré. Le prochain rapport de synthèse devra également être déposé dans le dossier de renouvellement d'accès précoce. Pour chaque renouvellement ultérieur, le rapport de synthèse déposé devra être le plus récent possible, en tenant compte du dépôt du dossier 3 mois avant

Integration of patients' perspective

Almost 80% of approved PUT-RD include a PROM (pre-autorisation EAA).

Patients association involvement for the choice of the PROM, if necessary

Example of PROMs frequently used in EAPs:

- **specific questionnaires: EORTC-QLQ-C30 in oncology, DLQI in dermatology, …**
- **generic questionaires: SF-12, SF-36, PedsQL, …**

How to optimize the data for their use in assessment?

Early « enough » access, so that data are available in the dossiers for the first assessment for reimbursment (or for a timely re-assessment)

Simplification of data collection for clinicians, pharmacists, and patients

Use of existing data sources, e.g. registries (see current work of HAS to enhance data discoverability)

Data quality and exhaustivity

Adapted methodology for the analysis of the data

Patients association involvement for the choice of the PROM

Clinician's expertise for drafting the data collection

Re-use of data for research purposes, in the context of post-autorisation studies (linkage with other databases or use for comparison vs an external control)

Back-up slides

A unique cooperation for EA in rare diseases in France

- Collaboration between the French National Registry for Rare Diseases (BNDMR), HAS, ANSM (regulator) and French Ministry of Health.
- The BNDMR warehouse gathers data collected through the app BaMaRa, in the format of a Minimal Data Set for rare disease, already used by healthcare professionals.
- In 2023, development of an additional Minimal Data Set to capture data on efficacy of the treatments (**Treatment - Minimal Data Set**) that can **be used for data collection in EA.**
- **A dedicated template of PUT-RD published by HAS in July 2023 for EA in RD (here).**
- Improves predictability for manufacturers in terms of the format of data requested and optimizes data collection. Enhance the re-use of data for research purposes.
- **The systematic involvement of rare disease networks reinforce the relevance of the data collected.**

First EAs with BaMaRa data collection coming soon…

Thank you for your attention!

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www.has-sante.fr

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The Potential for Collecting Real-World Data in Early Access to Inform HTA/Payer Decisions

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Closing Session: Building Better RWE for Decisions – What's Next?

RWE4Decisions Symposium

REAL-WORLD EVIDENCE OVER THE MEDICINE'S LIFECYCLE TO INFORM HTA/PAYER DECISIONS

23 NOVEMBER 2023
BIP MEETING CENTER, BRUSSELS

Keynote address from INAMI-RIZIV

Pedro Facon

Deputy CEO, National Institute of Health and Disability Insurance, Belgium (INAMI-RIZIV)

Looking ahead to the Belgian EU Presidency

Closing Session: Building Better RWE for Decisions – What's Next?

Niklas Hedberg

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Matti Aapro MD

Oncologist, Genolier Cancer Center

Simone Boselli

Public Affairs Director, EURORDIS-Rare Diseases Europe

Anna Filonenko

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Closing remarks

Looking ahead to 2024 – the RWE4Decisions agenda

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REAL WORLD EVIDENCE
RWE4Decisions Symposium

Thank you for your contributions!

Lunch will follow

The recording will be available on our website
www.rwe4decisions.com

Stay in touch on
secretariat@rwe4decisions.com
and keep up to date on social media

See you in November 2024!