MEMORANDUM

Health Innovation - the European Health Data Space and Real-World Evidence

10 November 2020

An event of the Federal Ministry of Health associated programme within Germany's Presidency of the Council of the European Union.

RWE4Decisions REAL WORLD EVIDENCE

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On 10 November, the **RWE4Decisions initiative** held a conference at which it launched a call for a multi-stakeholder Learning Network on Real-World Evidence within the European Health Data Space. The Conference was hosted under the auspices of the German EU Presidency and brought together payers, HTA authorities, health policy decision-makers, patient representatives, clinicians, researchers, industry representatives, data analytics groups and academics.

MODERATOR

Jacki Davis

Dr. Véronique Trillet-Lenoir
Member of the European Parliament

Dr. Véronique Trillet-Lenoir, Member of the European Parliament, opened the conference outlining that scientific advancement requires health data to be shared and processed, and undesirable bias avoided. National initiatives to share data exist, but interoperability at an EU level is essential. Data analysis needs to go hand-in-hand with scientific rigour, to bridge the gap between real-world data (RWD) and real-world evidence (RWE). RWD complements rather than replaces data collection from controlled clinical trials. The challenge is to find the right balance between privacy protection and data utility, and trust is a key factor for success.

Stella Kyriakides
European Commissioner for Health

Stella Kyriakides, EU Commissioner for Health, introduced the European Commission's health priorities and the EU Health Data Space. She said that the digitalisation of the EU's health systems is fundamental to improving the lives of patients. The European Health Data Space will enable and empower cooperation, strengthen citizens' access to and portability of their data, and eliminate barriers to the cross-border provision of digital health. The goal is to step up health data exchange and support research on new preventive strategies, treatments, medicines, medical devices and outcomes. In all these areas, RWD plays a vital role, but requires a common governance and interoperability framework for optimal data exchange.

Session 1:
ASSESSING THE VALUE OF REAL-WORLD EVIDENCE IN THE INNOVATION PROCESS

Dr. Karen Facey
Senior Research Fellow at the University of Edinburgh

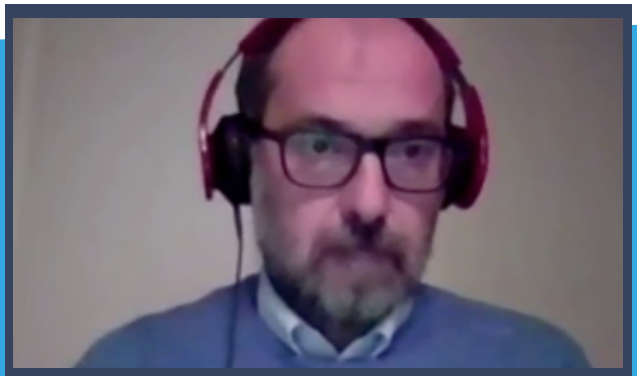
Simone Boselli
Public Affairs Director at EURORDIS-Rare Diseases Europe

Prof. Maurizio Scarpa
Coordinator of MetabERN, Regional Coordinating Centre for Rare Diseases, Udine University Hospital, Italy

Mercedes Echauri
Vice-President Market Access Europe and Canada at Takeda

Dr. Karen Facey
Senior Research Fellow at the University of Edinburgh

Dr. Karen Facey, Senior Research Fellow at the University of Edinburgh introduced TRUST4RD – Tool for Reducing Uncertainties in the evidence generation for Specialised Treatments for Rare Diseases. She outlined that the key concept of TRUST4RD is to understand what RWD can help to resolve uncertainties that commonly occur when determining the value of new treatments for rare diseases. Uncertainties are related to the size and characteristics of the population; the natural history of the disease and its current management; new treatments; and the health ecosystem in terms of treatment implementation. More dialogue with all stakeholders is essential to identify key evidence gaps in determining value; identify potential RWD solutions; and to trade-off between where evidence could be generated vs. where it's needed.



Simone Boselli
Public Affairs Director at EURORDIS-Rare Diseases Europe

Simone Boselli, Public Affairs Director at EURORDIS-Rare Diseases Europe remarked that gene therapies or other Advanced Therapy Medicinal Products (ATMPs) can treat previously untreatable diseases, but must be accessible to patients. This requires a continuum of evidence generation. Collecting RWD is essential as it gives an indication of how these new therapies are working.

Mercedes Echauri, Vice-President Market Access Europe and Canada at Takeda, commented that RWE can help to design good clinical trials that improve the treatment of rare diseases. This should not be done unilaterally by industry but with all stakeholders in a diligent and transparent manner.

Mercedes Echauri
Vice-President Market Access Europe and Canada at Takeda

Prof. Maurizio Scarpa
Coordinator of MetabERN, Regional Coordinating Centre for Rare Diseases, Udine University Hospital, Italy

Prof. Maurizio Scarpa, Coordinator of MetabERN, Regional Coordinating Centre for Rare Diseases, Udine University Hospital, Italy, pointed out that the presence of (27) national health systems is limiting homogeneous therapy access to patients. Networking is thus essential. Data needs to be connected in an organized, accessible and interoperable way. Thanks to the TRUST4RD network and tools, patients, policymakers, payers and industry can be connected, in order to better understand the efficacy and safety of a novel therapy and prolong the lives of rare disease patients.

Key takeaways from discussion:

- Multi-stakeholder dialogues to develop understanding of challenges and potential innovative solutions in medicines' development are particularly important in the field of rare diseases.
- HTA/Payer bodies should come together to agree a common core protocol for post-launch data collection of highly innovative technologies in a timely manner.
- People with the necessary data analysis skills are essential to take this forward. HTA and Payer bodies need training in RWD analytics.
- Duplication of initiatives needs to be avoided to create a network that connects everyone: industry, regulator, payer, HTA body, clinician, patient.
- Educate to ensure that rare diseases are not forgotten from curricula.

Session 2:
STAKEHOLDER ACTIONS AND COLLABORATION TO IMPROVE LEARNINGS ON REAL-WORLD EVIDENCE

Dr. Marc Van de Casteele
Coordinator at the Belgian National Institute for Health and Disability Insurance (INAMI/RIZIV)

Dr. Antje Behring
Acting Head of Drug Department at the German Federal Joint Committee (G-BA)

Dr. Liisa-Maria Voipio-Pulkki
Director General of Strategic Affairs and Chief Medical Officer at the Finnish Ministry of Health

Dr. Peter Arlet
Head of the Data Analytics and Methods Task Force at the European Medicines Agency (EMA)

Dr. Alexander Natz
Secretary General of the European Confederation of Pharmaceutical Entrepreneurs (EUCOPE)

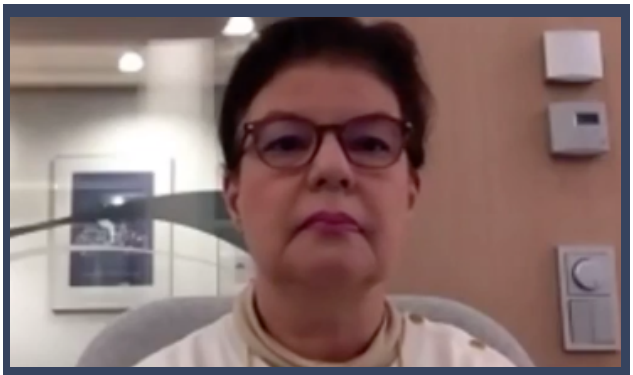
Dr. Marc Van de Casteele
Coordinator at the Belgian National Institute for Health and Disability Insurance (INAMI/RIZIV)

Dr. Marc Van de Casteele, Coordinator at the Belgian National Institute for Health and Disability Insurance (INAMI/RIZIV) introduced the RWE4Decisions Stakeholder Actions and the call for the creation of a EU Learning Network on RWE within the European Health Data Space. He described the key findings of a INAMI-led case study workshop which took place in September 2020: an open and confidential discussion of RWE generation plans; the planning of iterative dialogues; and the use of RWE studies with clear protocols and analytical plans with robust data capture and quality control mechanisms.

Dr. Antje Behring
Acting Head of Drug Department at the German Federal Joint Committee (G-BA)

Dr. Antje Behring, Acting Head of Drug Department at the German Federal Joint Committee (G-BA), pointed out that a major challenge is to agree on a common understanding on questions to be asked and end points to be measured. Another challenge relates to the completeness and quality of collected data in order to make reliable, trustworthy decisions. This involves collaborating with all stakeholders, and a change in the mindset of doctors and HTA bodies.

According to Dr. Liisa-Maria Voipio-Pulkki, Director General of Strategic Affairs and Chief Medical Officer at the Finnish Ministry of Health, it is essential to develop a simple, common language when talking to policymakers that describes the role of RWE in this continuum of evidence. For people designing digitalised health systems, key issues are the quality, timeliness, accessibility, confidentiality, and traceability of the original data, while ensuring the safety, security, and transparency of AI algorithms.

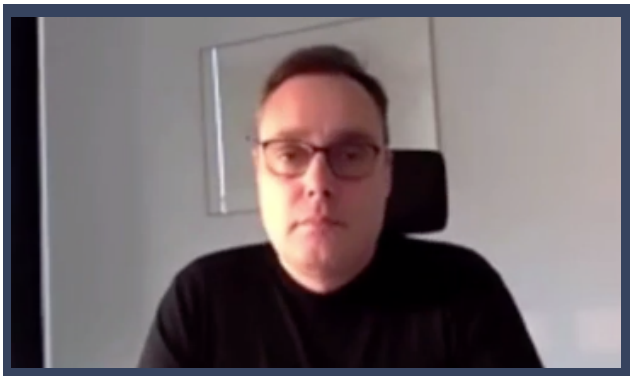


Dr. Liisa-Maria Voipio-Pulkki
Director General of Strategic Affairs and Chief Medical Officer at the Finnish Ministry of Health

Dr. Peter Arlett
Head of the Data Analytics and Methods Task Force at the European Medicines Agency (EMA)

Dr. Peter Arlett, Head of the Data Analytics and Methods Task Force at the European Medicines Agency (EMA), suggested that data quality is one aspect of characterising a dataset together with the time of data elements included and the populations they represent, as this will dictate what research, regulatory and HTA questions can be addressed. This requires investment in data science, statistics and epidemiology, and training of regulators and other stakeholders. DARWIN is a proposal for a Europe-wide network of RWD where data can be accessed and analysed to support decision-making by medicines regulators, if stakeholders collaborate, also HTA bodies and payers.

Dr. Alexander Natz, Secretary General of the European Confederation of Pharmaceutical Entrepreneurs (EUCOPE), believes that industry is aware that methodology is key: it's not about just putting lots of data on the table; we need to know what we are looking for. RWE4Decisions is a good starting point because it is payer-led, with the goal of bringing products to patients earlier. Moreover, RWE was never designed as a substitute for clinical trial data but as an addition to that data.



Dr. Alexander Natz
Secretary General of the European Confederation of Pharmaceutical Entrepreneurs (EUCOPE)

Key takeaways from discussion:

- It's critical to have both a multi-stakeholder approach as well as a cross-border approach.
- Ingredients for success include upskilling decision-makers in using RWE; technology to link people and analyse data; good governance to ensure data is dealt with securely and ethically; funding for sustainable multi-stakeholder collaboration.
- Money and the political will are needed to put in place the people and the structures.
- The bureaucratic burden needs to be lowered to use this data.
- The proposed Learning Network on RWE, which is HTA/ payer led, and the EU Regulatory Network's proposed DARWIN should complement each other.
- Defining the outputs of the Learning Network will have a bearing on the costs and related funding model.
- Practicing clinicians who work with RWD every day need to be asked what end points of clinical studies are important to them and their patients.
- Transparency of data sets and methodologies is essential to build up trust.
- A common legal basis for sharing data in the EU is needed.

Session 3:
CANCER AS A CASE STUDY FOR THE USE OF REAL-WORLD EVIDENCE

Dr. Christine Chomienne
Vice-Chair of Horizon Europe Mission Board for Cancer

Dr. Anja Tebinka-Olbrich
Head of Unit AMNOG EBV at the GKV-Spitzenverband

Dr. Tit Albreht
Head of the Centre for Health Care at the National Institute of Public Health of Slovenia

Dr. Tomáš Skácel
Head of Medical Affairs Oncology Europe & Canada at AstraZeneca

Robert Greene
Patient Advocate and Founder of the HungerNdThirst Foundation

Dr. Denis Lacombe
Executive Director of the European Organisation for the Research and Treatment of Cancer (EORTC)

Dr. Christine Chomienne
Vice-Chair of Horizon Europe Mission Board for Cancer

Dr. Christine Chomienne, Vice-Chair of Horizon Europe Mission Board for Cancer, spoke on real-world evidence and the mission to conquer cancer. She said that the Board has five intervention areas: ensure equitable access; prevent what is preventable; optimise diagnostics and treatment; support quality of life; and understand. These will be implemented by 13 citizen- and patient-centred recommendations for actions, taking into account what has already been done at the EU, national and regional levels, and continuing to work with Europe's Beating Cancer Plan. A recommendation is to create a European Cancer Patient Digital Centre where cancer patients and survivors can deposit and share their data for personalised care. The repository would include a summary of treatments and integrate patient-reported outcomes useful for the cancer patients' own use, and everyday life data provided by patients and survivors themselves. Data will serve as a resource to improve understanding of cancer and its impact on patients' and survivors' lives.

Dr. Anja Tebinka-Olbrich
Head of Unit AMNOG EBV at the GKV-Spitzenverband

Dr. Anja Tebinka-Olbrich, Head of Unit AMNOG EBV at the GKV-Spitzenverband, responded that new accelerated processes to faster market access pose challenges for the HTA assessment and also for pricing, particularly in oncology. These approvals are based on uncertain and incomplete evidence, and in Germany this creates an issue as there is automatic reimbursement after market authorisation.

Dr. Tit Albreht, Head of the Centre for Health Care at the National Institute of Public Health of Slovenia stressed that quality of life of patients is the ultimate objective, and requires various types of evidence and data. In spite of the recent deluge of quantitative data due to COVID19, qualitative data remains vital, such as from surveys and studies on socio-economic status.

Dr. Tit Albreht
Head of the Centre for Health Care at the National Institute of Public Health of Slovenia

Dr. Tomáš Skácel
Head of Medical Affairs Oncology Europe & Canada at AstraZeneca

Dr. Tomáš Skácel, Head of Medical Affairs Oncology Europe & Canada at AstraZeneca added that getting the right treatment for the patient at the right time is crucial, and increasing overall survival for the patient is the ultimate goal. However, a sole reliance on randomized controlled clinical trials as the main source of data generation for the new medicines is not sustainable. Randomized clinical trials are not able to provide data which is broadly representative of all cancer patient populations.

Robert Greene, Patient Advocate and Founder of the HungerNdThirst Foundation, remarked that cancer patients should be actively involved in every stage of planning and implementation. For cancer patients' data, the continuity of data is crucial (before, during and after) which can be best achieved with RWD leading to RWE.

Robert Greene
Patient Advocate and Founder of the HungerNdThirst Foundation

Dr. Denis Lacombe
Executive Director of the European Organisation for the Research and Treatment of Cancer (EORTC)

Dr. Denis Lacombe, Executive Director of the European Organisation for the Research and Treatment of Cancer (EORTC), acknowledged that RWD/big data constitutes an invaluable source of information. However, it is important to address what RWD may not be doing and assess how to improve the use of RWD where it raises challenges such as for taking decisions for access to treatments. He also suggested that it's important to think about what is being done with the data, as the challenges are different depending on whether data is being collected for diagnostic surveillance or treatment. Whatever type of RWD is used, it is important to determine what type of certainty we can bring to patients and the community (quality and standardization of the data, GDPR application/ anonymisation, centralized versus federated models, data sharing rules and principles).

Key takeaways from discussion:

- Research is needed on methodologies and how to approach the important datasets.
- A priority is to inform patients, carers and citizens about health.
- Data must be readily available and fit for purpose instead of locked away in inaccessible silos.
- Sharing of scientific data needs to be FAIR, which means data has to be findable, accessible, interoperable, and reusable.
- Involving citizens is key, as is using different sources of data – including RWD – in a way that enables multi-stakeholder and multi-decision-maker decisions.
- The next steps are to overcome data disparities, standardize data, and achieve compatibility for disease registries.

Concluding session:
EVIDENTIARY CHALLENGES FOR HIGHLY INNOVATIVE TECHNOLOGIES - THE WAY FORWARD TO IMPROVE SHARED LEARNINGS ON REAL-WORLD EVIDENCE FOR DECISION-MAKERS

Jo De Cock
CEO of the Belgian National Institute for Health and Disability Insurance (INAMI/RIZIV) and thought-leader of the initiative

Dr. Cláudia Furtado
Head of the Health Technology Assessment, Pricing and Reimbursement Division & Information and Strategic Planning Division at INFARMED

Simone Boselli
Public Affairs Director at EURORDIS

Dr. Wim Goettsch
Special Advisor HTA at the Dutch Zorginstituut Nederland (ZIN)

Jakub Boratyński
Acting Director in charge of Digital Society, Trust and Cybersecurity at the European Commission (DG CONNECT

Jo De Cock
CEO of the Belgian National Institute for Health and Disability Insurance (INAMI/RIZIV) and thought-leader of the initiative

Jo De Cock, CEO of the Belgian National Institute for Health and Disability Insurance (INAMI/RIZIV) and thought-leader of the initiative, said that in light of the proposal for an EU Health Data Space, a revised EU Pharmaceutical Strategy and a Regulation for EU collaboration on HTA, there is a need for an EU Real-World Evidence Action Plan to stimulate alignment and collaboration amongst ongoing initiatives and respond to key challenges by:

- Ensuring the development of a framework for cross-country collaboration on analyses.
- Supporting an infrastructure for sharing evidence generation plans and post-licensing evidence generation.
- Ensuring data quality, accessibility, security and privacy.

- Developing evidence standards and agreeing on common data sets.
- Promoting comprehensive and aligned guidance across bodies.
- Ensuring systematic patient involvement in order to capture RWE.
- Promoting the use of digital data in health care.

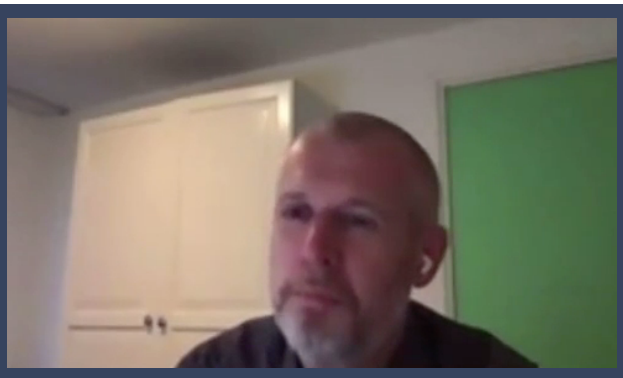
A Multi-Stakeholder Learning Network on RWE should include HTA bodies/payers, the EMA, patient representatives, researchers, clinicians, industry and academics, to improve evidence-informed decisions for market access and reimbursement of highly innovative technologies. It should harness the use of data in the evaluation of the truly added-value of pharmaceuticals, and address the operational, technical and methodological gaps. Such a network will develop practical learnings on the potential use of RWE through a 'learning by doing' approach, share experiences, pool resources, and build trust.

Dr. Cláudia Furtado
Head of the Health Technology Assessment, Pricing and Reimbursement Division & Information and Strategic Planning Division at INFARMED

Dr. Cláudia Furtado, Head of the Health Technology Assessment, Pricing and Reimbursement Division & Information and Strategic Planning Division at INFARMED agreed that a collaborative approach to real-world evidence for HTA/payer decisions is crucial. This will be a key part of the discussions during the upcoming Portuguese EU Presidency (starting in January 2021), in line with the priorities on medicines availability, access and affordability.

Simone Boselli, Public Affairs Director at EURORDIS, emphasised the need to look at the role of RWE at every stage in the cycle of development and access to therapies, and to include the patients and clinicians in a meaningful way to assess outcomes.

Simone Boselli
Public Affairs Director at EURORDIS



Dr. Wim Goettsch
Special Advisor HTA at the Dutch Zorginstituut Nederland (ZIN)

Dr. Wim Goettsch, Special Advisor HTA at the Dutch Zorginstituut Nederland (ZIN), argued that a better alignment of existing national methods to use RWE was needed. As a next step, we should identify current gaps, support implementation of agreed methods, and develop a programme for developing new methods that are closely linked to HTA practice.

Jakub Boratyński
Acting Director in charge of Digital Society, Trust and Cybersecurity at the European Commission (DG CONNECT)

Jakub Boratyński, Acting Director in charge of Digital Society, Trust and Cybersecurity at the European Commission (DG CONNECT), recognised that there are many synergies between the RWE Learning Network and the objectives of the European Health Data Space which can lead to aligned ways forward. There is a need to work on initiatives that stimulate a single digital market for health and a way to encourage innovation in digital health technologies. Governance is key in this.

As to next steps, Jo De Cock concluded that INAMI-RIZIV is willing to drive forward demonstration projects in 2021, and welcomes the participation of all interested stakeholders in this voluntary initiatives in order to share experience, to pool resources. The initiative aims to build trust and mutual learnings in the use of RWE for healthcare decision-makers. He thanked the German Presidency for their support and commitment and looked forward to progressing the Learning Network, working also with the Portuguese and Slovenian Presidencies.

Key takeaways from discussion:

- It's critical to have both a multi-stakeholder approach as well as a cross-border approach.
- Demonstration projects are necessary so that the results can feed into the Learning Network. It's vital to move to a continuum of care, having clinical data inform decision making including budgetary decisions.
- Robust methodologies are needed to allow combinations of data from clinical trials and RWE. The Learning Network should identify current gaps, and support implementation of agreed methods. This work should lead to guidelines to influence how treatments are used.
- Collaboration is needed for a standardized approach to RWE to address the fragmentation and to identify learnings and obstacles to developing a common approach. Industry must be involved, and patients and clinicians have to be involved in a meaningful way to assess outcomes.
- There is a need for policies to support continuation of this project in synergy with other initiatives.

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