Tool for reducing uncertainties in the evidence generation for specialised treatments for rare diseases
In 2017 the **multi-stakeholder initiative** was set up to:

Facilitate a shared understanding of the challenges faced by manufacturers, regulators, HTA, Payers and patient groups in the development and use of real world evidence to address uncertainties for these technologies.

The initiative builds on work already undertaken by:

- **Outcomes based pricing and reimbursement of innovative medicines**
- **The use of real world data throughout an innovative medicine’s lifecycle**
- **Recommendations from the European Working Group for Value Assessment and Funding Processes in Rare Diseases (ORPH-VAL)**
Multi-stakeholder participation

STAKEHOLDERS

- Prof. Lieven Annemans
  University of Ghent
- Dr Karen Facey
  University of Edinburgh
- Jo De Cock
  CEO – INAMI
- John Bowis
  FIPRA (Chair)
- Yann Le Cam
  CEO – EURORDIS

OBSERVER

- Dr Karen Facey
  University of Edinburgh
The approach

To provide a **mutual understanding of the challenges and trade-offs** in evidence development for highly specialised technologies

The rationale

Approaches that are agreed upon through a multi-stakeholder dialogue has the potential to **increase trust and uptake** of such evidence in health care decision-making
Development of Consensus Paper providing a technical but pragmatic methodology

A taxonomy of uncertainties relating to these challenges to delineate their nature and role in HTA and Payer decision-making.

Guidance to decision-makers on real-world evidence generation options to address these uncertainties and to support understanding of their scientific validity.

INAMI funded, endorsement by participants
Addressing uncertainties in the evidence generation for highly specialised treatments in complex or rare conditions

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Co-author: Dr Karen Facey, HTAi

TRUST4RD building blocks:

1. Typology of uncertainties – related to the disease, medicine or health ecosystem
2. Qualitative assessment of importance/impact of a given uncertainty
3. Overview of available data sources
4. List of issues related to different data sources
5. Permanent communication line between industry and HTA bodies/payers
Assessing the impact and importance of uncertainties

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Disease</th>
<th>Health Ecosystem</th>
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| ▪ Magnitude of treatment effect  
▪ Possibility of waning effect  
▪ Impact of biomarker on treatment effect  
▪ Dose required for optimal effect  
▪ Relevance of treatment effect to patients  
▪ Impact on quality of life  
▪ Impact on society and caregivers  
▪ Adverse events and safety  
▪ Which patients treatment works best | ▪ Natural history of the disease  
▪ Relationship between surrogate and hard endpoints (e.g. long-term survival)  
▪ Extent of unmet need (impact of disease on quality of life and survival)  
▪ Incidence and prevalence of the disease | ▪ Current pathway and standard of care  
▪ Patient acceptability and compliance (not therapy related)  
▪ Provider prescription patterns  
▪ Consequences to healthcare system (e.g. extra costs)  
▪ Consequences to society (e.g. reduced absenteeism) |

Some uncertainties may have a larger impact on relative effectiveness and value for money than others
Data sources

- Experimental evidence about current management
- Experimental evidence about new medicine
- Real World Evidence about current management
- Real World Evidence about new medicine

4 types of data sources can address uncertainties
The way forward…

List of issues

Issues will occur with the available data sources. It is important that these issues are explicitly listed and discussed, leading to suggested solutions.

A permanent communication line

A dialogue can lead to solutions, using the building blocks of the tool.
Process and deliverables: overview

Ongoing dialogue / consultations with stakeholders - final endorsement