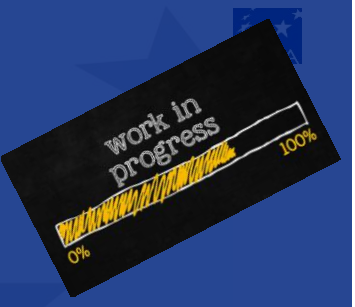
TRUST – 4 RD



Tool for Reducing Uncertainties in the evidence generation for Specialised Treatments for Rare Diseases

1

Objective

To present a guidance that can be used to define and manage

Uncertainties & evidence gaps

in the assessment of value and value for money

of so-called highly specialised treatments for complex or rare diseases.

with a focus on Real World Evidence (RWE)

2

Scope

"highly specialised treatments for complex or rare diseases"

2011 EC cross-border health care directive:

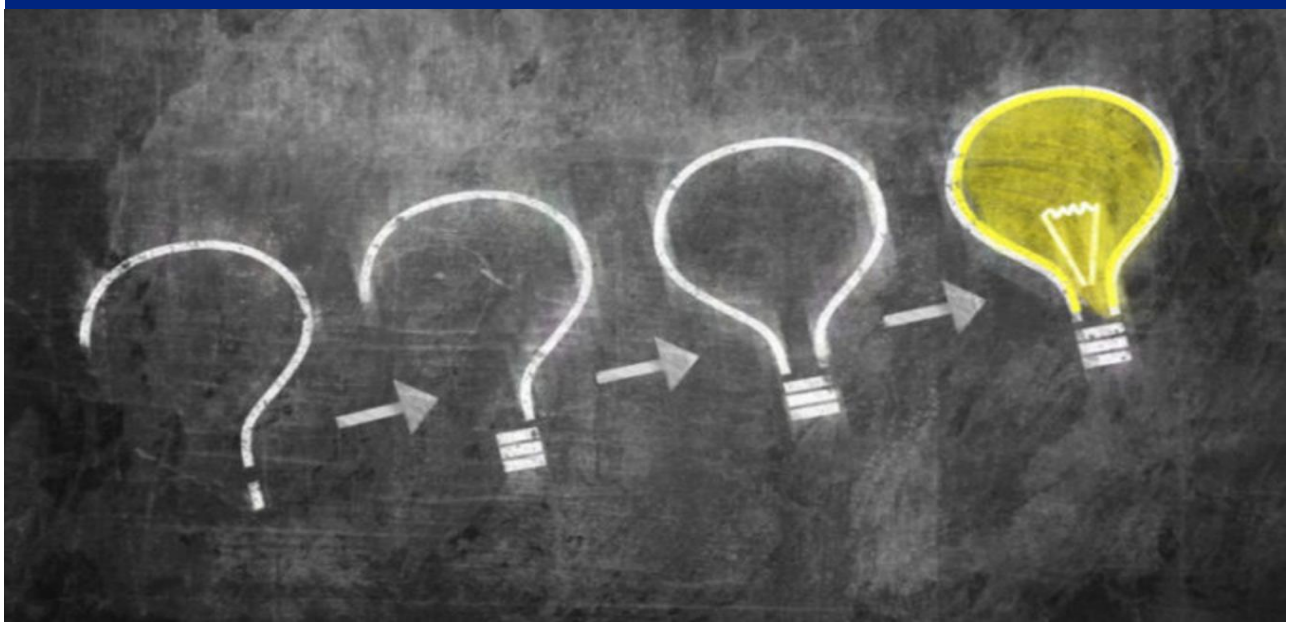
"for conditions having particular issues about diagnosis and access to care"

European Reference Networks 2017:

"No country alone has the full knowledge and capacity to treat these complex or rare diseases"

3

"Evidential uncertainty very likely to occur"



Multi-stakeholder initiative

HTA Bodies, Payers and Ministries	▪ **INAMI/RIZIV, NICE, G-BA, ZIN, HAS, EUnetHTA** ▪ **Austrian Ministry of Health, Belgian Ministry of Health**
Regulators	▪ **European Medicines Agency**
Patient Representatives	▪ **EURORDIS, Duchenne Parent Project**
Clinicians	▪ **Luca Sangiorgi** – ERN BOND (Rare Bone Disorders) ▪ **Cedric Hermans** - Saint-Luc University Hospital, Brussels
Clinical Research	▪ **European Organisation for Research and Treatment of Cancer** (EORTC)
Observers	▪ **European Commission (DG SANTE)**
Industry	▪ **EFPIA/EuropaBio OMP Task Force** ▪ **EUCOPE**
Authors	▪ **Lieven Annemans, Ghent University** ▪ **Karen Facey, University of Edinburgh**

Task Force: EURORDIS and Industry. Secretariat: FIPRA (Chair – John Bowis OBE)

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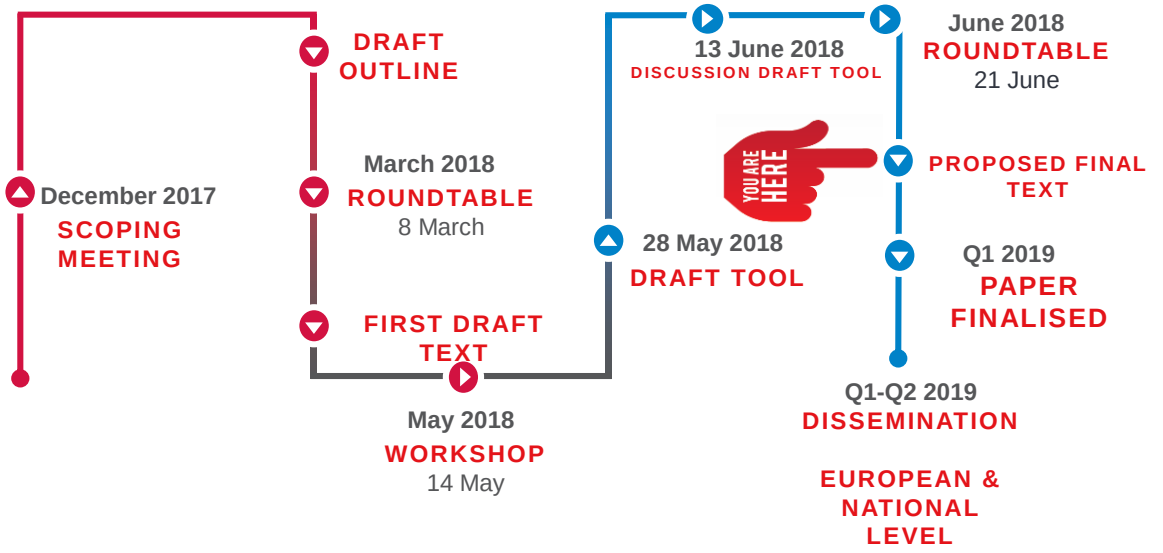
Building on existing initiatives

The paper builds further on existing initiatives from

- the European Commission and the EMA,
- the Innovative Medicines Iinitiative (IMI) ,
- EunetHTA,
- MoCA (Mechanism of Coordinated Access to OMPs),
- ISPOR,
- ORPH-VAL,
- Annemans L and Pani L
- Hampson G et al.
- …

Timeline



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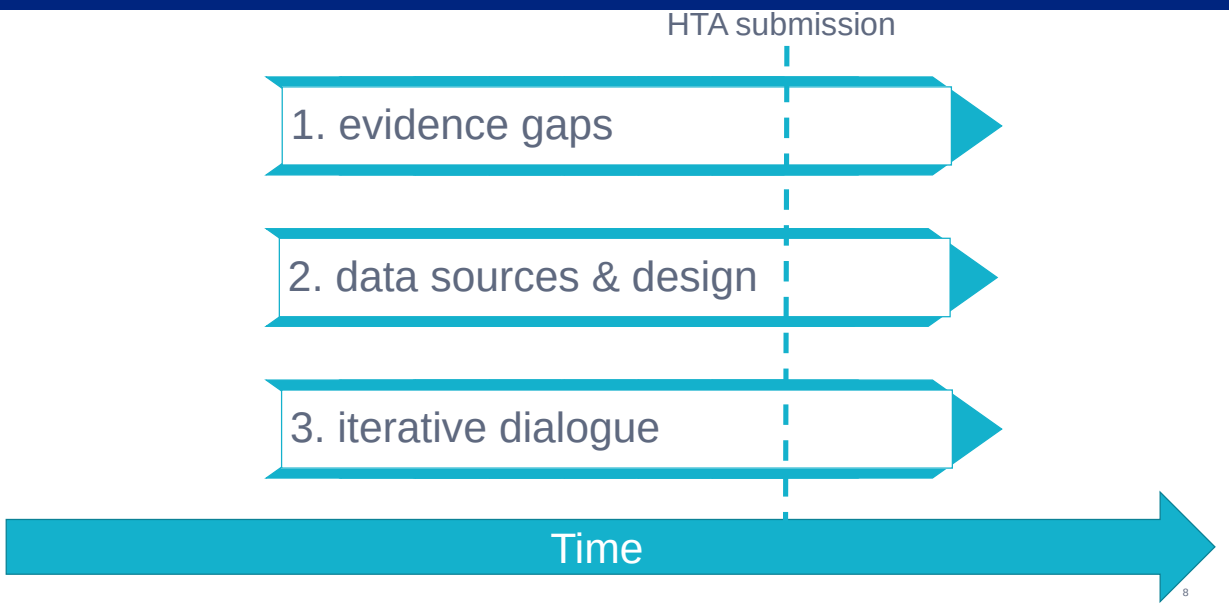
Concept



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1. evidence gaps

Uncertainty related to	Examples
Population and epidemiology	- Incidence and prevalence - Exact size of target population (high risk, 2nd line,…) - …
Disease and standard of care	- Natural course of the disease - Unmet burden - Standard of Care, endpoints, outcomes - …
New therapy	- Effect size in real life - Effect on final clinical endpoints - Sustainability of effect - …
Health Eco-system	- Prescribing behaviour - Compliance/persistence - Cost offsets - …

define importance

2. Data sources and design

	Experimental interventional design	RWE / routine practice
Current treatment(s)	- previously published comparative trials	- disease and/or population registries, - claims databases, - electronic patient records, - biobanks, - surveys, - chat rooms and patient communities.
New treatment	- RCT vs standard of care - pragmatic trials - case series compared with historical controls - nested randomisation study in a disease or population registry	- disease and/or population registries, - claims databases, - electronic patient records, - biobanks, - surveys, - chat rooms and patient communities.

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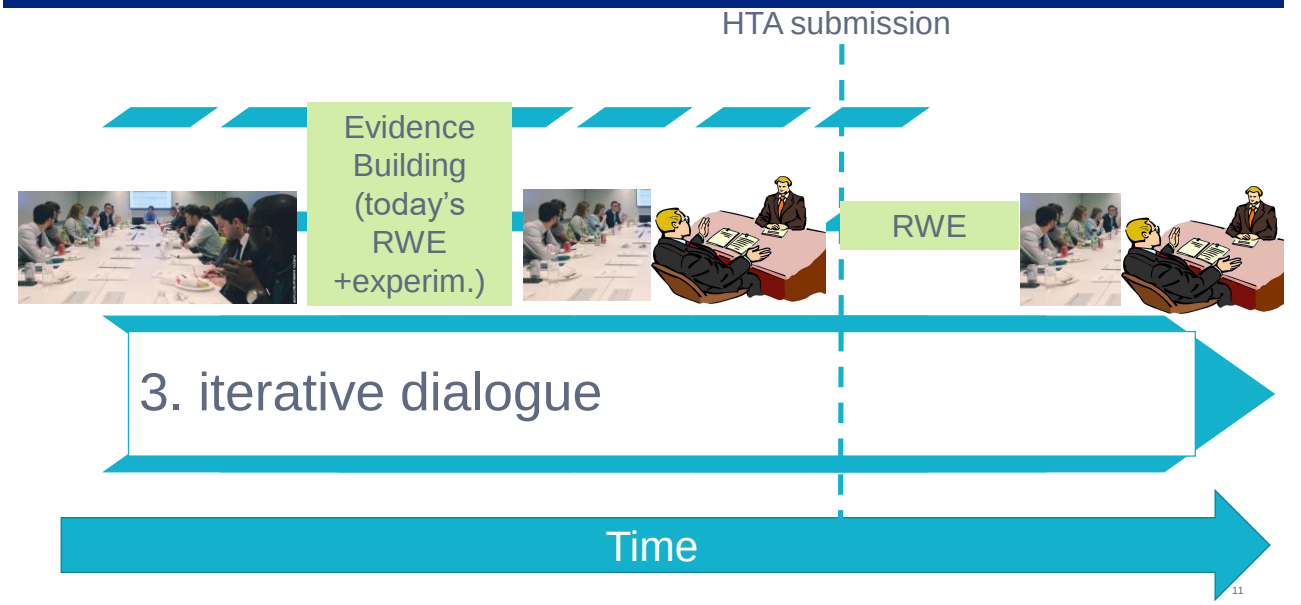
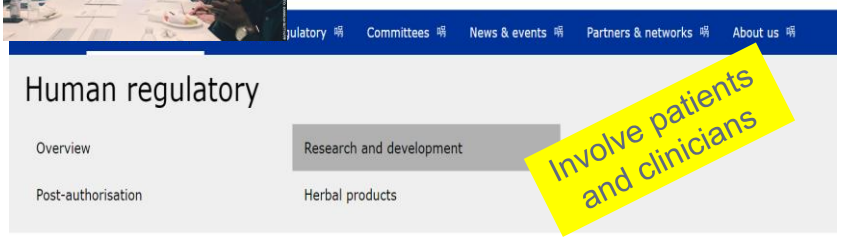
3. Dialogue

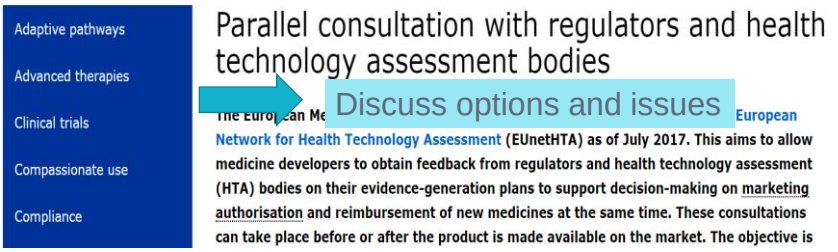


First Dialogue: early and parallel

Company:

- **Early model**
- **Target Product Profile (TPP)**
- **First Evidence**
- ***Evidence generation plans***
- ***Inventory of data gaps (avoidable/unavoidable)***





Early dialogue: example of content

before trial – early dialogue

Description of uncertainty		Importance	Proposed solution / data source	Issues	Way forward
New therapy	Effect on surrogate endpoints (e.g. response rate)	++	RCT	No randomisation possible	Single arm trial with matched historical controls
New therapy	Effect on final clinical endpoints (e.g. event rates)	+++	Follow up trial patients over time	Still trial based	Registry post launch
Disease related	Relationship surrogate-final clinical endpoint (survival)	+++	Registry of existing therapies pre-access	Historical relationship not the same as anticipated new relationship Survival only affected in the long term	Measure historical relationship and assess potential value of therapy based on surrogate outcome and this historical relationship.

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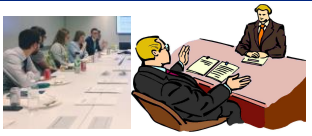
Gaps meet data

Uncertainty related to	Data sources /design → RWE
Population and epidemiology	- comparative trial current SoC - disease and/or population registries, - claims databases, - electronic patient records, - biobanks, - surveys, - chat rooms and patient communities
Disease and standard of care	
New therapy	- RCT vs standard of care - pragmatic trial - case series compared with historical controls - nested randomisation study in a disease or population registry
Health Eco-system	- disease and/or population registries, - claims databases, - electronic patient records, - biobanks, - surveys, - chat rooms and patient communities

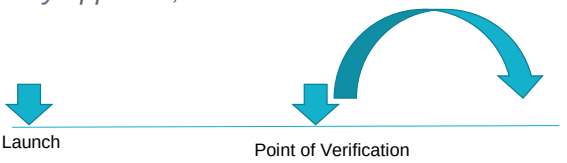
Second Dialogue: pre-submission



- **Final HE model**
- **Value dossier**
- **Pivotal Evidence**
- **Post-launch evidence generation plans**
- **Remaining data gaps**
- **Prepare for a possible outcomes based agreement**

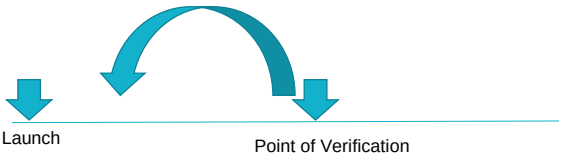
1.Coverage upon evidence development

- *Temporary approval, then final decision*



2.Performance Linked Reimbursement (outcomes guarantee)

- *Not as good as promised → industry pays back*



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Post Launch real world evidence (RWE)

- product, disease and/or population registries,
- claims databases,
- electronic patient records,
- biobanks,
- surveys,
- chat rooms and patient communities
- …

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Third Dialogue: point of verification

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Summary and recommendations

- **Proposal for a systematic approach: TRUST4RD**
  - Taxonomy of evidence gaps
  - Setting priorities (important vs unimportant gaps)
  - Gaps meet data pre-launch (large potential of RWE pre-launch)
  - Post-launch evidence is jointly prepared pre-launch
  - Mandatory Dialogue – Dialogue – Dialogue involving patients and clinicians

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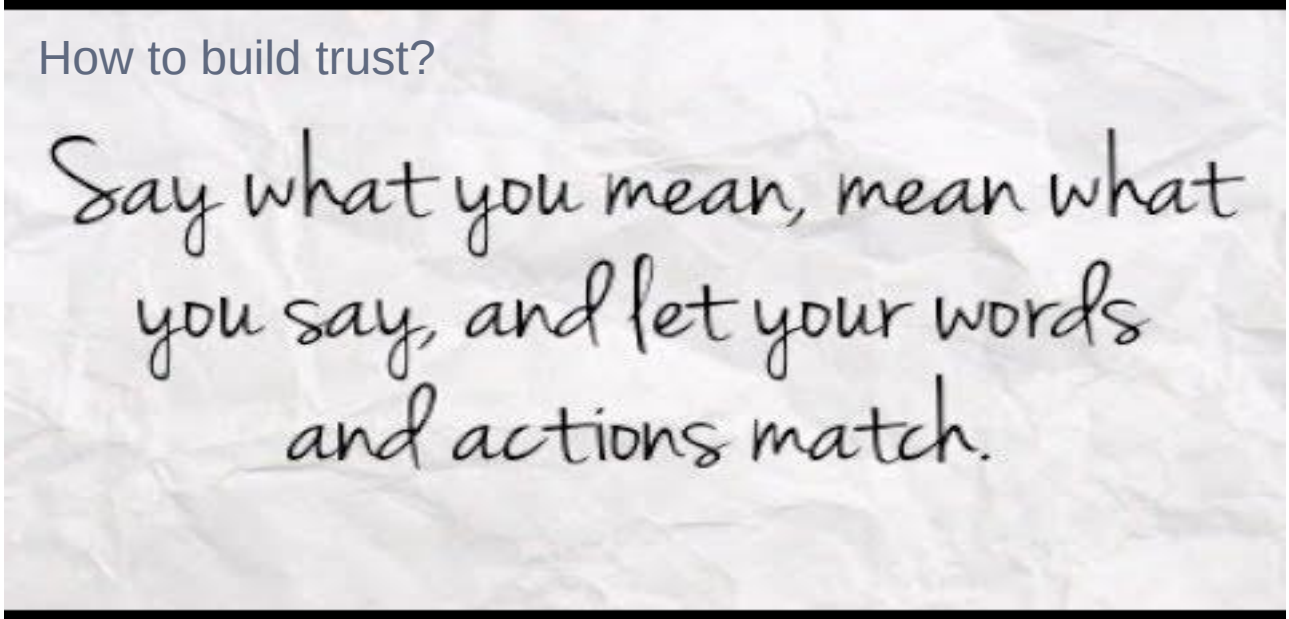
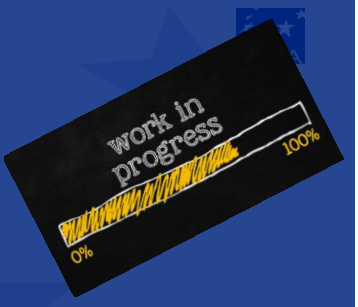
How to build trust?



TRUST – 4 RD



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