EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Study on submission of RWD/RWE in MAAs and EoIs - 2018-2019

Preliminary results

Presented by: Xavier Kurz
Data Analytics and Methods Task Force

RWD/RWE in MAAs and EoIs in 2018-2019

Objective: **Characterise RWD/RWE** included in centralised marketing authorisation applications (MAA) and extensions of indications (EoI) submitted in 2018-2019 and **explore its contribution** to benefit-risk decision-making.

Methods:

- All centrally authorised products with submissions of MAAs and EoIs between Jan 2018 and Dec 2019
- Exclusion of MAAs for generics, informed consent, well established use & duplicate applications
- Manual review of final/latest version of CHMP AR Report and Risk Management Plan
- Other reports and documents consulted for additional information as needed (e.g. D180 CHMP Rapp/co-Rapp report for withdrawn products, PASS protocols…)
- Extraction of data using standard form by 7 investigators (Sep-Dec 2020)
- Verification by 2 independent reviewers of samples of MAAs/EoIs reviewed by the investigators

Study team members

- Catherine Cohet
- Chantal Quinten
- Kelly Plueschke
- Marcia Rückbeil
- Maria Gordillo Maranon
- Robert Flynn
- Ruben Duijnhoven
- Valerie Strassmann
- Xavier Kurz

Working definition of RWD/RWE

Real-World Data (RWD): **“**routinely collected data relating to patient health status or the delivery of health care from a variety of sources other than traditional clinical trials”

Real-world evidence (RWE): **“**information derived from analysis of real-world data”

INCLUDED AS RWD/RWE

- Non-interventional pre- or post-authorisation studies with primary or secondary data collection
- Use of real-world data source (e.g. registry, electronic health care records, medical charts, etc.) in the context of clinical trials (e.g. external control groups)
- Analyses of patient-based observational data in the context of the MAA (e.g. natural history of disease, drug utilisation of reference)
- Information from published articles of product-related non-interventional studies (e.g. on safety or effectiveness of the product in other indications)

NOT INCLUDED AS RWD/RWE

- Non product-related literature review (e.g. on epidemiology of the disease)
- Interventional studies (Phase I, II), pre-clinical studies, toxicological studies, dose-response studies, drug-drug interaction studies
- Clinical trials without use of RWD/RWE
- Open-label follow-up studies of clinical trial patients
- Routine pharmacovigilance activities in RMP
- Surveys not based on individual patients (e.g. surveys of physicians to assess awareness of risk minimisation measures)

RWE in MAAs and EoIs – Overview

Phase 1. Descriptive analyses for initial MAA and EoI by

- Time of use of RWE (pre-, post-authorisation or both)
- If pre-authorisation: main vs. supportive evidence
- Type of application (full MAA, CMA, Exceptional, Under evaluation, Withdrawn)
- Orphan status
- ATMP
- Objective for use of RWE (e.g. safety, drug utilisation, effectiveness)
- Study design (e.g. cohort study, case-control)
- Type of data source (e.g. hospital data, disease registry)

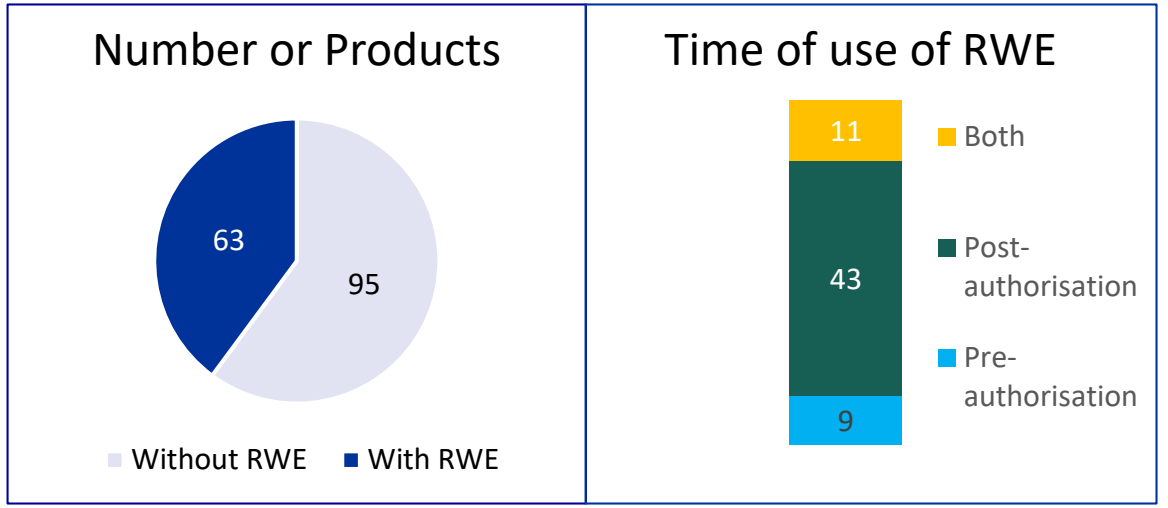
RWE in MAAs and EoIs – Preliminary results

- RWD/RWE used in **40% of MAAs** (mainly post-authorisation) and in **18% of EoIs** (mainly pre- or post-authorisation)

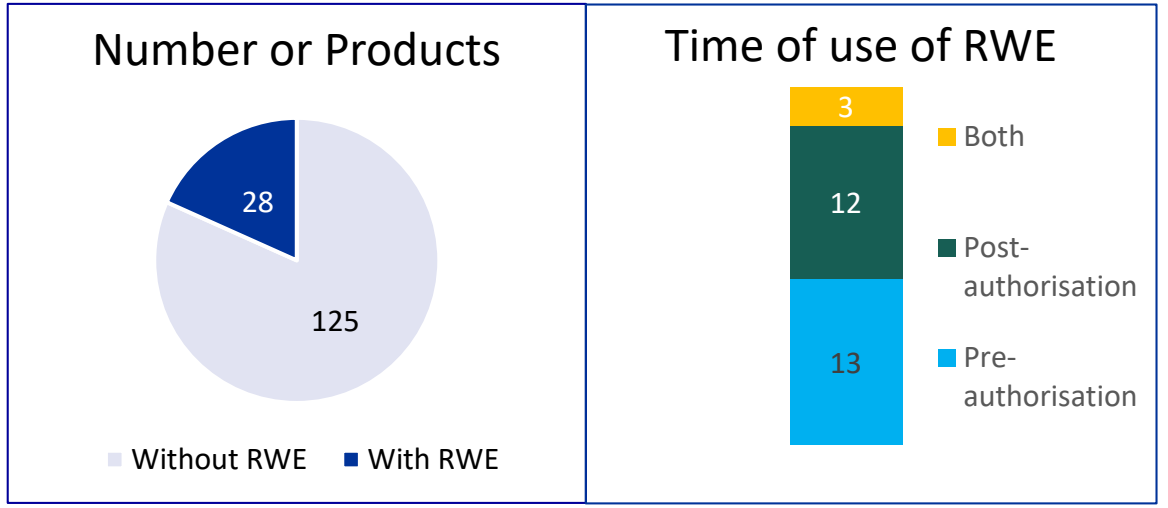
- Majority of products: **Antineoplastic** and **Immunosuppressants** (35% MAA and 42% EoI)
  - ➢ Possible reasons: Single arm trial designs, Identification of patients for non-interventional study/Feasibility analysis, Patterns of drug utilisation, Need to collect data on long term safety/effectiveness

- When used pre-authorisation: mainly **supporting** study looking at **efficacy/effectiveness**
- When used post-authorisation: mainly **RMP Category 3** (for studies included in RMP) looking at **safety**

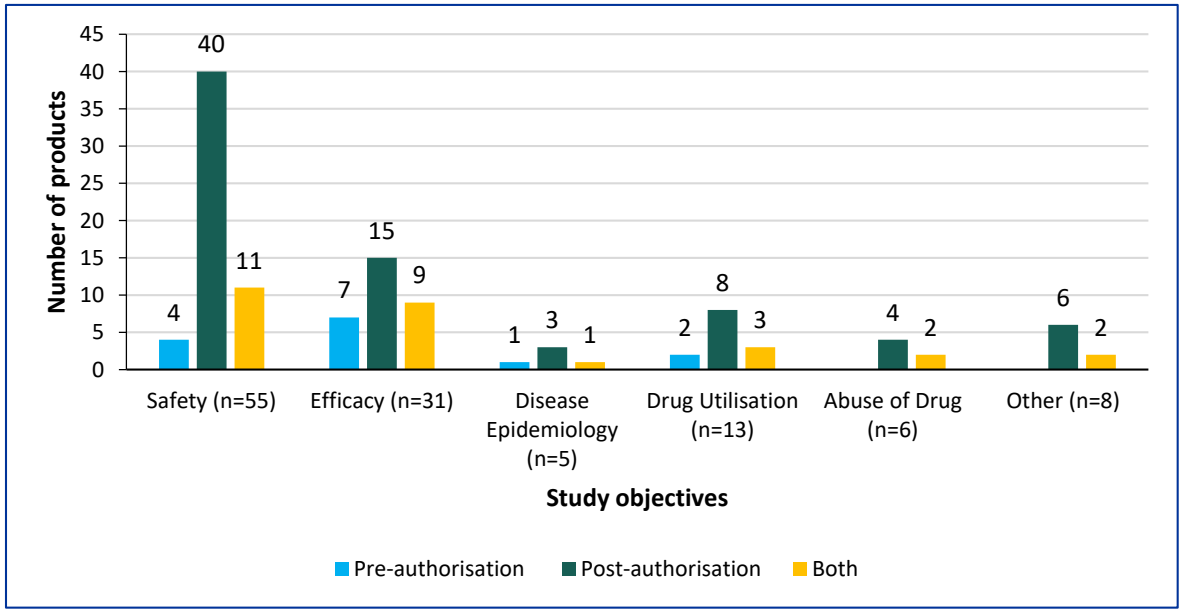
Initial MAA (n=158)

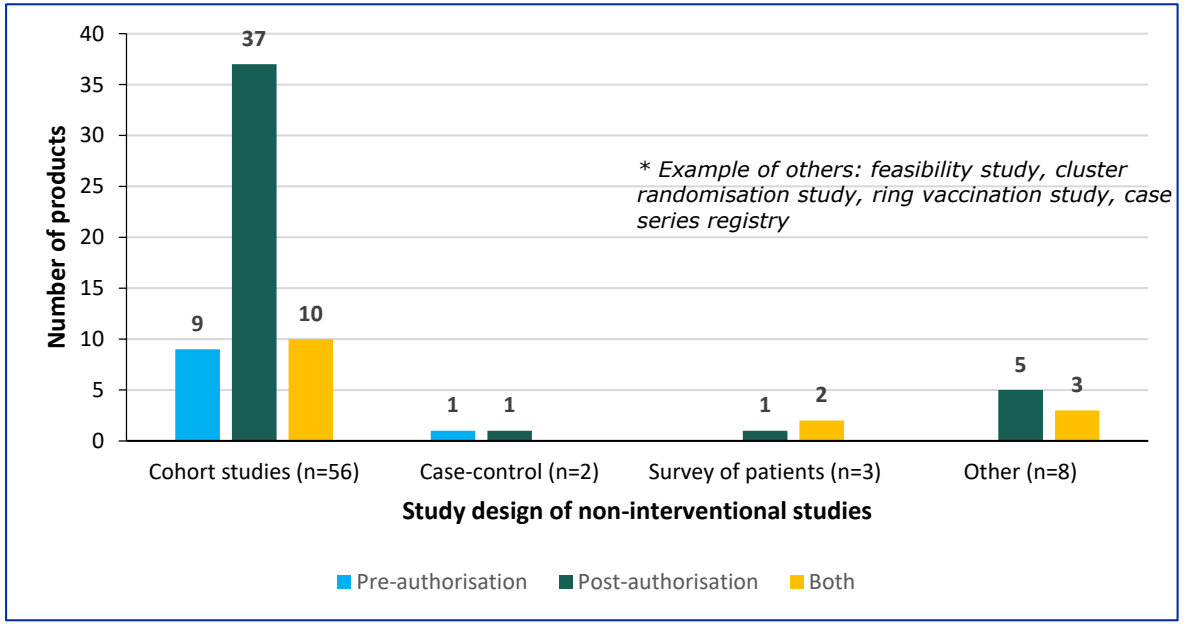


Extension of indication (n=153)

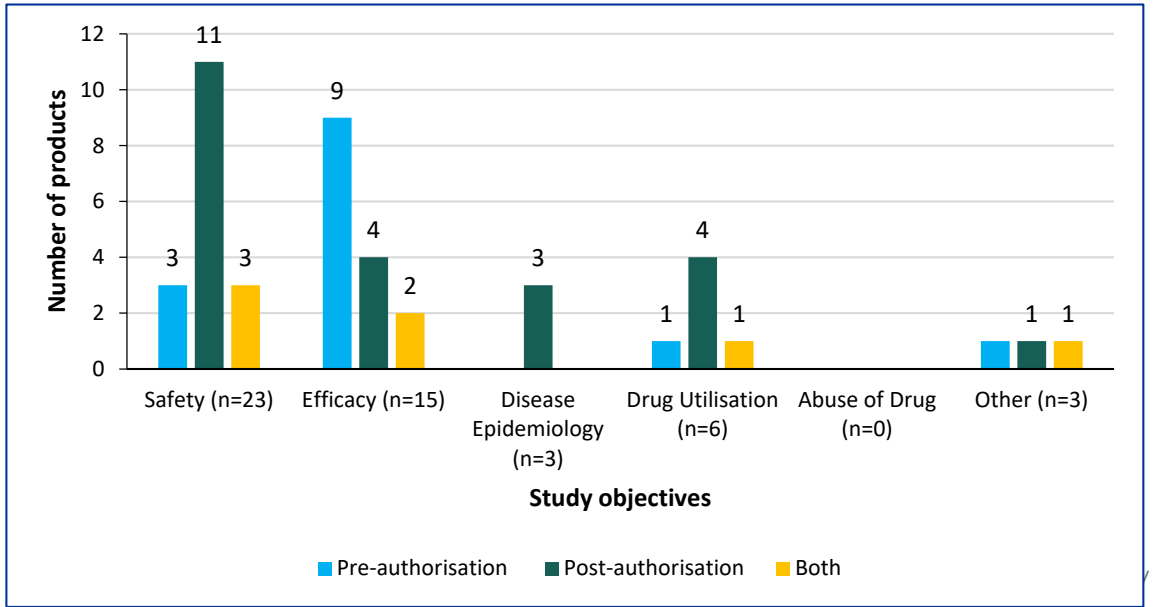


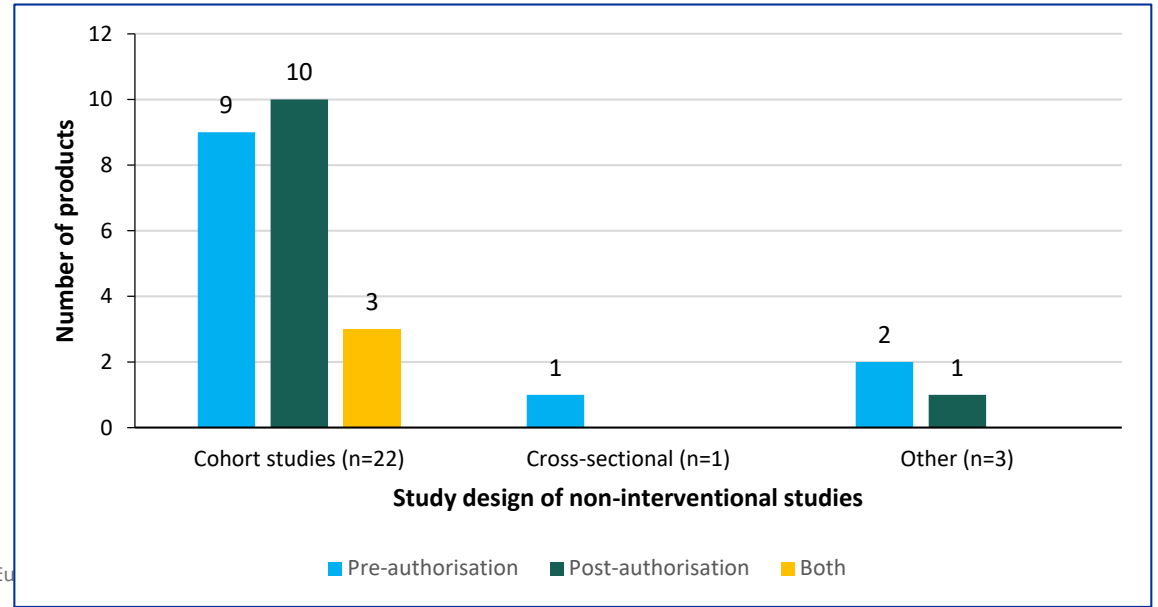
MAAs: RWE studies (n=138) submitted (n products=63)





EoIs: RWE studies (n=46) submitted (n products=28)

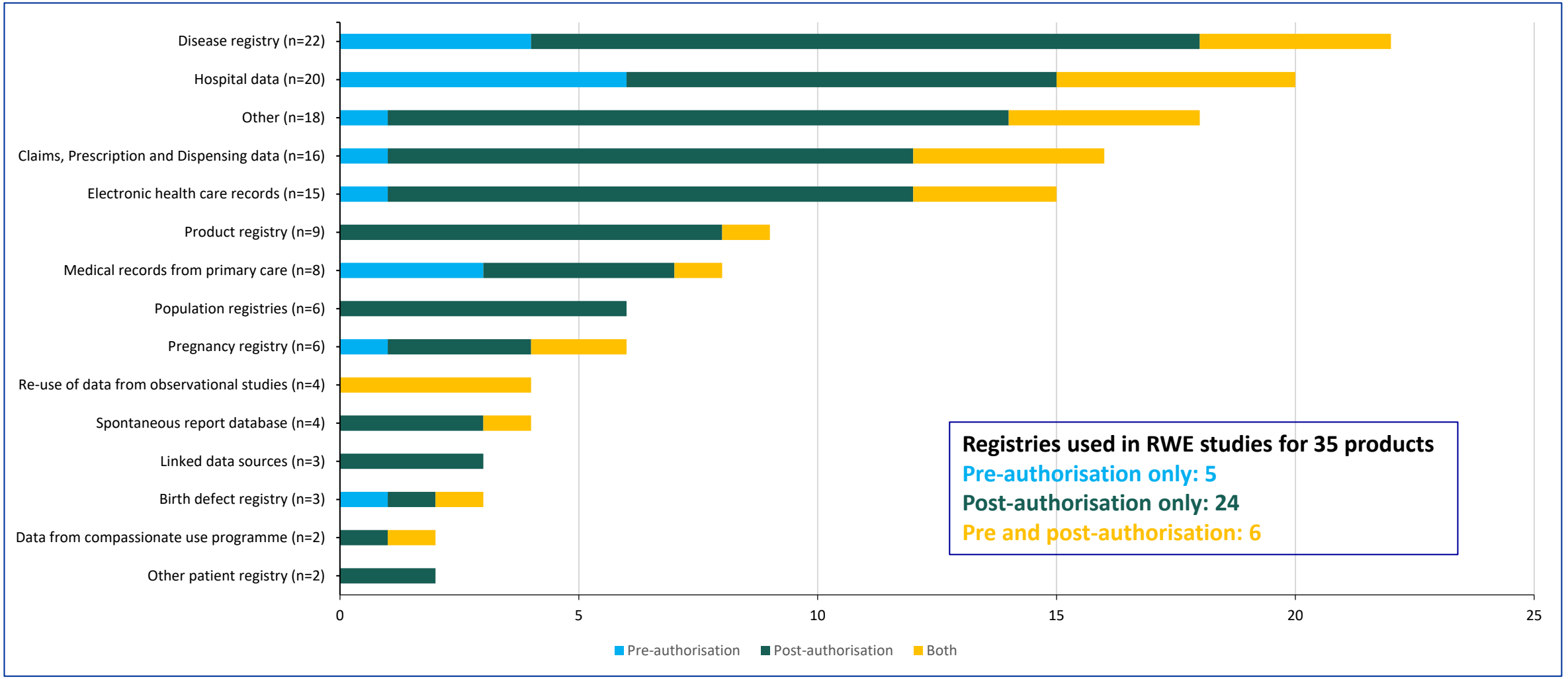




Preliminary results: MAAs

RWE studies (n=138), products submitted (n=63)

Type of data sources used

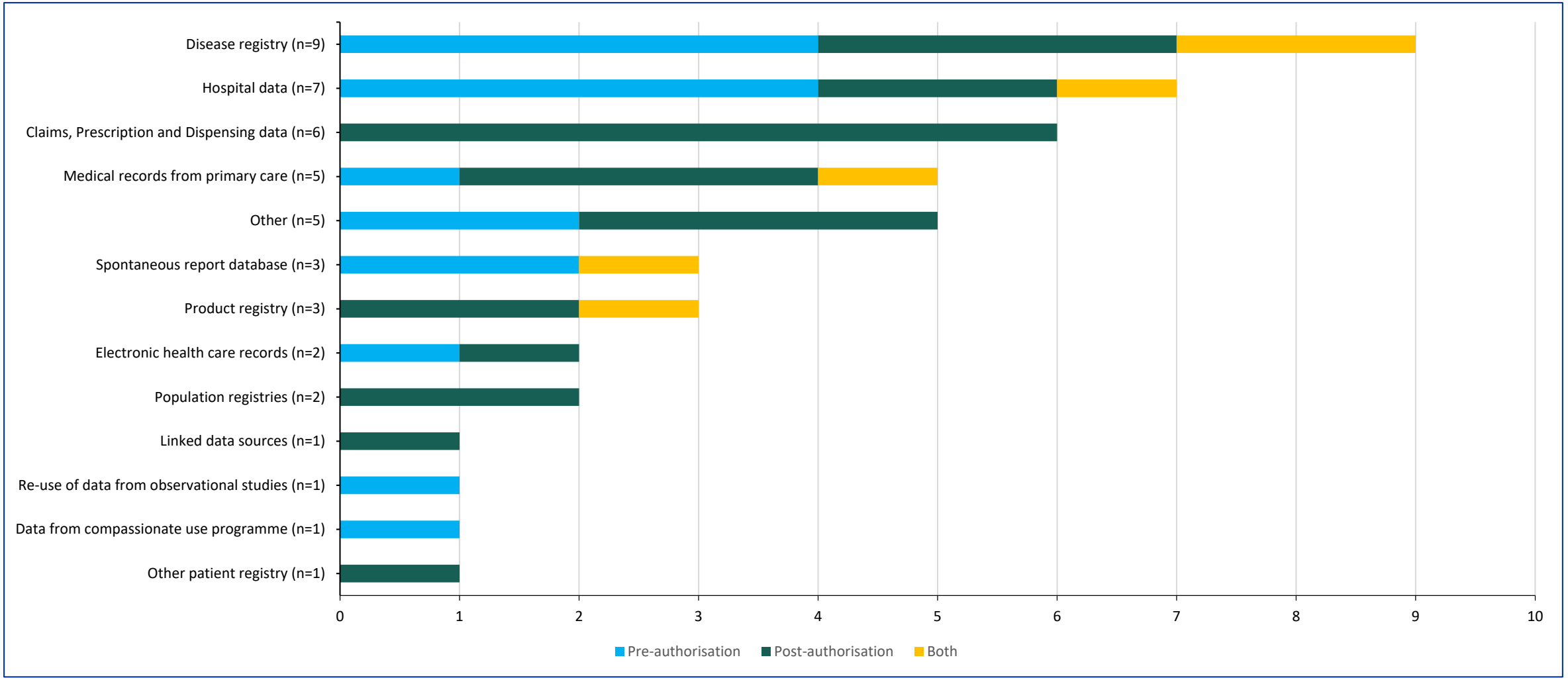


** Example of "Other": follow-up questionnaires of cases of medication errors, medical charts, data sources not specified. "Other" is mainly selected in combination with other specified data sources*

Preliminary results: EoI

RWE studies (n=46) submitted (n products =28)

Type of data sources used



** Example of "Other": follow-up questionnaires of cases of medication errors, medical charts, data sources not specified. "Other" is mainly selected in combination with other specified data sources*

Reminder: why we initiated the EMA patient registry initiative

EUROPEAN MEDICINES AGENCY

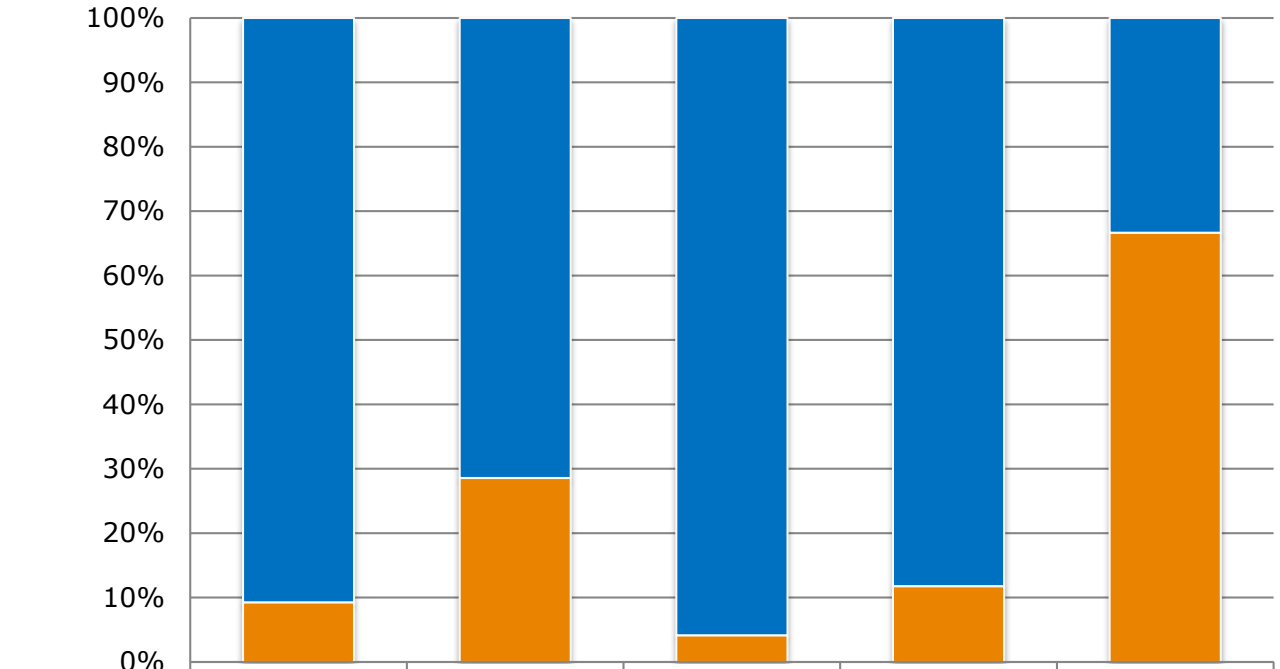
Number of registries imposed as an obligation at the time of autorisation for centrally-authorised products, 2005-2013

Overall, use of a registry imposed for 9% of the products authorised

65% of registries are product registries

80% of registries are new registries

Bouvy et al. PDS 2017;26(12):1442-50



	all (n=335)	orphan (n=70)	non-orphan (n=265)	conditional (n=17)	exceptional circumstances (n=21)
no registry	304	50	254	15	7
registies	31	20	11	2	14

RWE in MAAs and EoIs – Feedback from Committees

- Further work needed to evaluate the **concrete impact and usefulness** of RWE in the evaluation and decision-making: how is it used, do we follow consistent approaches?
  - ➢ *Requires committee input (selection of type of RWD/RWE, objectives to be prioritised, how to evaluate RWE impact). Involvement of the Cross-committee Task Force on Registries.*

- Currently no **framework** for using RWE in submissions (RWE information often limited): **need for guidance** targeted to various stakeholders (industry, academia, regulators, registry owners etc.)
  - ➢ *Draft guideline on registry based studies currently under amendment following public consultation*
  - ➢ *Observational Studies Rapid Analytics Project including pilots with committees to collect uses cases*
  - ➢ *Link to Priority Recommendations on Guidance from the HMA-EMA joint Big Data Task Force*

- No **structure** in the way RWE is submitted: consideration for standard definitions/key words, quality assessment…
  - ➢ *Link to the Data Standards Strategy and LRS Metadata Project*

Manuscript in preparation

→ Phase 2 starting July 1st

Thank you for your attention