CBG MEB | MEDICINES EVALUATION BOARD

Perspective of the regulator on readiness of registry data

Marjon Pasmooij

GOOD MEDICINES USED BETTER

Patient Registry Initiative

Registry

An organised system that uses observational methods to collect uniform data on specified outcomes in a population defined by a particular disease, condition or exposure.

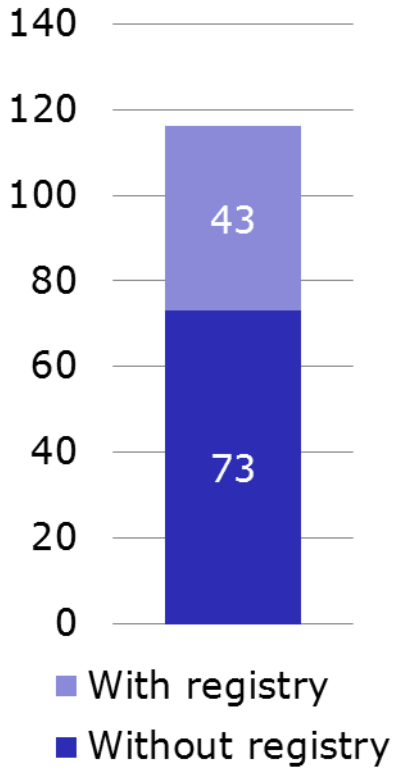
Regulators generally prefer *patient (disease) registries* over *product registries*

- They gather insights on clinical outcomes of conditions with different treatments, rather than on the outcomes of specific treatments
- They allow comparisons
- They are generally better integrated into health care systems.

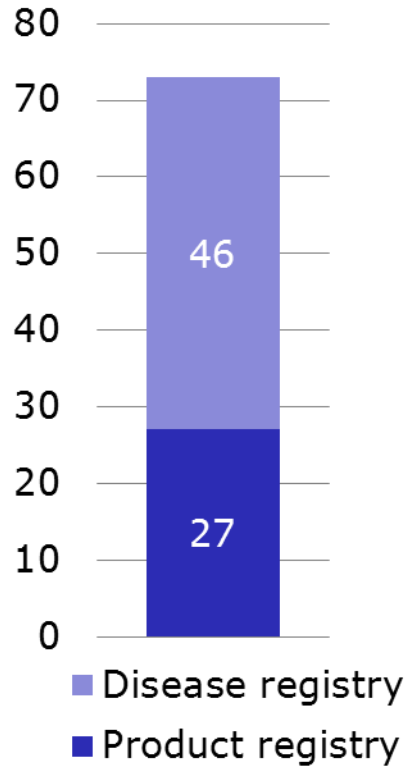
Registries supporting new drug applications

1 Jan 2007 to 31 Dec 2010

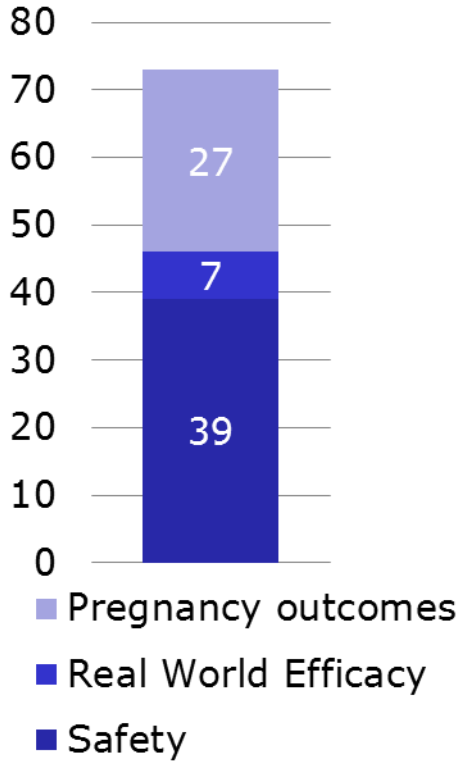
New Drugs



Type of Registry



Primary Aim



Key facts

43 new drugs with
1 to 6 registries

9 imposed registries

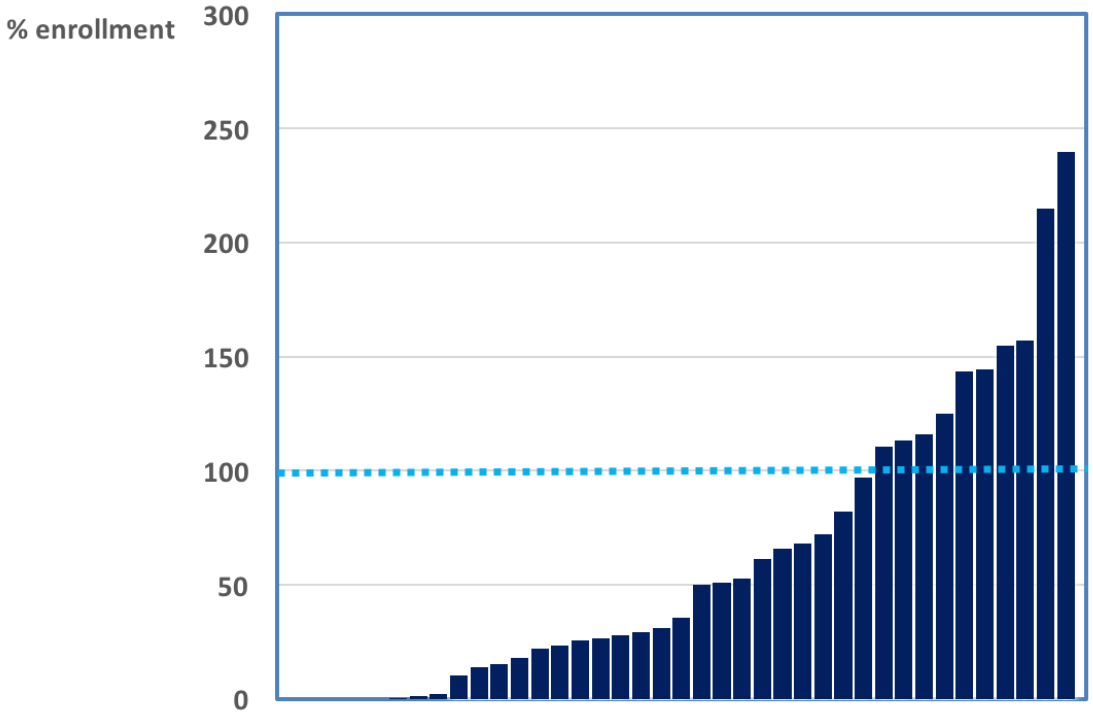
15 Orphan drugs

13 Conditional Approval /
Exceptional Circumstances

-> level of innovation and
orphan status predict
approval with registries

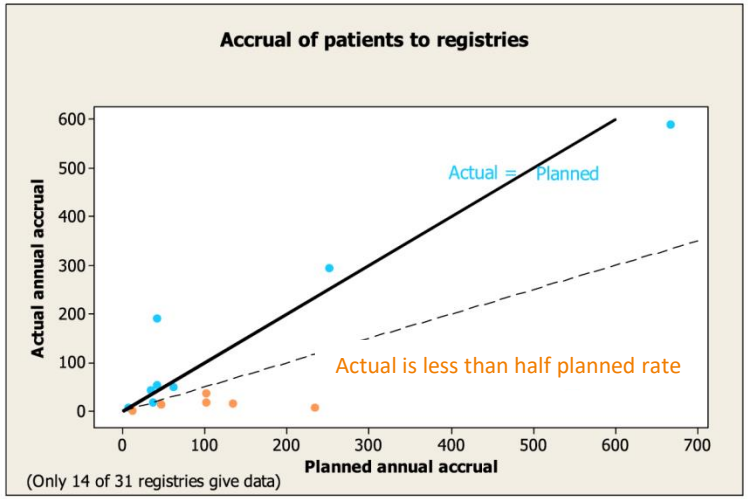
C. Jonker et al. Pharmacoepidemiol Drug Saf. 2017;1–7

Enrolment



Enrolment in 41 of 73 registries (registry studies) with predefined sample sizes (a median of) 5 years after approval

Jonker C et al. Clinical Therapeutics 2018



Bouvy J et al. Pharmacoepidemiol Drug Saf. 2017;1–8

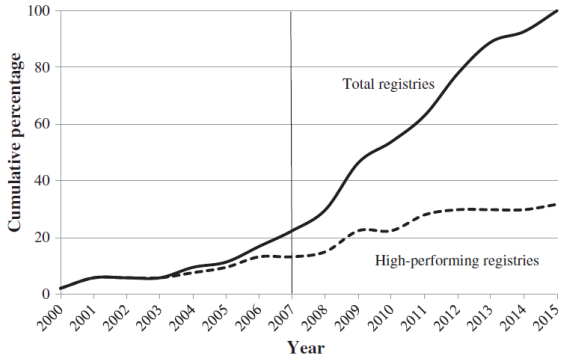


FIGURE 1 Cumulative distribution of postmarket product registries. Total registries represent the 54 registries identified that have initiated (nonpending status)

Zhao Y et al. Pharmacoepidemiol Drug Saf. 2018;1–8

Reasons for problems encountered

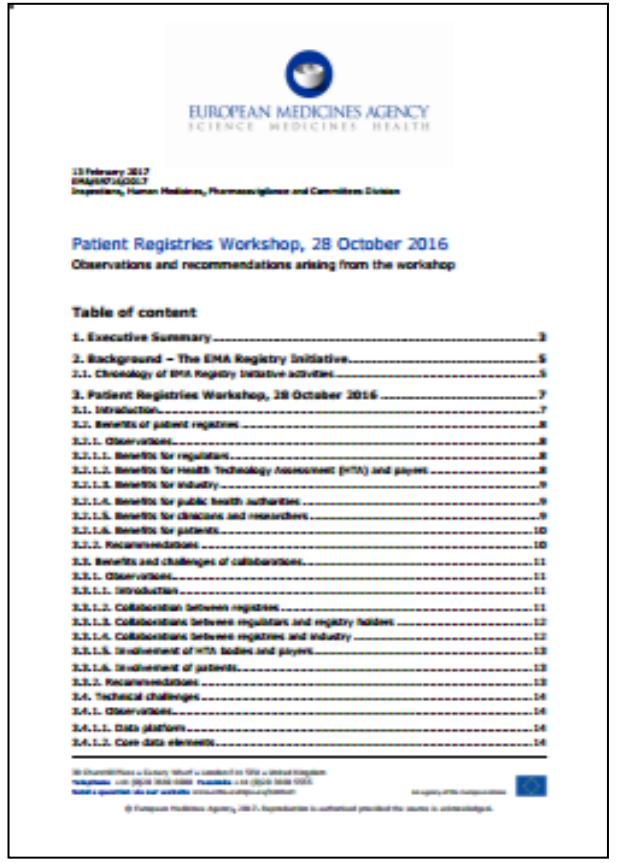
Approach to registries often suboptimal in scientific and resource terms

- Existing registries not fully exploited → duplication of efforts and inefficiencies
- Discrepancy between data collected by registries and data requested by regulators

- *Existing patient (disease) registries were not set up for regulatory purposes*
- *Challenges in using registries for regulatory studies:*
  - **Recruitment:** lack of physician engagement due to administrative burdens, patient consent, low product usage and competing registries
  - **Data quality**: representativeness of registry population, missing data
  - Lack of consistent data **quality control**
  - **Sustainability** (funding)
- So companies may prefer to establish individual product registries

The EMA's Patient Registry Initiative

- Launched, September 2015 – Cross-Committee Task Force
- ***Aims to facilitate use of patient (disease) registries by introducing and supporting a systematic approach to their contribution to the benefit-risk evaluation of medicines***
- **Pilot phase, 2016**: Stakeholder feedback encouraged an active role of EU network in supporting collaboration for greater utilisation of disease registries



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Patient Registries Workshop, 28 October 2016

Observations and recommendations arising from the workshop

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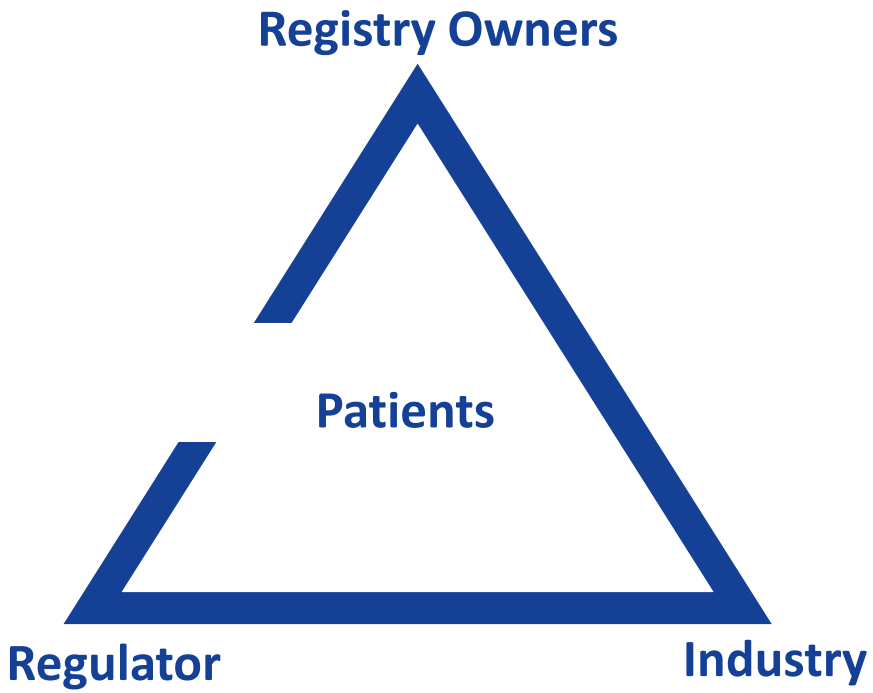
Strategy

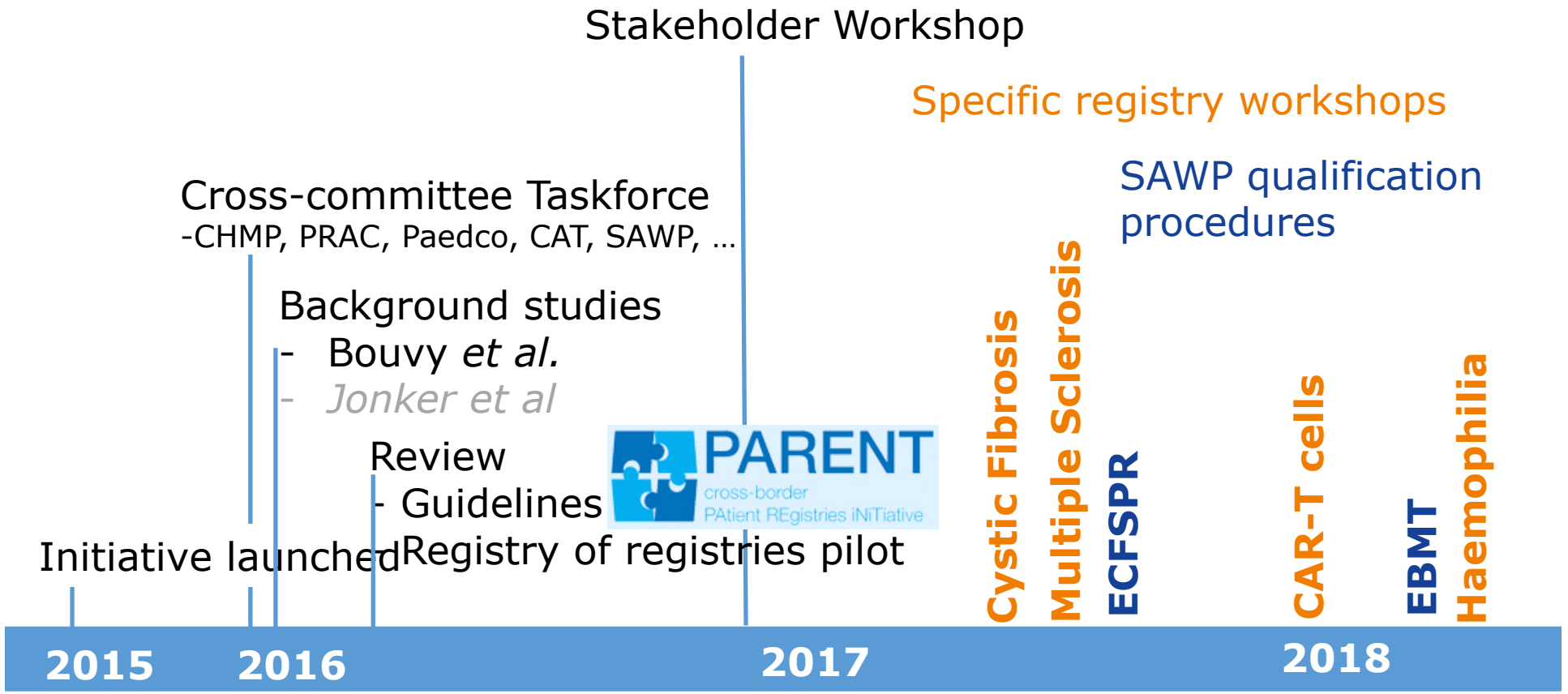
Patient Registry Initiative strategy - key components

- To promote dialogue between regulators, companies and registry holders to understand barriers and opportunities of using disease registries.

- To clarify concepts: **registry vs. study** that may be registry-based



Patient Registry Initiative



EMA registries workshops

Cystic Fibrosis Registries Workshop: 14th June 2017

Multiple-Sclerosis Registries Workshop: 7th July 2017

CAR T-Cell therapies Registries Workshop: 9th February 2018

Haemophilia Registries Workshop: 8th June 2018

Participants: regulators, companies, registry holders, health technology assessment bodies, patient and health care representatives

Diseases selection?

- ✓ Products recently authorised or authorisation process ongoing
- ✓ New products - business pipeline
- ✓ EU disease registries have requested support for harmonisation
- ✓ On-going qualification procedures for two EU-wide registry platforms

McGettigan, P *et al. 2019 Drug Safety*
https://doi.org/10.1007/s40264-019-00848-9

Lessons learned and challenges

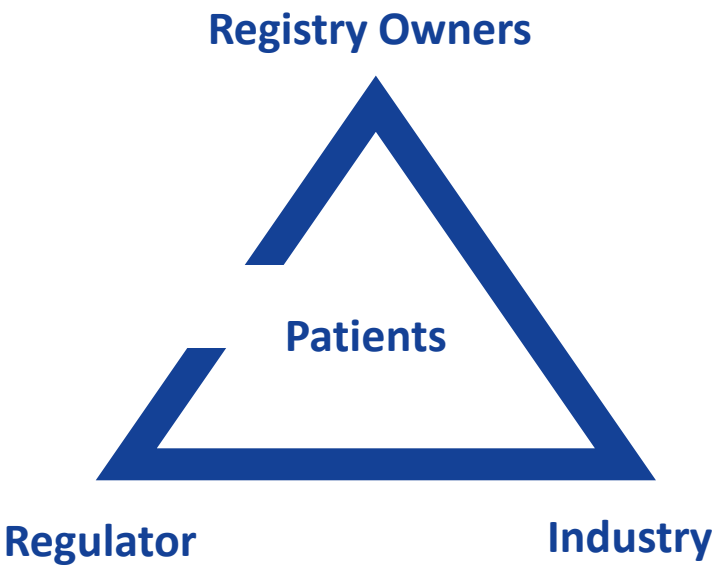
Governance

- **Regulators and marketing authorisation holders / applicants (MAHs/MAAs)**
  - Need to be aware of data that can be feasibly be collected by registries
  - Inform registries on their data needs - early discussions
  - Process for collecting and reporting adverse events defined / described in study protocol
- **Registry holders**
  - Develop policy for timely data sharing based on data protection and informed consent
  - Establish a system for centralised data application requests
  - Require sustainable funding for registries
- **All**
  - Transparency on access to, sharing of, and publication of data

How can regulators support use of disease registries?

- **Methodological guidance** on use of disease registries from a regulatory perspective
- **Scientific Advice** on PASS/PAES study protocol using registries, e.g. joint collaborative studies
- **Inventory of disease registries**

  https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/encepp-resource-database-inventory-patient-registries_en.pdf
- **Facilitation of interactions** between regulators, industry and registry holders during the entire life cycle of a product
- **Collaboration with EU initiatives**, e.g., EUnetHTA Joint Action 3, EC JRC European Platform on Rare Disease Registration
- **Qualification procedure**



Guideline on registry-based studies

24 September 2020
EMA/502388/2020

Guideline on registry-based studies

Draft

Draft approved by the Cross-Committee Task Force on Registries	May 2020
Draft sent to the EU Regulatory Network for consultation	9 July 2020
Start of public consultation	24 September 2020
End of consultation (deadline for comments)	31 December 2020

Comments should be included in the form published with this draft guideline, and should be sent to EMAregistries@ema.europa.eu by 31 December 2020.

- Recommendations on key methodological aspects that are specific to the use of patient registries by marketing authorisation applicants and holders (MAAs/MAHs)
- Aspects of patient registries that regulators consider important for their use in registry-based studies are included
- Checklist for evaluating the suitability of registries for registry-based studies

https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-registry-based-studies_en.pdf

RWD/RWE in applications submitted 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.

Xavier Kurz (EMA), submitted

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)

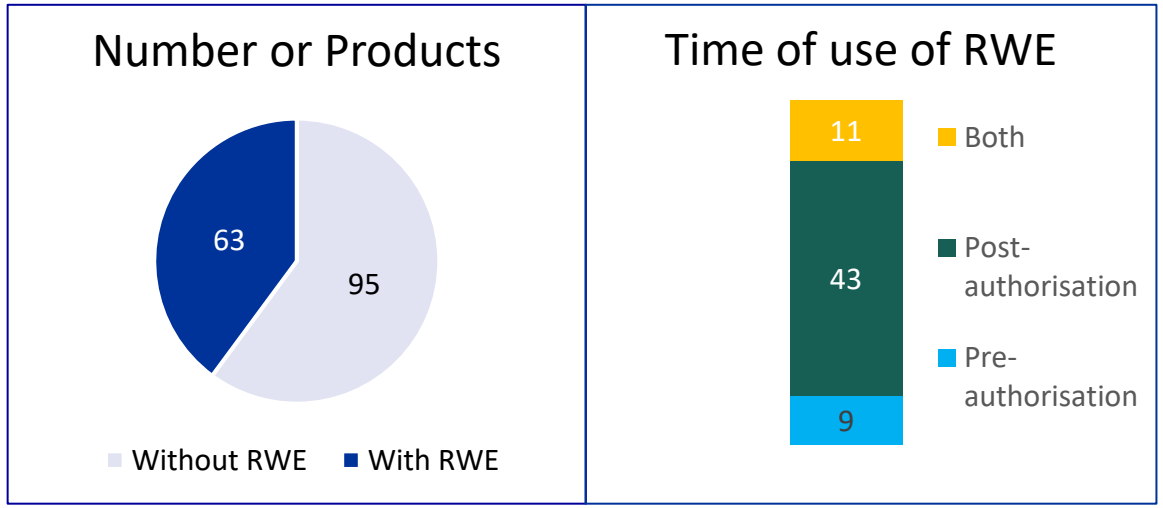
- Possible reasons: Single arm trial designs, Identification of patients for non-interventional study/Feasibility analysis, Patterns of drug utilisation, Need to collect data on long term safety/effectiveness

When used pre-authorisation: mainly **supporting** study looking at **efficacy/effectiveness**

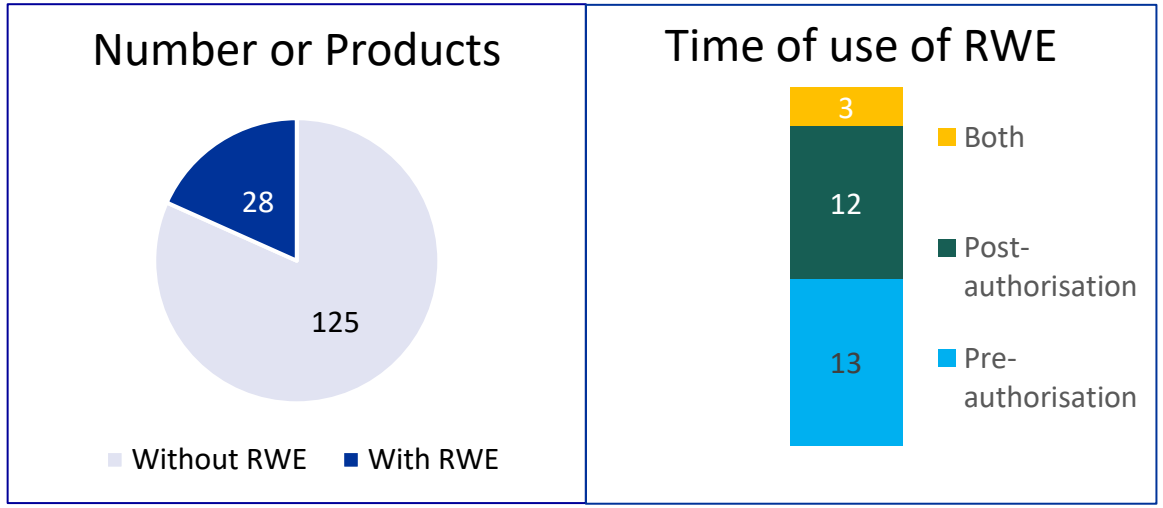
When used post-authorisation: mainly **RMP Category 3** (for studies included in RMP) looking at **safety**

Xavier Kurz (EMA), submitted

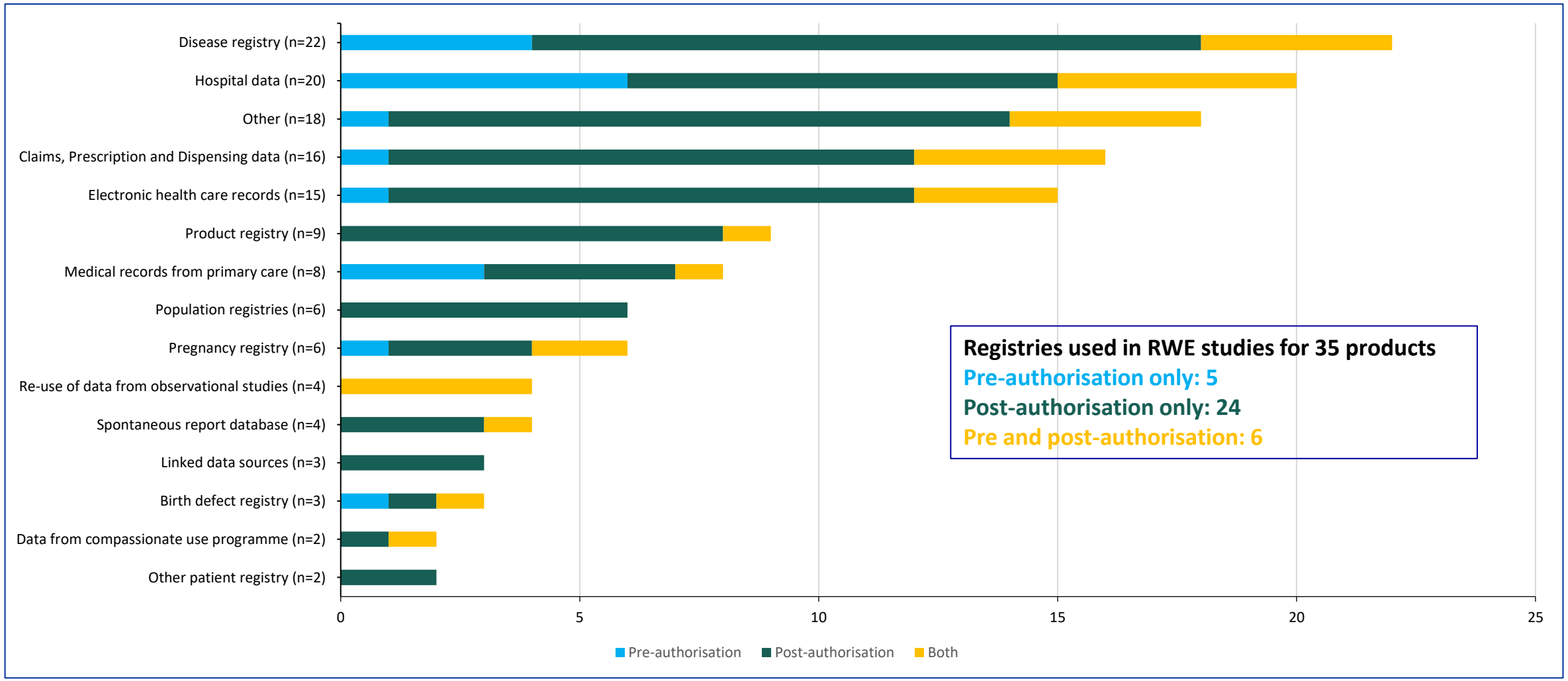
Initial MAA (n=158)



Extension of indication (n=153)



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



** 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*

Xavier Kurz (EMA), submitted

Conclusions

- Paradigm shift from “product registry owned by single company” to “(joint) collaboration with disease registry for long-term patient follow-up”
- Concerns about data quality of existing disease registries but workshops revealed high interest from companies and registry holders to collaborate
- Gap between the amount/type of data collected in disease registries and data requested by regulators
- Early interactions between regulators and registry holders may help bridge the gap
- EU regulatory network develops tools to support use of disease registries, such as methodological guidance (registry-based studies)

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