EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Guideline on registry-based studies

Consultation of Committees

EMA 25 years

Presented by: Xavier Kurz, Valerie Strassmann and Kelly Plueschke
EMA Data Analytics and Methods Task Force

In this presentation:

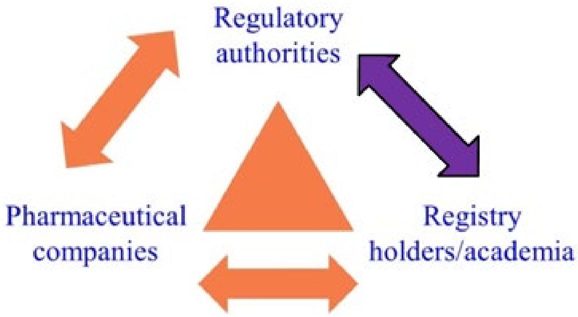
- Background
- Objectives and Scope
- Table of Contents
- Points for consideration
- Next steps - timelines

Background (1)

- EMA Patient Registry Initiative launched, September 2015
- Aims to facilitate use of disease registries by introducing and supporting a systematic approach to their contribution to the benefit-risk evaluation of medicines

Key components of the initiative

- To promote dialogue between regulators, companies and registry holders to understand barriers and opportunities of using disease registries.
- To provide guidance to clarify methodological concepts and regulatory requirements



Source: Nicola Ruperto, PRINTO

Background (2)

EMA Cross-Committee Task Force on Registries

Peter Mol – Chair – SAWP (CBG-MEB)
Kieran Breen – PCWP (European Parkinson's Disease Association)
Christian Gartner – BSWP (AGES)
Virginie Hivert – PRAC (Eurordis)
Carla Jonker (CBG-MEB)
Brigitte Keller-Stanislawski – PRAC (PEI)
Dolores Montero- (AEMPS)
Jan Span - CAT (CBG-MEB)
Milena Stain - CHMP (AGES)
Sabine Straus – PRAC (CBG–MEB)
Ulla Wändel Liminga – PRAC (MPA)

EMA: Priya Bahri, Julianna Fogd, Karin Hedenmalm, Xavier Kurz, Jane Moseley, Kelly Plueschke, Valerie Strassmann

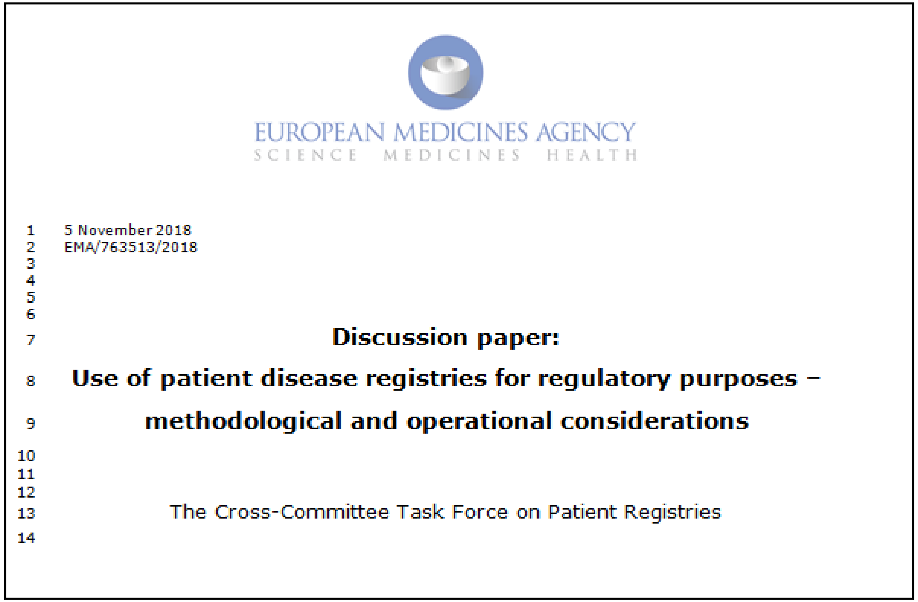
Background (3)

- Specific disease related multi-stakeholder workshops on :
  - Cystic fibrosis registries: 2017
  - Multiple sclerosis registries: 2017
  - Registries for CAR T cell therapies: 2018
  - Haemophilia (Factor VIII) registries: 2018
  - Use of registries in the monitoring of cancer therapies based on tumours' genetic and molecular features: 2019

- Follow-up actions:
  - Survey on safety data collection in registries
  - Further work on essential data elements for the cancer registries
  - Interactions with other disease registries based on lessons learned from the workshops

Background (4)

Discussion paper: Use of patient disease registries for regulatory purposes – methodological and operational considerations



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

5 November 2018
EMA/763513/2018

Discussion paper:

Use of patient disease registries for regulatory purposes – methodological and operational considerations

The Cross-Committee Task Force on Patient Registries

Consultation from November 2018 to June 2019

Comments received from 48 organisations

September 2019-March 2020: revision by Cross-Committee Task Force on Registries

Decision to develop a **Guideline on registry-based studies**

Scope and objective

Objective: to provide recommendations on key methodological aspects of registry-based studies and the relevant legal basis and regulatory requirements for MAAs/MAHs

Also relevant to patients and to persons involved in the funding, creation and management of registries, those participating in the collection and analysis of registry data, and those planning to use the registry to perform registry-based studies with a possible regulatory purpose.

Scope: studies based on *disease registries* or studies characterised by the presence or occurrence of a particular condition such as a pregnancy or birth defect.

Guideline does not address *product registries* as such data collection should be considered either a clinical trial or a non-interventional trial/non-interventional study.

Table of content (1)

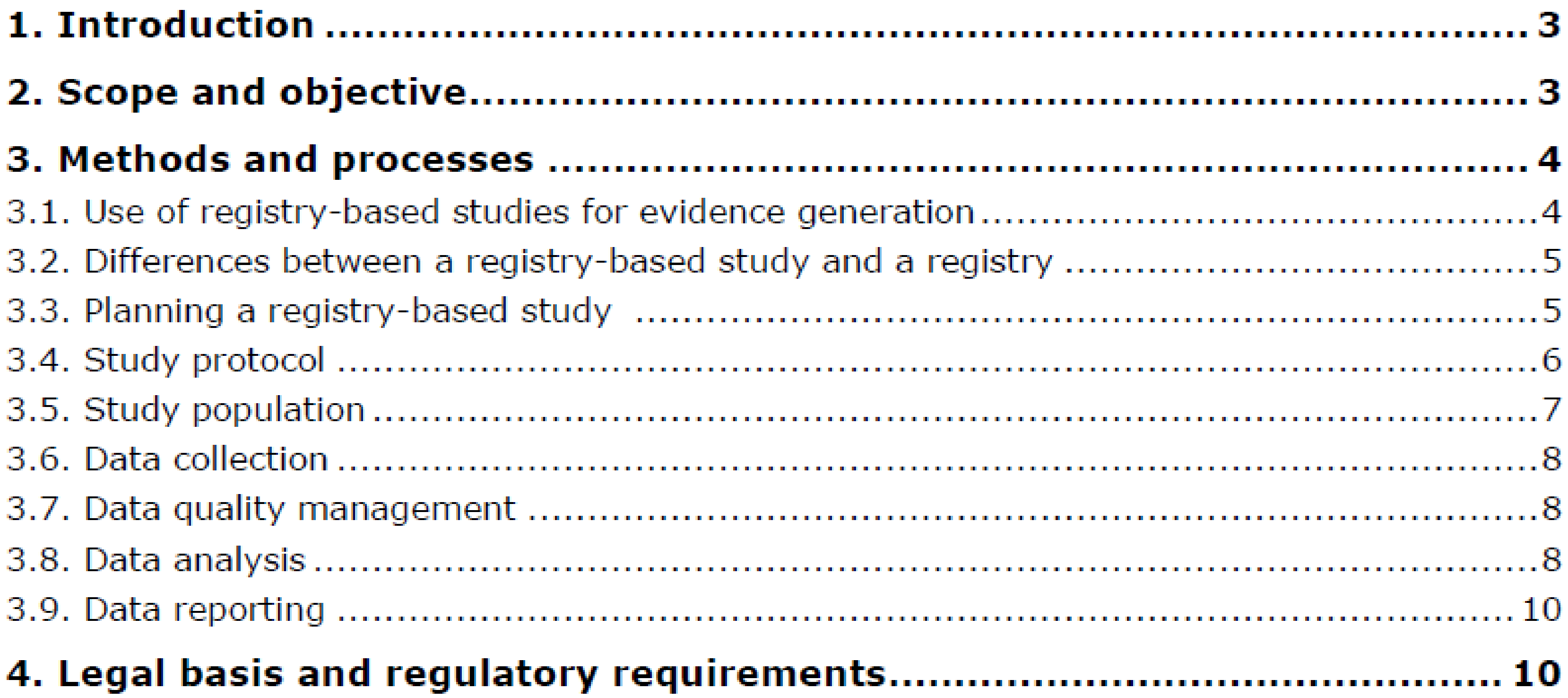
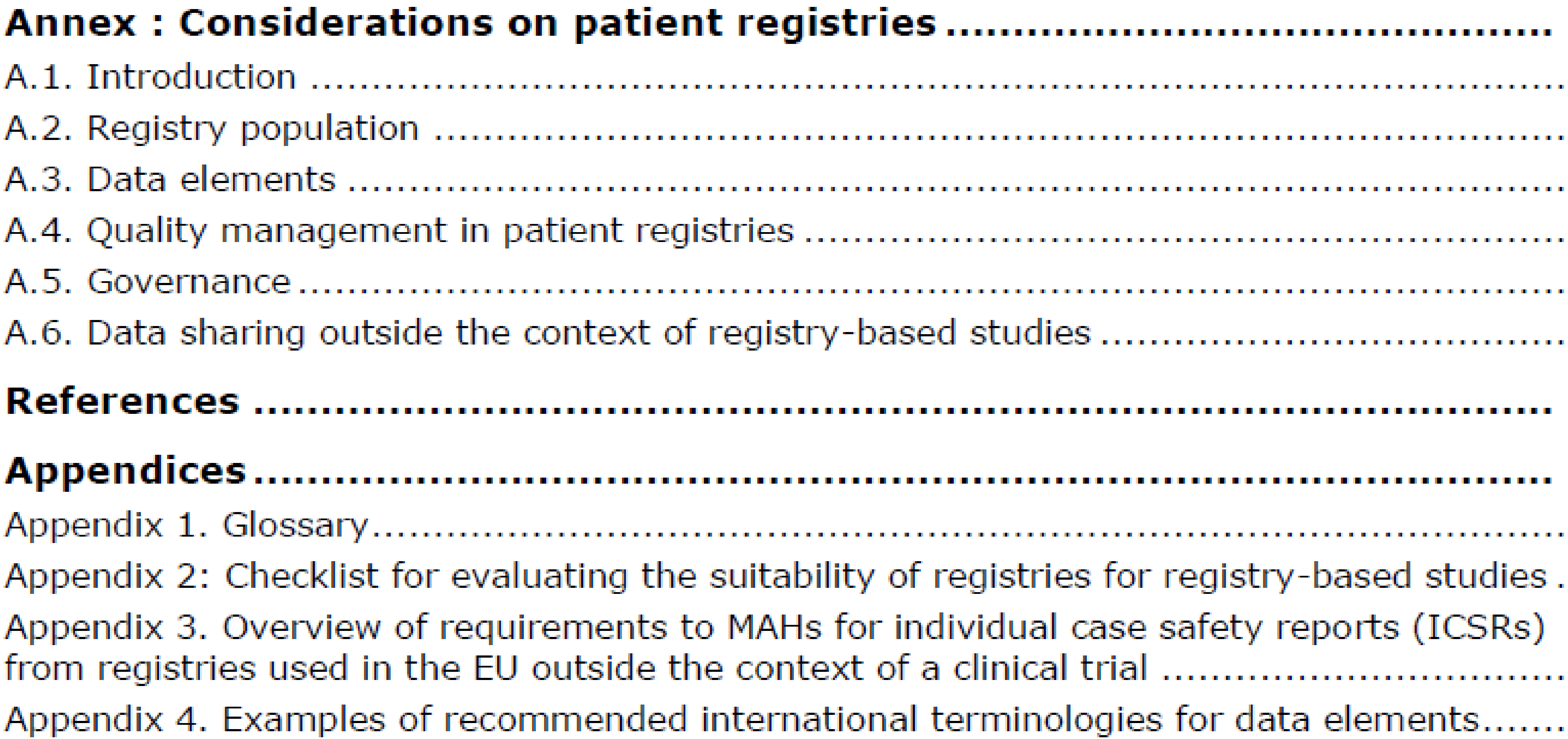


Table of content (2)



Points for consideration (1)

Definition

Registry-based study

Investigation of a research question using the infrastructure of (a) new or existing registry(-ies) for patient recruitment and data collection.

A registry-based study may be a clinical trial or a non-interventional trial/study.

Post-authorisation, a registry-based study may be a post-authorisation safety study (PASS), a post-authorisation efficacy study (PAES) or another type of study with other objectives

A registry-based study may apply primary data collection and/or secondary use of data collected through a registry for a purpose other than that of the given study.

Points for consideration (2)

	Registry-based study	**Registry**
1. Definition	Investigation research question or hypothesis.	Data collection system
2. Timelines	Driven by the collection/ extraction and analysis of data relevant to the study	Driven by schedules for data collection and data analyses which prompted the registry.
3. Patient enrolment	Defined by research objective(s)	Complete enrolment depending on the purpose of the registry
4. Data collection	Needed by the research question– additional data collection may be required.	Depending on the purpose of the registry; agreed core set of data elements to be collected
5. Analysis plan	Statistical analysis plan	Often descriptive and performed routinely
6. Data quality control	Additional quality assurance may be needed.	Applied routinely with a focus on core set of data elements.

Points for consideration (3)

Planning a registry-based study

Early discussions with regulators through Scientific Advice, the PRIME procedure or pre-submission meetings.

Early discussions should also take place if registry-based studies are planned post-authorisation; they should involve the concerned Rapporteurs (including PRAC) or Lead Member States as well as the MAA/MAH, registry holders and HTA bodies if relevant.

It is the responsibility of the MAA/MAH to involve in the discussion the holders of the registry(-ies) intended to be used.

Points for consideration (4)

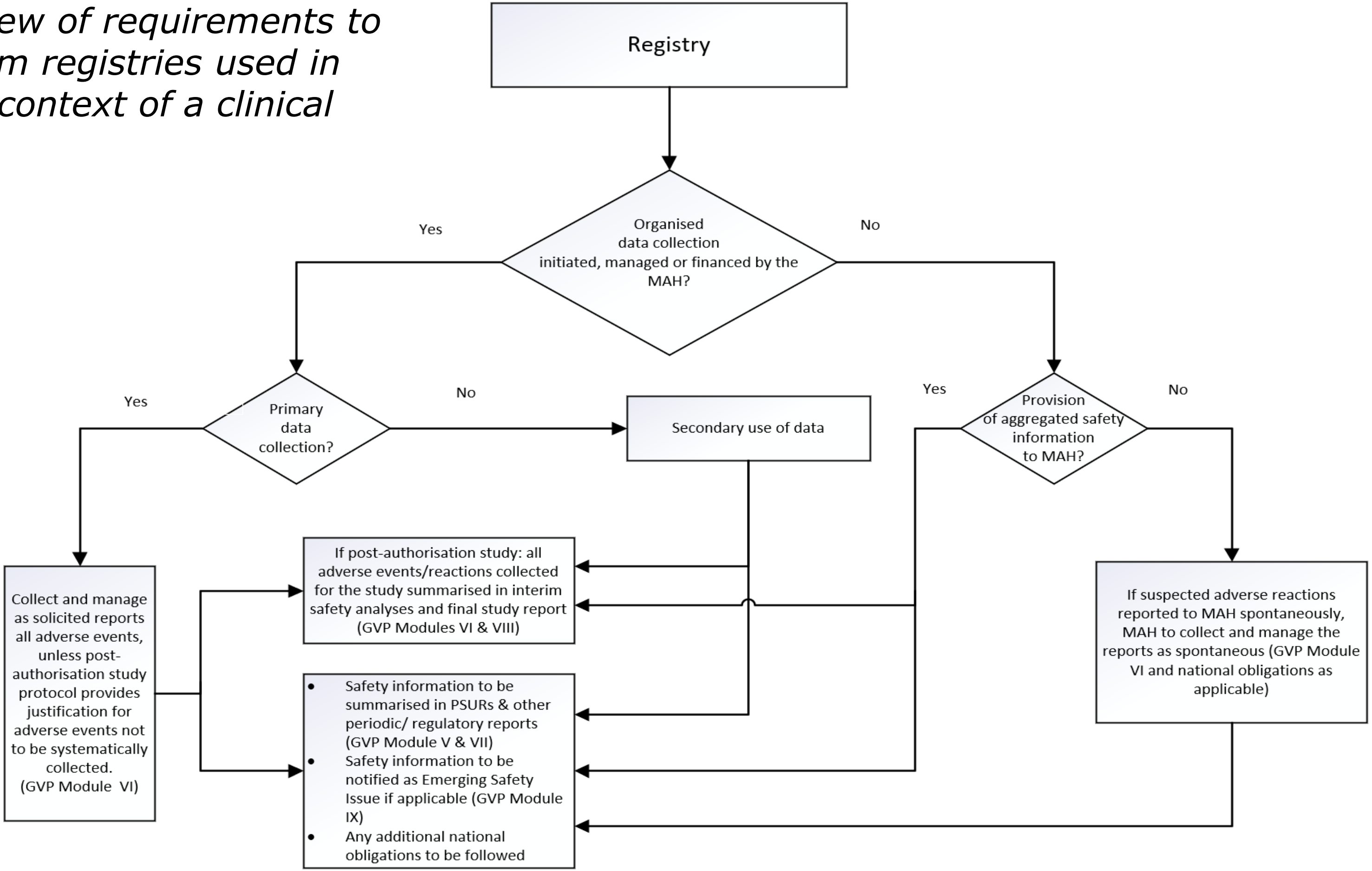
Planning a registry-based study

Feasibility analysis: performed by the MAA/MAH or research organisation initiating the registry-based study in collaboration with registry holders to facilitate the discussion with regulators and other parties

- Description of the registry(-ies) (check list proposed)
- Availability of the data elements needed for the study and of the capacity to collect any additional ones or introduce additional data collection
- Processes in place for AEs/ADRs and capacity to introduce additional data collection if needed.
- Data on the numbers of registered patients, active patients and patient flows
- Potential selection bias due to inclusion/exclusion criteria
- Potential confounding if some data elements are not available
- Analytical issues that may arise
- Any data privacy issues and governance-related issues
- Overall evaluation of the suitability of the registry for the specific study.

Points for consideration (5)

Appendix 3. *Overview of requirements to MAHs for ICSRs from registries used in the EU outside the context of a clinical trial*



Registry

Organised data collection initiated, managed or financed by the MAH?

Yes

No

Primary data collection?

Yes

No

Secondary use of data

Provision of aggregated safety information to MAH?

Yes

No

Collect and manage as solicited reports all adverse events, unless post-authorisation study protocol provides justification for adverse events not to be systematically collected. (GVP Module VI)

If post-authorisation study: all adverse events/reactions collected for the study summarised in interim safety analyses and final study report (GVP Modules VI & VIII)

- Safety information to be summarised in PSURs & other periodic/ regulatory reports (GVP Module V & VII)
- Safety information to be notified as Emerging Safety Issue if applicable (GVP Module IX)
- Any additional national obligations to be followed

If suspected adverse reactions reported to MAH spontaneously, MAH to collect and manage the reports as spontaneous (GVP Module VI and national obligations as applicable)

Next steps

- June 2020: presentation to Committees
- June-July 2020: consultation of Committee members in writing (deadline: 31 July 2020)
- August 2020: amendment of Guideline as needed
- Mid-September 2020: public consultation
- Q4 2020: workshop with stakeholders (t.b.c.)

Any questions?

Further information

EMAregistries@ema.europa.eu

Official address Domenico Scarlattilaan 6 • 1083 HS Amsterdam • The Netherlands
Send us a question Go to www.ema.europa.eu/contact
Telephone +31 (0)88 781 6000

Follow us on **@EMA_News**