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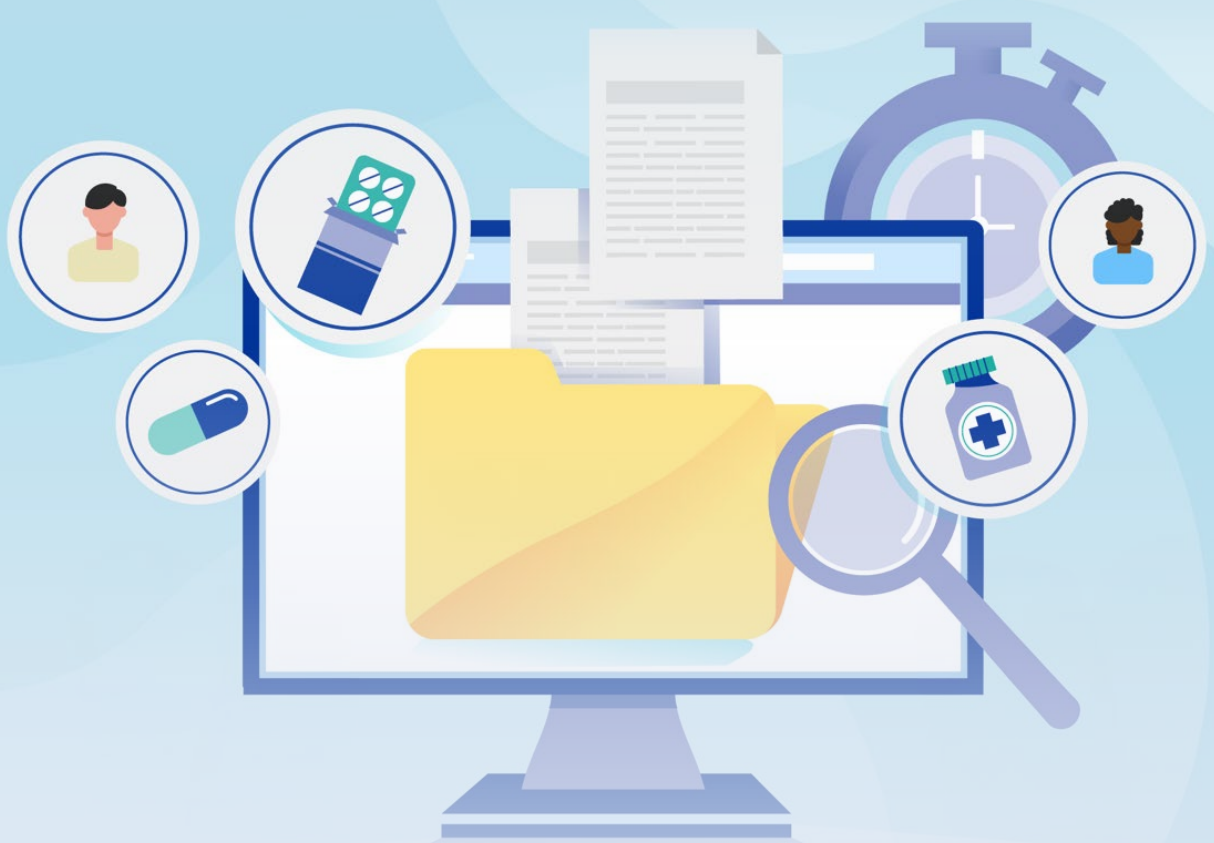
3.1 Clinical trials raw data pilot: interim results

Joint PCWP/HCPWP meeting – 02 July 2024

Presented by Marcia Rueckbeil
European Medicines Agency – Data Analytics and Methods Task Force

Content

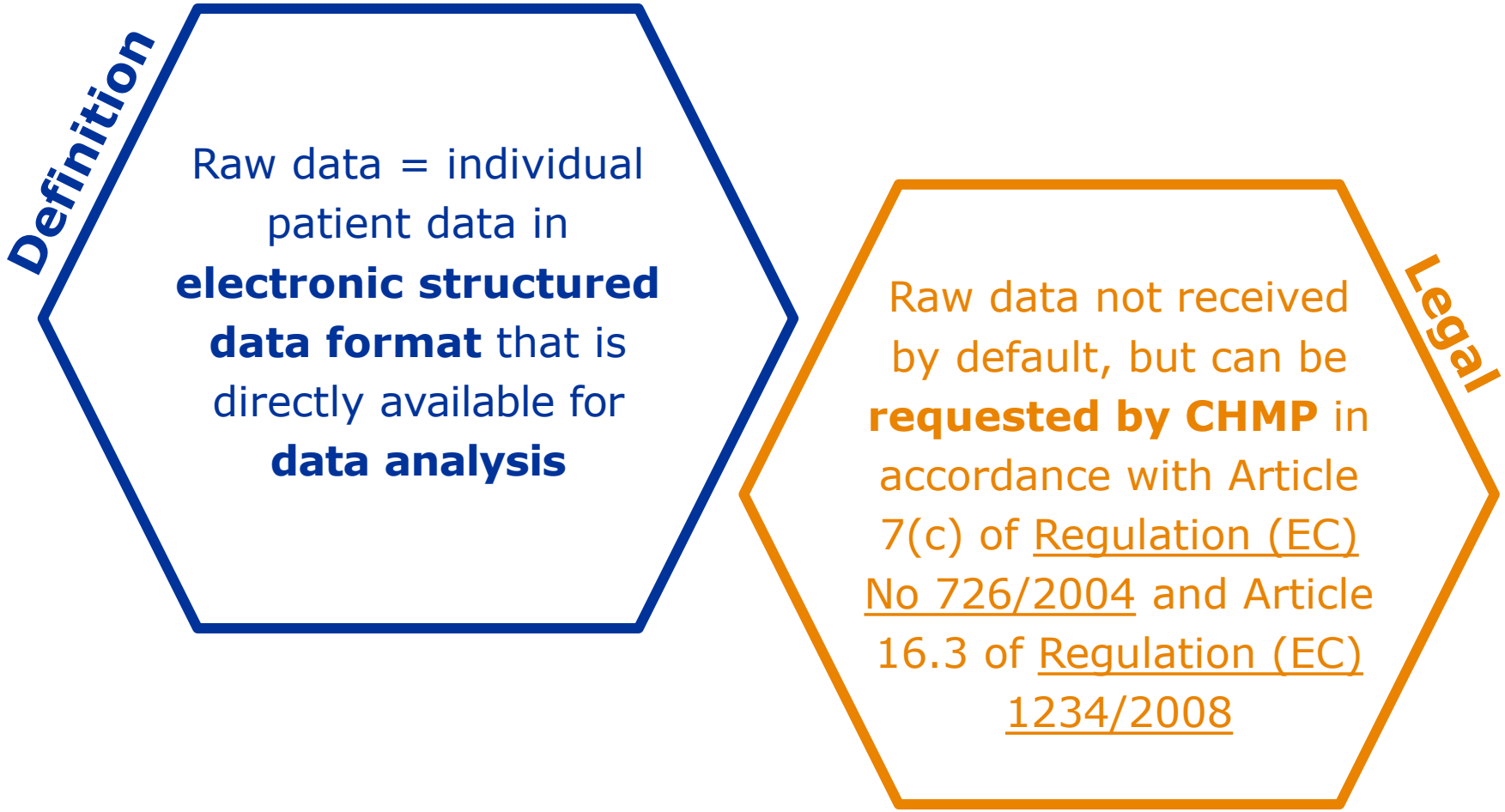


1 **Pilot reminder and status update**

2 **Interim pilot results**

Definition of 'Raw Data' and current legal basis

Now: Individual patient data in PDF format already provided by companies for all submissions, but format does not directly enable data analysis.



Expected benefits of raw data access and analysis

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Expected benefits of the clinical studies' raw data analysis for selected key stakeholders

EU patients & HCPs

- Faster access to innovative, safe and effective medicines
- Enhanced confidence in regulatory decision-making
- Refined product labelling/ targeting of subgroups within the recommended indications
- Facilitation of cross-product analyses

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- Enhanced understanding of clinical study results to inform regulatory decision making
- Fewer questions of data interpretation to the applicant/marketing authorisation holder (MAH)
- Facilitation of cross-product analyses
- Optimised use of inspection resources

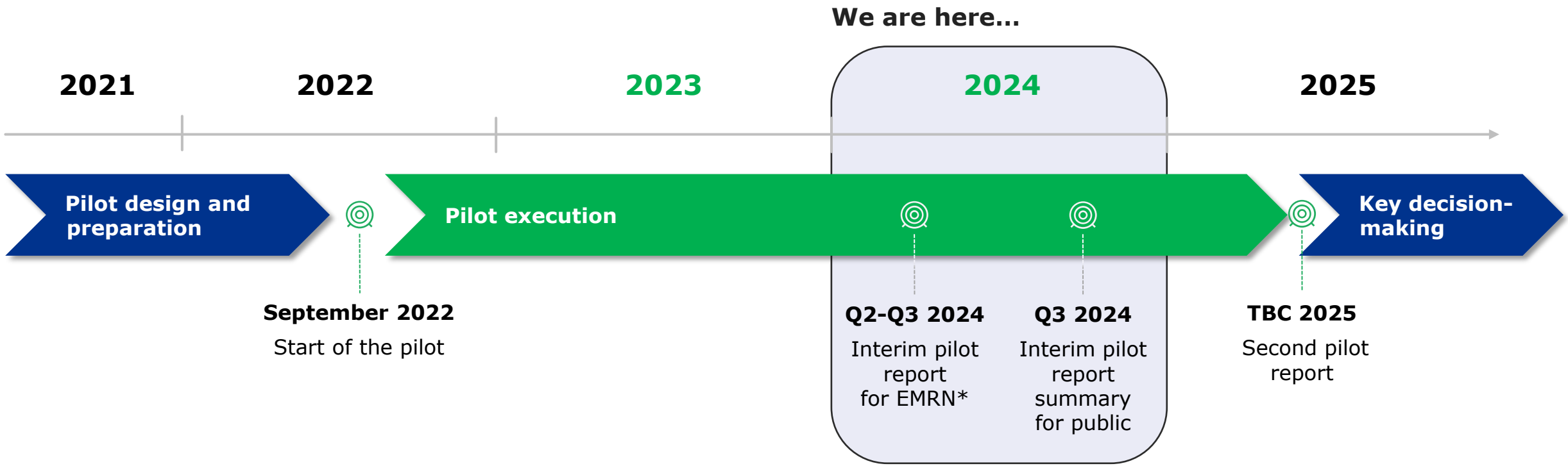
Applicants/MAHs

- Workload reduction due to fewer complex questions
- Shorter clock-stops
- Earlier authorisation

Raw data pilot phases and key timelines

Purpose of pilot

Determine the **benefits of raw data access** and analysis to support the scientific assessment of medicinal products; identify the **target operating model**, **capacity and capability requirements**, and **technical requirements** for receiving, validating, storing, managing and analysing raw data.



** EMRN – European Medicines Regulatory Network*

Raw data pilot overview

Timelines: Approx. **10 regulatory procedures over 2 to 3 years** from September 2022.

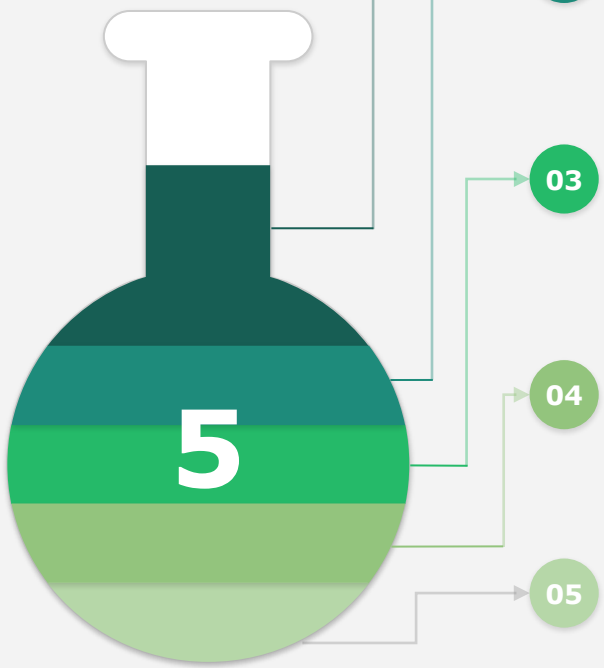
Procedure scope: **Initial marketing authorisation applications** and **post-authorisation applications**.

Participation: Procedures are based on **voluntary participation of CHMP Rapporteur teams** and **applicants/MAHs**.

Analysis scope: **Three analysis objectives** including Clinical Efficacy & Safety, Pharmacokinetic-Pharmacodynamic (PK-PD) and Good Clinical Practice (GCP) site selection.

Resourcing scenarios: **Three resourcing scenarios** for data analysis being explored: the CHMP Rapporteur teams, EMA staff and/or EMA contractors (DKMA).

Included pilot procedures up to December 2023*



01 **Initial MAA: new active substance**
In the area of neurology

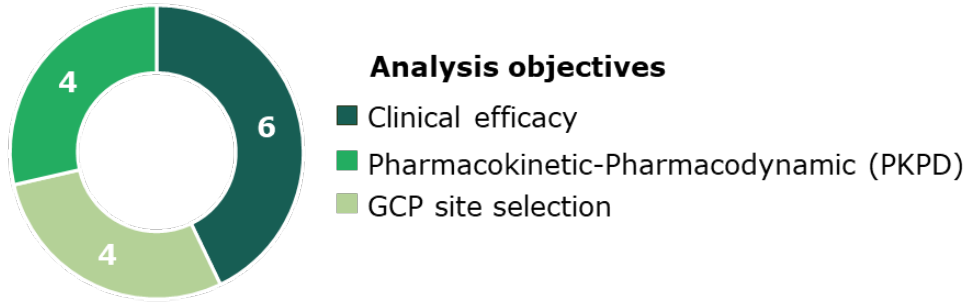
02 **Initial MAA: biosimilar**
In the area of endocrinology

03 **Type II variation****
In the area of oncology

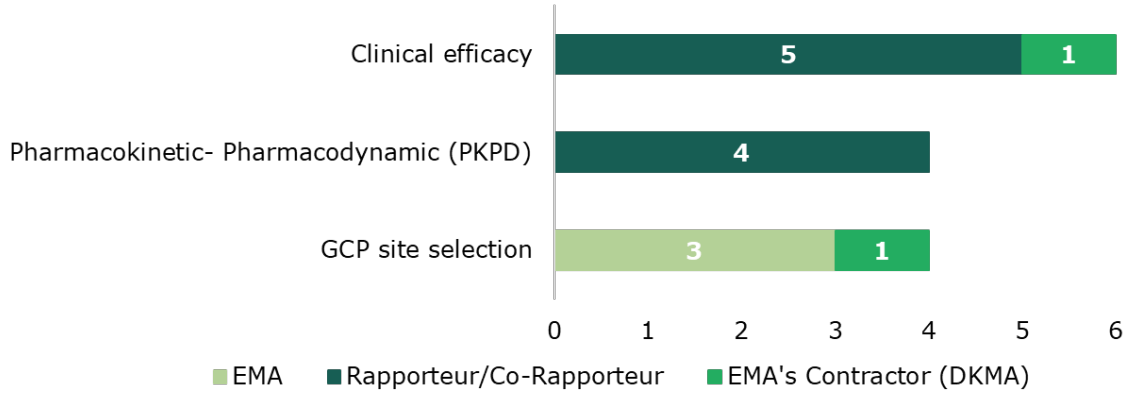
04 **Type II variation**
In the area of dermatology

05 **Initial MAA: new active substance**
In the area of gastroenterology

Analysis objectives



Resourcing scenario



Among the *Clinical efficacy* analyses performed by Rapporteur/Co-rapporteur **one of them** was conducted by a **NCA as Member State providing comments**.

** The presentation shows the numbers at the time of the analysis and drafting of the interim report. Currently, 7 procedures are included.*
***This submission was postponed to Q2 2024; under the new timelines, it was agreed not to include the procedure in the pilot.*

Interim raw data pilot report

In **December 2023**, the cross-Agency's raw data pilot team conducted **surveys** to gather feedback from all pilot participants

4 AREAS OF FEEDBACK

- Added value for assessment and decision making
- Capacity and capability
- Governance and processes
- Technical aspects

64% RESPONSE RATE

47 feedback received out of 74*

60 different PARTICIPANTS

- CHMP Rapporteur/ Co-rapporteur
- Data analyst
- Rapporteur/Co-Rapporteur assessment team
- NCA staff involved in provision of member state comments informed by raw data analysis
- EMA pilot procedure coordinator
- EMA product lead
- EMA GCP officer
- GCP inspectors
- Applicant/MAH

** Some participants provided feedback for more than one procedure*

Preliminary learnings and insights as reported by pilot participants

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Added value for assessment and decision making

- **Fewer questions to the Applicant/MAH**, as some were resolved via raw data analysis
- Improved **understanding of the information submitted** in the MAA dossier
- Helps build **consensus** on methodological issues **amongst Rapporteurs**
- Potential to **optimise** the use of limited **inspection resources**

Capacity and capability

- Additional EMRN expertise needed in the field of **statistical programming**, PK-PD modelling, biostatistics, and **clinical trial data standards**
- Conduct of additional tasks on raw data **allowed assessment to be performed** according to timelines

Governance and processes

- Most **resourcing scenarios tested successfully** for analyses supporting the clinical efficacy & safety assessment and selection of sites for GCP routine inspection
- **NCAs providing member state comments** on the assessment conducted raw data analyses

Technical aspects

- **Data package requirements** by other international regulators deemed suitable
- **Data submission, storage and analysis** worked adequately for the pilot but will require optimisation to upscale in case of larger volume of raw data submissions
- **Choice of software under investigation** for all areas: clinical efficacy, PK-PD modelling, GCP

Selected recommendations for the second part of the pilot

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Added value for assessment and decision making

- Continue **enrolling procedures for the pilot**

Capability and capacity

- Continue **raising awareness of stakeholders** regarding use of raw data analysis in regulatory decision-making by providing regular updates to the European Medicines Regulatory Network and public fora

Governance and processes

- **Test EMA's support** in carrying out **analyses in support of benefit-risk assessment**
- Consider testing a resourcing scenario where **a contractor outside the EMRN acts as data analyst**

Technical aspects

- Acquire **relevant PK-PD analytical software** at EMA

Next steps & Discussion points

- Interim pilot report
  - Dissemination to the European Medicines Regulatory Network (Q2-Q3 2024)
  - Public dissemination (Q3 2024)
- Reflections on the preliminary learnings & recommendations?
- Any other comments?

Thank you

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Further information

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Back-up slides

New EU pharmaceutical regulation (proposal)

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Article 6

Centralised marketing authorisation application

1. Each application for a centralised marketing authorisation of a medicinal product for human use shall specifically and completely include the particulars and documentation as referred to in Chapter II of [revised Directive 2001/83/EC]. In the case of applications in accordance with Article 6(2), Article 10 and Article 12 of [revised Directive 2001/83/EC], this shall include the electronic submission of raw data, in accordance with Annex II of that Directive.

Recital 45

Marketing authorisation applications, like any other application submitted to the Agency, should follow the digital by default principle and hence be sent to the Agency in electronic form. Applications should be assessed based on the file submitted by the applicant in accordance with the different legal basis provided by [revised Directive 2001/83/EC]. At the same time, the Agency and the relevant committees may take into account any information that is in its possession. Applicants shall be requested to generally submit raw data, in particular with regard to the clinical trials performed by the applicant in order to ensure a full assessment of the quality, safety and efficacy of the medicinal product.

Network priority: clarify benefit of access to 'raw data' (1)

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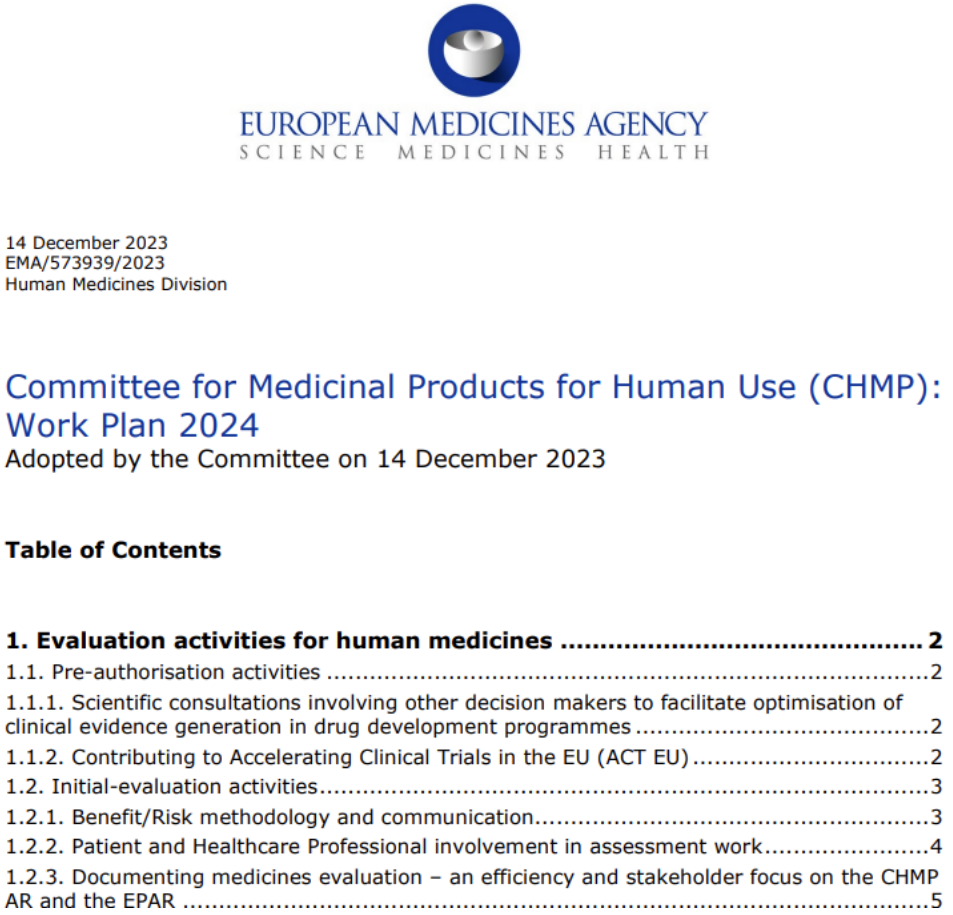
Key objective

Explore the analysis of raw data from Marketing Authorisation (MA) dossiers to the assessment of initial marketing authorisation applications and selected post-authorisation procedures.

Activities in 2024

- Continue the proof-of-concept pilots of analysis and visualisation of raw data from MA dossiers to learn of the practicalities and benefits of such an approach
- Expand Network Community on Raw Data to regularly share developments on the raw data proof of-concept pilots and foster close collaboration across the Network into using raw data for regulatory decision-making
- Produce the proof-of-concept pilots' interim report to reflect on the pilot conduct



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14 December 2023
EMA/573939/2023
Human Medicines Division

Committee for Medicinal Products for Human Use (CHMP): Work Plan 2024
Adopted by the Committee on 14 December 2023

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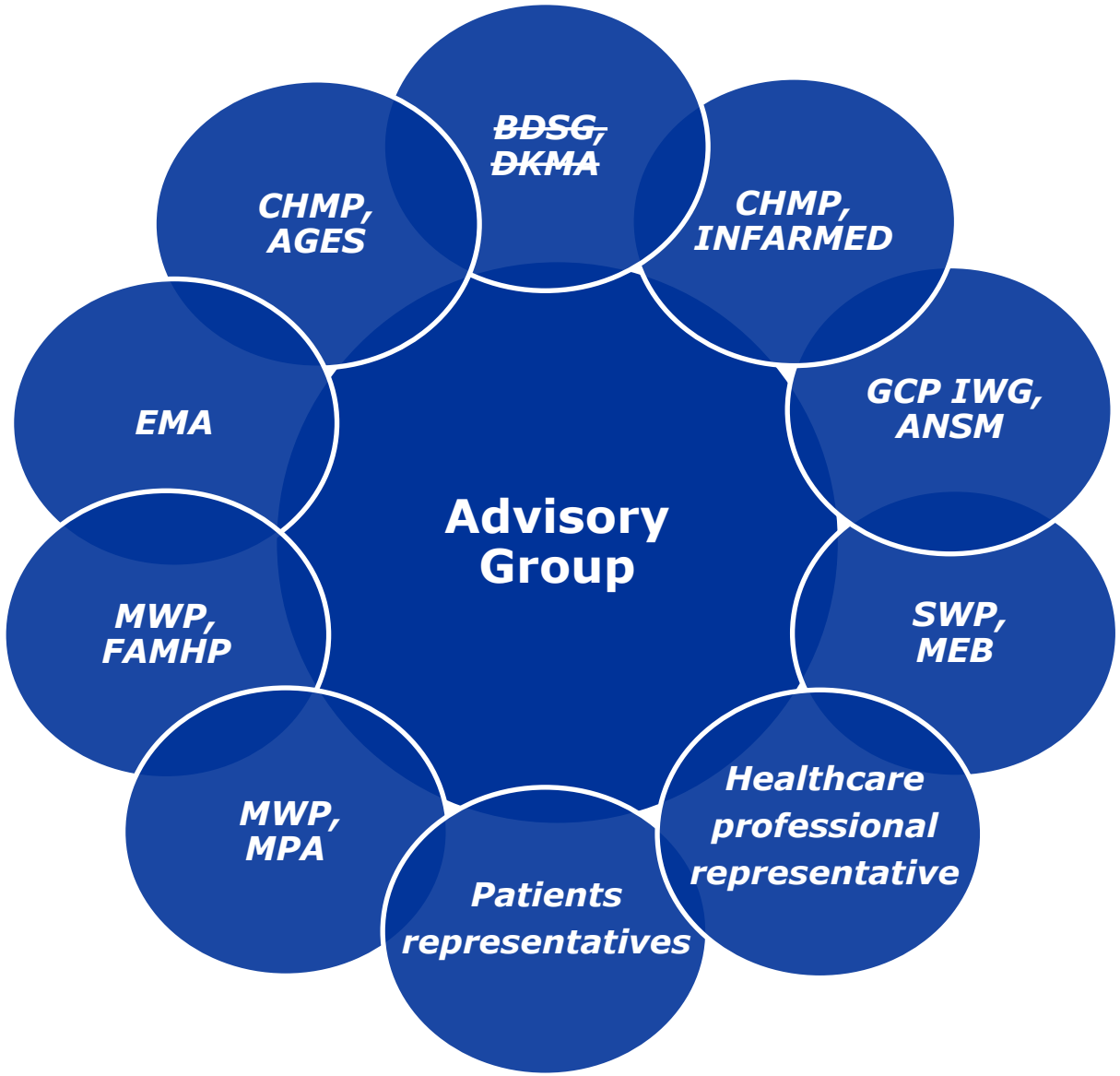
Network priority: clarify benefit of access to 'raw data' (2)

Big Data Steering Group work plans

A proof-of-concept pilot will be performed to clarify the benefits and practicalities of access to individual patient data […]. Learnings from the pilot will help the EU medicines regulatory network to make an informed decision on the place of raw data in regulatory decision-making.

Network – Advisory Group on Raw Data



Excluded pilot procedures up to December 2023*

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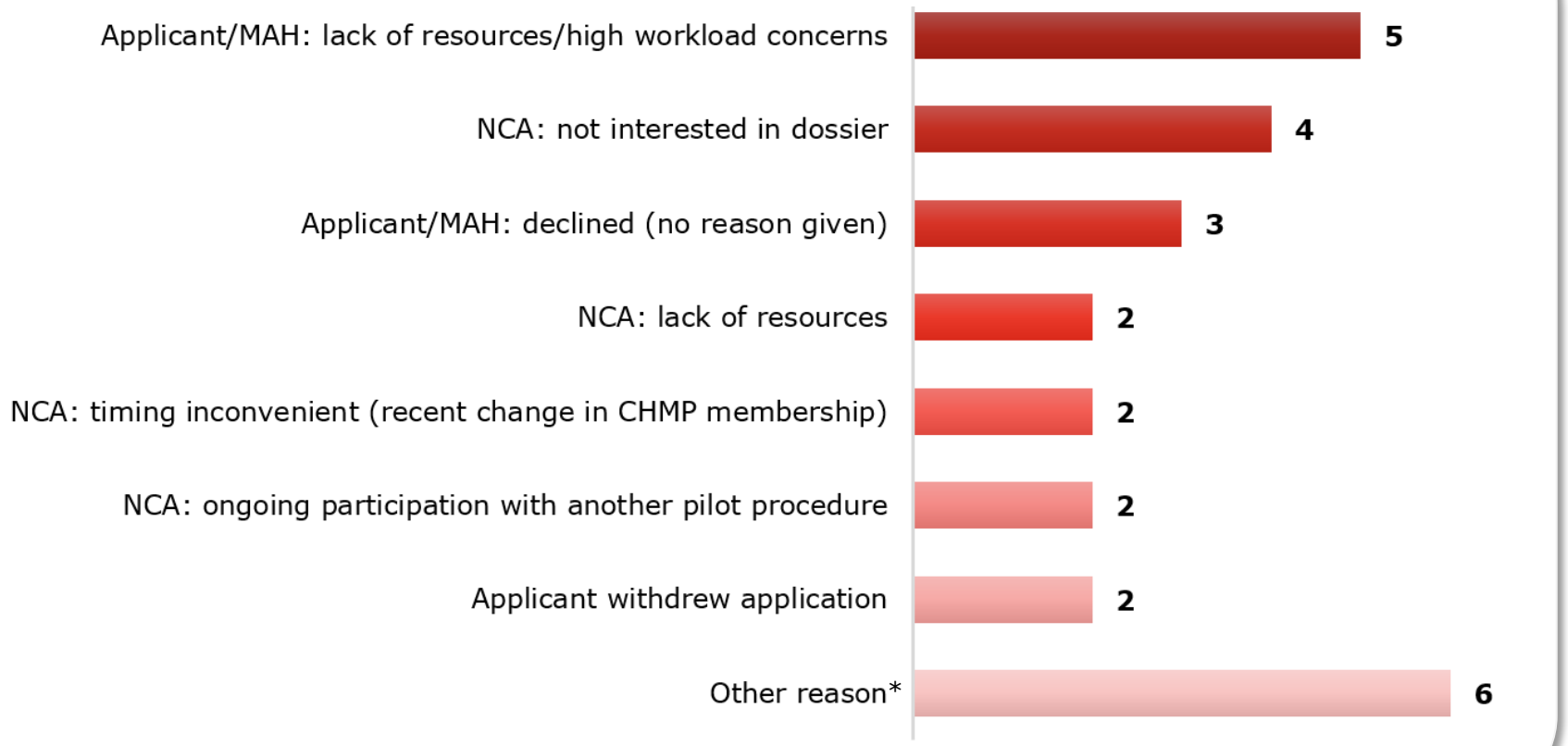
Overall, 36 procedures screened for pilot inclusion - **Reasons for exclusion**



** Other reasons:*

- *Procedure already underway at the time of the pilot invitation*
- *Submission date postponed due to a negative outcome from another international regulator*
- *Participation of the Applicant/MAH under the conditions of the Agency's policy in access to documents (Policy 0043) waiver*
- *Applicant/MAH declaring that the raw data package for EMA required updates since its submission to another international regulator due to a divergence between the regulators' data cut-offs*
- *Stringent upcoming submission timeline for the Applicant/MAH*
- *No response from the Applicant/MAH upon invitation for pilot participation*

**The presentation shows the numbers at the time of the analysis and drafting of the interim report. Currently, 7 procedures are included.*