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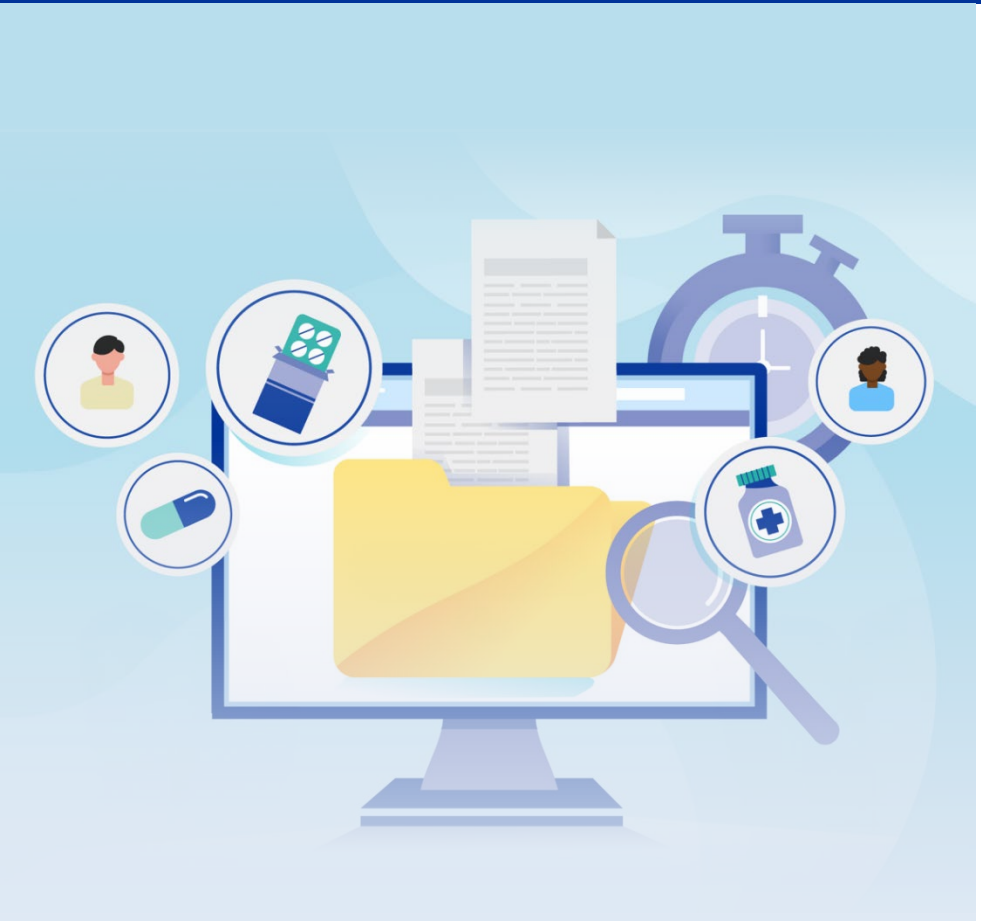
EMA's Clinical study data pilot – an update

Industry Stakeholder Platform on the Operation of the Centralised Procedure for human medicines - 22 November 2024

Presented by Eftychia Eirini Psarelli
EMA - Data Analytics and Methods Task Force

Content



1. **Pilot status update**
2. **Interim learnings incl. feedback from applicants/MAHs**
3. **Recommendations**
4. **Collaboration with Industry**

Mandate of the pilot

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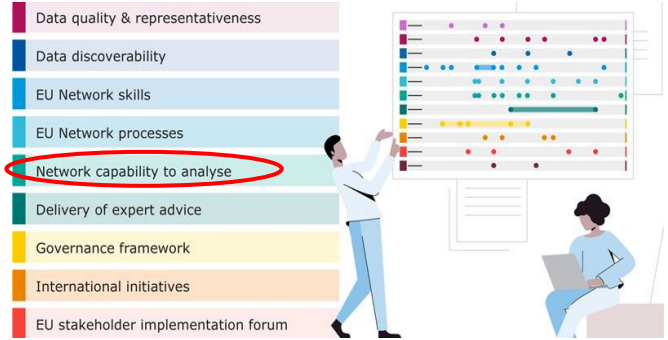
HMA/EMA BDSG work plan
(2023-2025)



MWP 3-year workplan
(2022-2024)

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15 January 2024
EMA/CHMP/478317/2023
Human Medicines Division

Revised consolidated 3-year work plan for the Methodology Working Party (MWP)

Chairperson: Kit Roes
Vice chair: Kristin Karlsson

Work plan period: May 2022 – December 2024

CHMP workplan
(2024)

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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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Expected benefits of clinical study access and analysis

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Expected benefits of the clinical studies' 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

European Medicines Regulatory Network

- 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

Clinical study data pilot phases and timelines *(as per initial plan)*

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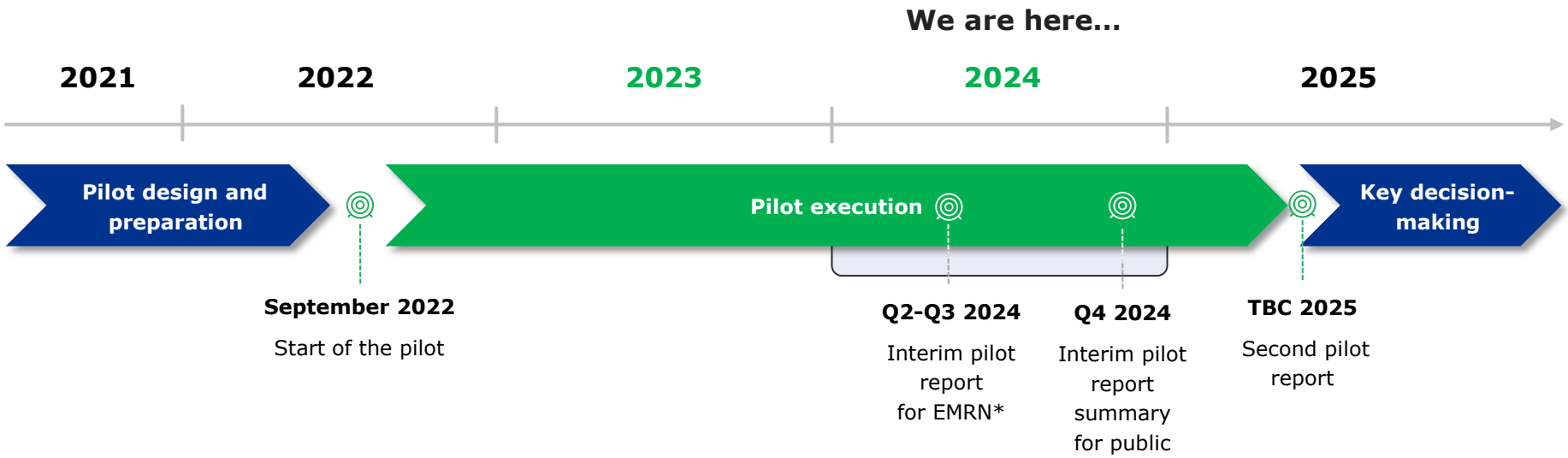
Purpose of pilot

Determine the **benefits of early clinical study data access** (at time of submission) 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 clinical study data.



Clinical study data pilot overview – initial design

Timeline:

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

9 procedures included so far.

Scope:

Initial marketing authorisation applications and **post-authorisation applications**. Focus on **benefit-risk assessment**.

Participation:

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

Analysis objective:

Three analysis objectives included: Clinical Efficacy, Pharmacokinetic-Pharmacodynamic (PKPD), GCP site selection.

Resources:

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

Procedures included in the pilot

Pilot's half-way point *was reached by December 2023…*

Procedure number	Therapeutic Area	Type of procedure
1	*Neurology* 	*iMAA-Full MAA*
2	*Endocrinology* 	*iMAA-Biosimilar*
3	*Oncology* 	*Post auth. Type II variation*
4	*Dermatology* 	*Post auth. Type II variation*
5	*Gastroenterology* 	*iMAA-Full MAA*

...up to now, November 2024

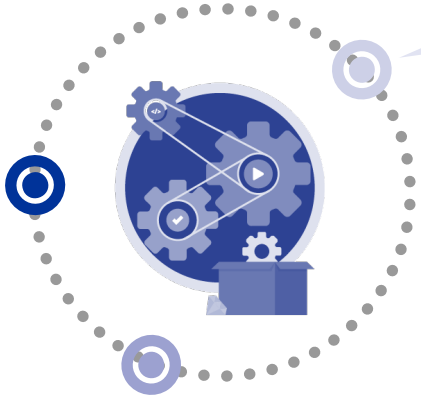
Procedure number	Therapeutic Area	Type of procedure
6	*Oncology* 	*iMAA-Biosimilar*
7	*Gastroenterology* 	*iMAA-Full MAA*
8	*Oncology* 	*iMAA-Full MAA*
9	*Oncology* 	*iMAA-Full MAA*

Interim clinical study data pilot report

In **December 2023**, the cross-Agency's clinical study data pilot team conducted **surveys** to gather feedback from all pilot participants (e.g. Rapporteur teams, applicants/MAHs, etc.)

4 AREAS OF FEEDBACK

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



>60% RESPONSE RATE

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 clinical study data analysis
- EMA pilot procedure coordinator
- EMA product lead
- EMA GCP officer
- GCP inspectors
- Applicant/MAH

Key preliminary learnings

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Added value for assessment and decision making

- **Fewer questions to the applicant/MAH;** resolved with clinical study data analysis [potential to reduce overall assessment time]
- Improved **understanding of the information submitted** in the MAA dossier [potential for better opinion on indications and warnings]
- **Consensus** on methodological issues **amongst Rapporteurs** [potential to reduce outstanding issues during decision-making discussion]
- Potential to **optimise** the use of limited **inspection resources** [shorter time needed to plan and conduct inspections]

Capacity and capability

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

Governance and processes

- **Most resourcing scenarios** tested successfully for analyses supporting the clinical efficacy and GCP routine inspection
- **Non-Rapporteur NCAs appear engaged,** with provision of Member State comments based on clinical study data analyses
- **Data package requirements** by other international regulators deemed suitable [no additional work for applicants]

Technical aspects

- **Data receipt, storage and analytics infrastructure** for EMRN will require optimisation to upscale
- **Choice of software under investigation** for all areas: clinical efficacy, PK-PD modelling, GCP [established off-the-shelf options available]

Feedback from applicants (1/2)

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*"The **communication** was very **smooth** with our EMA counterparts both via email and the meetings which were scheduled."*

*"We attended a **data submission meeting** with the EMA shortly after filing to orient the EMA team with the data. This meeting was very **similar to** that which normally takes place with the **FDA**, it was very practical in nature. For us **no changes are needed**."*

*"In the future it would be **beneficial to have the opportunity to discuss the electronic submission plan with EMA**. Further, It would be beneficial to have pre-submission interaction **aligned with the current process for FDA**."*

*"The Applicant would like to highlight that **alignment pre-submission was sparse**, so there was **no alignment with EMA on the adequacy of the data files / programs to be submitted** for the pilot."*

Feedback from applicants (2/2)

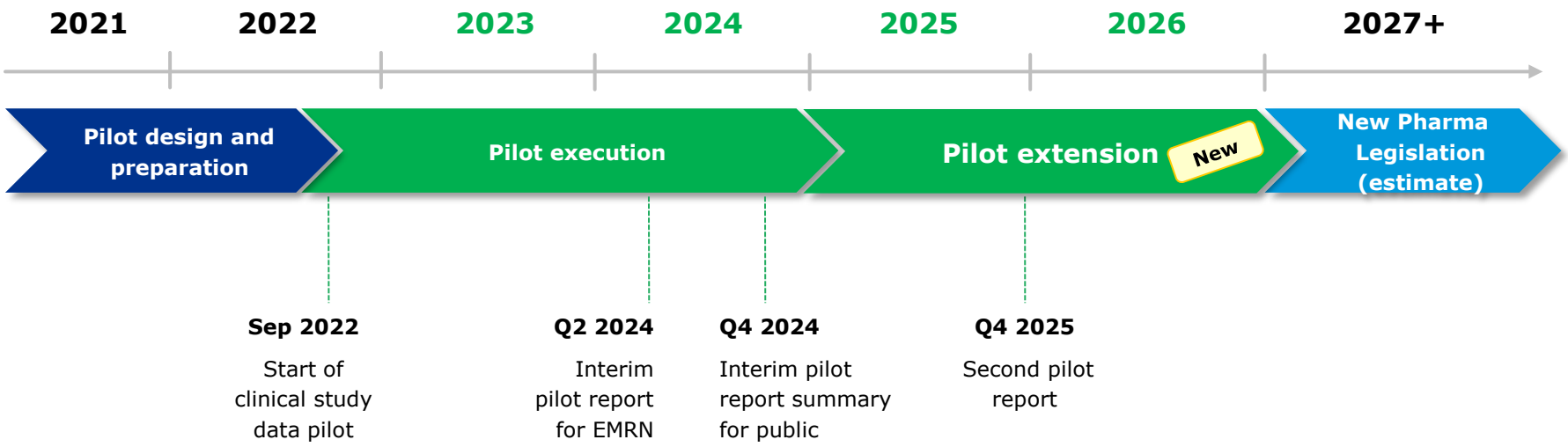
*"The **guidance** provided was acceptable and **helpful**."*

*"The **questions in the LoQ** (which informed on raw data) **were clear**. It was **appreciated** that **EMA share in detail** which analysis were performed, how they were performed and why they were performed."*

*"Generally, the questions were clear and indicated which analyses they wanted us to conduct and/or replicate. Where there was any further clarification required there was a very **helpful interaction with the analyst team**."*

Extension of pilot

New



Selected recommendations for the second part of the pilot

Added value for assessment and decision making

- Continue **enrolling procedures for the pilot**

Capability and capacity

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

Governance and processes

- **Update guidance to applicants/MAHs** for the second phase of the pilot, e.g. change in timelines, modes of participation
- **EMA to carry out analyses** in support of benefit-risk assessment

Technical aspects

- Identify necessary upgrades of systems and process to **optimise applicants'/MAHs' eSubmission process**, e.g. the inclusion of the clinical study data package in eCTD structure
- **Strengthen exchange** with other international regulators on activities related to **data standardisation** and data governance, fostering **alignment regarding data submission requirements** and **electronic submission plans**
- **Foster engagement with applicants/MAHs** (e.g. via the Industry Focus Group on Raw Data or relevant industry fora)

Industry Focus Group on Raw Data – est. 2022

-Intensify collaboration with Industry

-Promote dialogue

-Opportunity for members to share their views on specific pilot's aspects

- Guidance for Industry
- Application of EMA's data transparency policy
- Second pilot's phase and areas for collaboration

Industry Focus Group on Raw Data membership

Upcoming presentations and useful links

- 5th HMA/EMA Big Data Stakeholder Forum:

28 November 2024

- **Interim pilot report** and updated **guidance** for industry available at EMA's Big Data website
- Open to receiving **new pilot proposals** from applicants/MAHs

Please reach out to rawdatapilot@ema.europa.eu

Back-up slides

Definition of clinical study data

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- Individual Patient Data (IPD) / clinical study data is **defined** as:
  - 'data, including imaging data, at an individual patient level which is directly assessable in terms of reanalysis or additional analyses'
  - 'individual patient data in electronic structured data formats, e.g. CDISC Study Data Tabulation Model (SDTM) or CDISC Analysis Data Model (ADaM)'

- Clinical trial data **already provided by marketing authorisation applicants and sponsors** in modules 4 & 5 of all MAA dossiers
  - EMA currently receives this data in the form of PDF listings; in a format that does not support data analysis
  - In contrast to PDF listings IPD / raw data is directly assessable in terms of reanalysis, additional analyses or visualisation

EMA's Raw Data project

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Aim

- **Determine the regulatory benefit of access to clinical study data** via **pilots of analysis of clinical study data** , before coming back with **recommendations to the Committee for Medicinal Products for Human Use** (CHMP).
- Ultimate aim is for **Network to understand and take informed decisions** on the place of analysis of **clinical study data for future regulatory submissions**.

How

- **Put in place procedures and safeguards to process clinical study data**, in accordance with data protection legislation.
- **Establish an Advisory Group on Raw Data** identified in HMA-EMA Joint Big Data Taskforce Phase II report (multi-disciplinary group with members from CHMP, EMA Working Parties, patients' representatives)
- **Perform a proof-of-concept pilot** in order establish the value of IPD and to build, step by step, capacity to analyse clinical study data.
- **Foster stakeholders' engagement** through a communication plan.

Assessment process including clinical study data analysis

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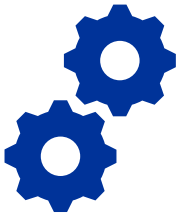
- For procedures chosen for PoC pilot, applicants/Marketing Authorisation Holders submit clinical study data in addition to regular dossier (how: Q&A guidance available)
- During assessment, questions may arise which Rapporteurs want to answer via clinical study data analysis
- Clinical study data analysis happens during assessment phases, e.g. btw. Day 1 to Day 80 for iMAAs
- Rapporteurs include description of results in assessment report (AR)
- CHMP may request replication of analysis results from applicant e.g. via LoQ/LoOI/RSI



Network – Advisory Group on Raw Data