Submission of individual patient data from clinical trials – an EMA update

EFSPI Regulatory Statistics Workshop 2023

Presented by Eftychia Eirini Psarelli on 13 September 2023
Methodology Workstream, Data Analytics and Methods Task Force, EMA

Disclaimer

The views expressed in this presentation are my personal views and may not be understood or quoted as being made on behalf of or reflecting the position of the European Medicines Agency or one of its committees or working parties.

Meet the Speaker

Eftychia Eirini Psarelli

Title: Seconded National Expert, Methodology, Data Analytics and Methods Task Force

Organisation: European Medicines Agency

Eftychia is statistician on secondment at EMA in the Methodology Workstream of the Data Analytics and Methods Task Force, where she has been managing EMA's Raw Data project, focusing on utilising raw data to generate evidence for better and more efficient regulatory decision making. Prior to joining the EMA in July 2020, she spent 8 years as a Senior Statistician at the Liverpool Clinical Trials Centre within the University of Liverpool, UK, where she has gained experience in clinical trial design and analytics.

Outline

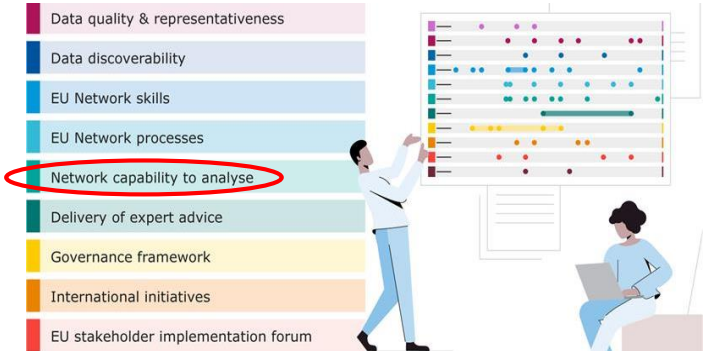
- Introduction to EMA's Raw Data project
- Approach taken
  - Proof-of-concept pilots
  - Interaction with Industry
  - Guidance for Industry
- Status update (incl. initial learnings)
- What's next?

Introduction

Mandate of the raw data pilot (1)

HMA/EMA Big Data Steering Group work plan (2023-2025)

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.



CHMP workplan (2023)

Proceed with 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.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15 December 2022
EMA/911829/2022
Human Medicines Division

Committee for Medicinal Products for Human Use (CHMP): Work Plan 2023
Adopted by the Committee on 15 December 2022

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Mandate of the raw data pilot (2)

EMA MWP 3-year workplan (2022-2024)

To *deliver an improved access to raw data* (e.g. clinical or pharmacometrics), it is proposed to actively engage with the Network Advisory Group on Raw Data with members across committees and working parties *to examine the practical aspects of patient level data visualisation and analysis, with an initial focus on clinical trial data*. Training will be required in processes and relevant software to facilitate this.

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15 December 2022
EMA/CHMP/58124/2023
Human Medicines Division

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

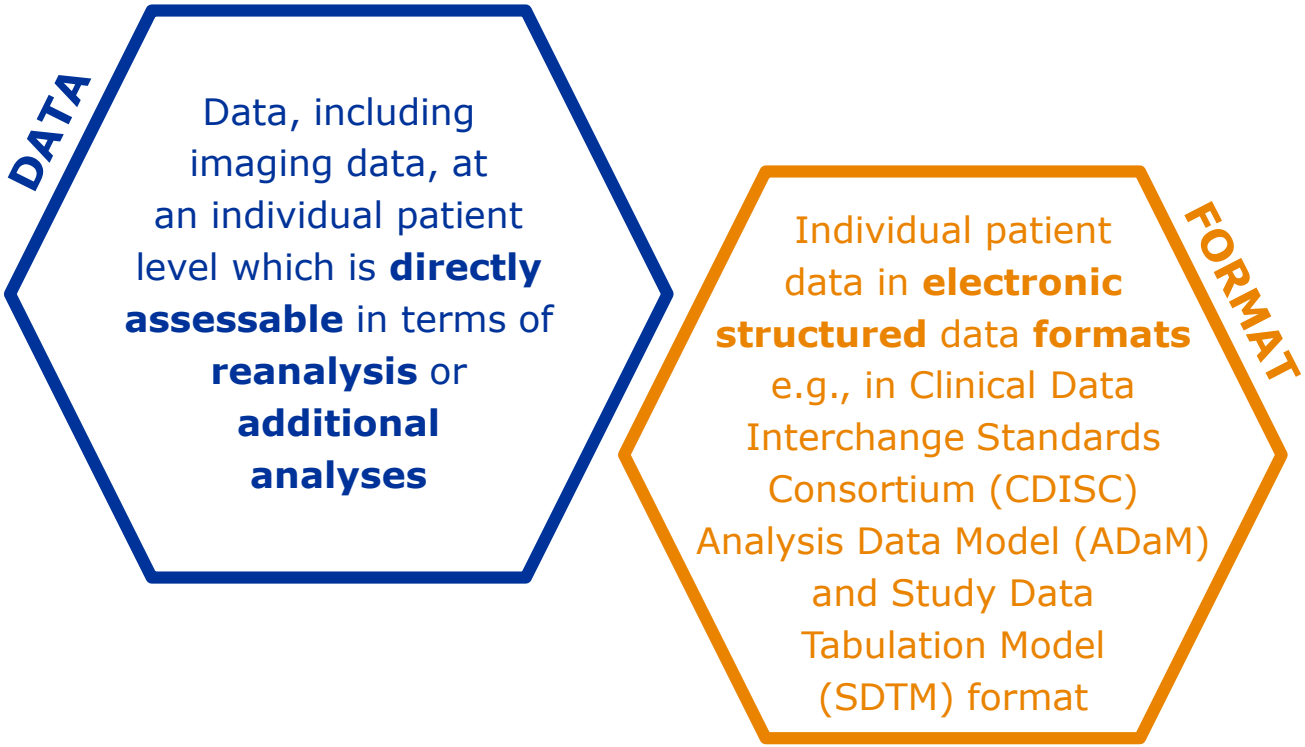
Chairperson: Kit Roes

Vice chair: Kristin Karlsson

Work plan period: May 2022 – December 2024 (with a first review point after one year)

Definitions

Raw data / Individual Patient Data (IPD) / Patient Level Data (PLD) / is **defined** as:



EMA's Raw Data project

- **Determine the regulatory benefit of access to raw data** via **pilots of analysis of raw data** from clinical trials, 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 **raw data for future regulatory submissions.**

- **Put in place procedures and safeguards to process clinical trial raw data,** in accordance with data protection legislation.
- **Perform a proof-of-concept pilot** in order establish the value of IPD and to build, step by step, capacity to analyse raw data.

Approach taken

Proof-of-concept pilots

Proof-of-concept pilot – summary

- **Timeline:** Approx. **10 regulatory procedures over two years** from September 2022.
- **Scope: Initial Marketing Authorisation Applications (iMAAs)** and **post-authorisation applications** (e.g., variations or extensions). No restrictions for clinical characteristics of dossier.
- **Participation:** Procedures will be selected based on **voluntary participation of CHMP Rapporteurs** and **assessment teams**. Eligible applicants or marketing authorisation holder (MAHs) will be asked to confirm their voluntary participation by signing a participation letter.
- **Data Standards:** Raw data to follow CDISC standards (SDTM, ADaM), data packages for other **international regulators** in general **accepted.**
- **Usage:** Analyses that are considered relevant to the assessment will be **shared with the Applicant or MAH via the assessment report (AR)** and be used for decision-making by the CHMP. The Applicant or MAH might be asked to **replicate these results via the LoQ/ LoOI/ RSI**.
- **Resources:** Three **resourcing scenarios for who is doing the analysis** are going to be explored: (1) the Rapporteurs' assessment team, (2) EMA or (3) EMA contractor (DKMA).

Approach taken

Interaction with Industry

Industry Focus Group on Raw Data

Est. August 2022

-Strengthen collaboration with Industry

-Promote dialogue

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

- Guidance for Industry
- Application of EMA's transparency principles
- Consultation on pilot's outcomes (learnings to be collected)

Industry Focus Group on Raw Data membership

efpia

EuropaBio

medicines for europe
better access. better health.

EUCOPE

EFSPI

AESGP

janssen

PHARMACEUTICAL COMPANIES OF Johnson&Johnson

Continuous engagement (list not exhaustive)

-Bi-annual meetings of Big Data Steering Group and Industry stakeholders

-Bi-annual Industry Stakeholder Platform on operation of the centralised procedure for human medicines

-Newsletters

- Big Data Highlights
- Clinical Trials Highlights

Approach taken

Guidance for Industry

PoC pilot guidance

- Public communication via EMA's website in July 2022
  - Updated information on the pilot for Industry in October 2022

- Additional documents published
  - Updated Questions & Answers document for applicants/MAHs (details & technical) in March 2023
  - Pilot participation letter
  - Raw data submission cover letter template
  - Data Protection Notice, Records of data processing
  - Application of EMA's transparency principles to the raw data proof-of-concept pilot

Closer look at transparency aspects (1)

- Application of Policy 0043 to the raw data PoC pilot
  - *Any type of documents held by EMA can be subject to a request for access to documents submitted by any citizen of the European Union (EU) […]. This also includes individual patient data submitted as appendices to Clinical Study Report (CSR) in module 5.3 of a Marketing Authorisation Application (MAA).*
  - *Access to such documents would be refused during the relevant ongoing regulatory procedure.*
  - *EMA will consult the concerned third-party regarding the possible presence of commercially confidential information (CCI) and personal data, with a view to redacting/anonymising both categories of data as necessary.*
  - *IPD in PDF format are already regularly submitted to EMA by companies as part of Annex 16 of Clinical Study Reports. EMA regularly receives request to access patient line listings and releases the data once anonymised.*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19 December 2022
EMA/949891/2022
European Medicines Agency

Application of EMA's transparency principles to the raw data proof-of-concept pilot

1. Purpose and context

- Further to the dedicated discussion between the European Medicines Agency (EMA) and the Industry Focus Group (IFG) on Raw Data[1] concerning EMA's Policy 0043[2] and its application during the raw data proof-of-concept pilot on 15 November 2022, the present paper was developed with the aim to clarify EMA's existing data transparency principles, including its current practice and processes.

Closer look at transparency aspects (2)

- Application of Clinical Data Publication (Policy 0070) to the raw data PoC pilot
  - *Individual patient data would only be considered for publication under phase 2 of Policy 0070 which is not implemented at this time*
  - *Webinar to prepare to re-start publishing clinical data from September 2023, in line with related Policy 0070, held on May 2023*
- Application of Union data protection legislation (EUDPR & GDPR) to the raw data PoC pilot
  - Comprehensive data protection documentation available


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Status update

Number of pilot procedures

Initial learnings

PoC pilot status update

5
Included in the pilot

1. iMAA (new active substance) - neurology
2. iMAA (biosimilar) – endocrinology
3. Type II variation – oncology
4. Type II variation – dermatology
5. iMAA (new active substance) – gastroenterology

Focus on **benefit-risk** incl. modelling and simulation (M&S) analysis

Excellent collaboration with industry for included pilot procedures

- Interaction between Applicant and EMA to prepare official pilot participation
- Identification of the procedure during the pre-submission interactions

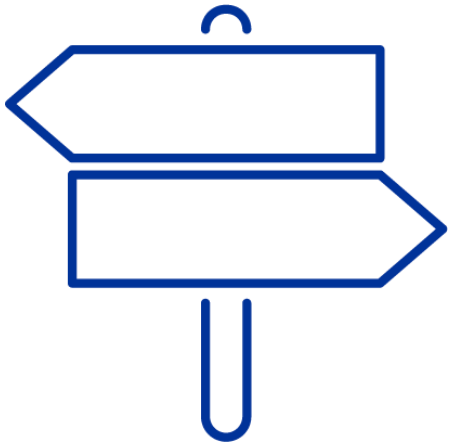
Data access and analysis – learnings so far

- **Submission of data** to EMA via Gateway (eCTD); **no change**
  - Data submission meeting taking place
- Raw data received **complies with CDISC standards** (SDTM, ADaM)
  - Pinnacle 21 was used by EMA's contractor (DKMA) for validation
  - XPORT transport file formats accepted as per FDA and PMDA (other file transport files accepted upon mutual agreement, e.g. JSON and XML)
  - Data definition files in CDISC XML format required
- **Software** being explored
  - SAS and R for statistical analysis
  - SAS JMP clinical for visualisation
  - M&S software (e.g. Monolix, GastroPlus)

What’s next?

Important upcoming milestones

- **Interim pilot report expected by early 2024**
  - Interim learnings on benefit to regulatory assessment and practicalities (operating model, capacity & capability, technical demands)
  - Feedback to be sought from all stakeholders involved, including Applicants/MAHs via surveys
  - Report's summary to be published on EMA's website (bearing in mind that most pilot procedures will have ongoing assessments)



How to take part in the raw data pilot?

If you are interested in participating in the PoC pilot or would like more information, please contact rawdatapilot@ema.europa.eu

Submissions up to Q1 2024 still eligible

Any comments or questions?

TO KNOW MORE

- Priority VI in HMA-EMA Joint Big Data Taskforce Phase II report
- HMA-EMA joint Big Data Steering Group (BDSG) workplan 2023-2025
- Information about the raw data proof-of-concept pilot for industry

Any questions?

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Back-up slides

Assessment process including raw data analysis

- For procedures chosen for PoC pilot, applicants/Marketing Authorisation Holders submit raw data in addition to regular dossier (Q&A published on website)
- During assessment, questions may arise which Rapporteurs want to answer via raw data analysis
- Raw 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 might request replication of analysis results from applicant e.g. via LoQ/LoOI/RSI

Looking into a future after the pilot

- Based on information collected, make recommendations to governance bodies on
  - Regulatory benefit of access to data
  - Practical learnings on operational, resource, technological, and data standard needs
- Communication with industry & public (e.g., publish summary of results, workshop)
- If decision to implement, further work expected – transitional phase
- Vision for alignment in requirements between international regulators