EMA's 'raw data' Pilot: Industry Focused Group (IFG) Member Perspective

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EMA's Definition of Raw Data

'Raw data', also referred to as 'Standardized Study Data' means individual patient data from clinical studies in structured format from which statistical analyses are derived.

Raw data includes the datasets in Study Data Tabulation Model (SDTM) and Analysis Data Model (ADaM) formats.

Source: EMA's "Information about the raw data proof-of-concept pilot for industry", Version 24OCT2023

Terms Used

CHMP: Committee for Medicinal Products for Human Use

HMA: Heads of Medicines Agencies

MAA: Marketing Authorization Applicant

MAH: Marketing Authorization Holder

IFG: Industry Focused Group

Current State of Data Submission to EMA

Currently receives data after statistical processing in aggregated format as clinical summaries, as well as in PDF listings.

The CHMP scrutinizes these summaries as part of the scientific evaluation of the benefits and risks of medicinal products.

This process results in several rounds of questions:

EMA's View on Potential Benefits of Raw Data

EU Patients:

EMA Launched Raw Data Proof-of-Concept (POC) Pilot

- To assess whether the analysis of ‘raw data’ from clinical trials by regulatory authorities improves the evaluation of MAA.
- To explore the practical aspects of the submission and analysis of such data.
- Open to applicants or MAHs that are about to submit MAA or post-authorization applications.
- If selected, they will include raw data already as part of their submissions.
- The pilot is expected to last up to two years and will include approximately ten regulatory procedures submitted to EMA from September 2022.
- The pilot will fully comply with data protection legislation requirements.
- Stems from on of the priority recommendations of the HMA-EMA joint Big Data Task Force.

Source: https://www.ema.europa.eu/en/news/ema-launches-pilot-project-analysis-raw-data-clinical-trials

Formation of Industry Focused Group (IFG)

Prior to launch of raw data pilot, EMA formed an IFG.

Call for member participation sought through European trade associations such as EFPIA, EUCOPE, EuropaBio.

Intent: To engage and seek stakeholder feedback in the design of raw data POC pilot.

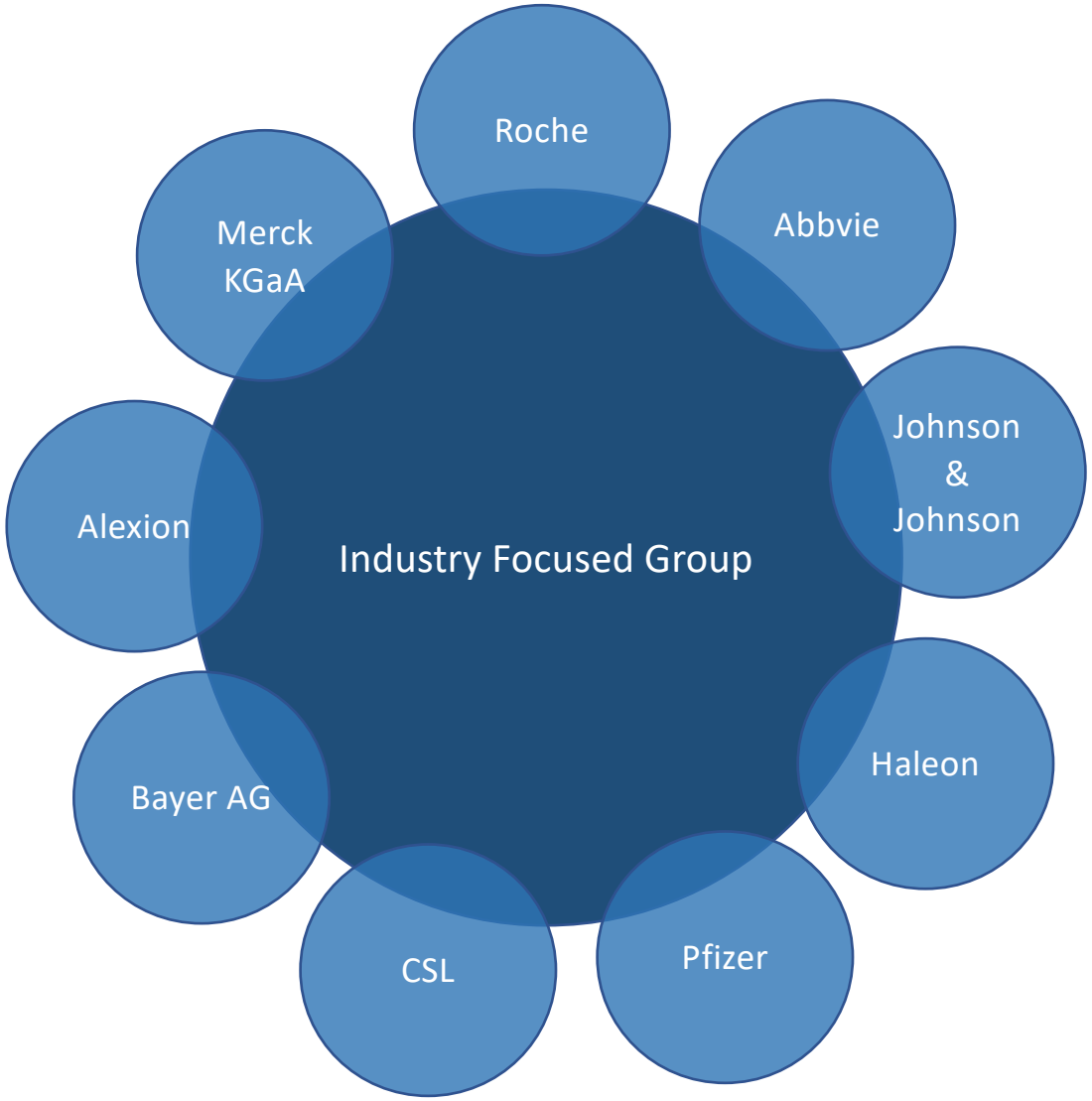
IFG Expectations and Expertise

Expectation: IFG member share their view on specific elements of design of raw data POC pilot.

Expertise:

Electronic structured data standards & formats (e.g. CDISC SDTM/ADaM).	Understanding of requirements of submission of electronic study data to international regulators.	Understanding of existing and potential benefits of submitting electronic study data to international regulators.

IFG Participants



Author may have missed a participating company due to changing attendance and participation.

IFG's Engagement with EMA

Started with a Kick-off meeting organized by EMA with IFG.

Draft versions of "Pilot Participation Letter" and "Q&A Document for Industry" shared with IFG for review.

IFG reviewed above documents and provided feedback.

Subsequent adhoc meetings with EMA as needed.

Examples of IFG Feedback

Clarification of definition of ‘raw data’.

Clarification of expectations around Analysis Results Metadata (ARM) and its format.

Data package prepared for other regulatory agencies acceptable?

Conformance checks?

Clarification about the analysis performed by the agency.

Concerns around data privacy.

Clarification About Other Data Packages

3.1. Are data packages as prepared for other international regulators suitable to be submitted to the Agency for the PoC pilot?

In principle, data packages prepared for other international regulators, such as FDA, PMDA or Health Canada, may be submitted to the Agency for the PoC pilot, provided they meet the mandatory criteria listed in Question 3.3. Accordingly, all versions of standards as supported by other international regulators are permissible for the pilot.

Furthermore, a direct dialogue between the appointed CHMP Rapporteurs and the applicant/MAH shall confirm that the data package contains data for all clinical studies which are considered of interest by the Rapporteurs (see Question 3.2).

Source: EMA's "Questions and Answers about the raw data proof-of-concept pilot for industry", Version 07MAR2023

Mandatory Files in the Data Package

- Signed participation Letter (if not submitted before).
- Datasets:
  - Datasets as SAS Transport Format (XPORT). Other formats (XML or JSON) also acceptable upon mutual agreement.
  - Datasets should comply with CDISC SDTM and ADaM data standards.
  - For non-interventional studies or analysis involving modeling and simulations, other data formats and standards may be agreed to with agencies.
- The data definitions files in CDISC Define-XML format.
- The Analysis Data Reviewer’s Guide and Study Data Reviewer’s Guide.
- Software programs for ADaM datasets and related to primary and secondary efficacy analysis including programs to generate figures and tables.

Source: EMA's "Questions and Answers about the raw data proof-of-concept pilot for industry", Version 07MAR2023

Optional Files in the Data Package

ARM highly recommended for primary and key secondary endpoints. ARM format can be XML or PDF.

BIMO datasets and documents which are provided in FDA applications.

The annotated case report form (aCRF).

Data for ISS and ISE.

Source: EMA's "Questions and Answers about the raw data proof-of-concept pilot for industry", Version 07MAR2023

Additional Clarification about Analyses Performed by the Agency

- Agency will share information about the analysis method and statistical software used and optionally software code.
- Applicants/MAHs will be asked to replicate the analyses via list of questions.
- Clarification about possible outcome of comparison of results.

EMA's Clarification about Data Transparency

Further to discussion with IFG, EMA developed a document titled "Application of EMA's transparency principles to the raw data proof-of-concept pilot".

Per EMA Policy 0043, any type of document (including IPLD) held by EMA can be subject to a request for access by any EU citizen.

Access to such documents would be refused during the relevant ongoing regulatory procedure.

EMA will consult third-party regarding the presence of commercially confidential information (CCI) and personal data, with a view of redacting or anonymizing both.

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 anonymized.

Source: EMA's "Application of EMA's transparency principles to the raw data proof-of-concept pilot", Version 19DEC2022

Summary

EMA's approach of proactively seeking stakeholder feedback is very admirable.

IFG's early involvement in review of draft documents helped in adding several clarifications.

IFG hopes for continued collaboration through duration of the pilot and beyond.

EMA's Interim pilot report expected in early 2024.

As EMA decides the future of standardized study data submission post-pilot, continued dialogue with the stakeholders (including IFG) would be very valuable.

Harmonization of requirements for standardized study data across regulatory agencies is critical to reduce burden on sponsors.

Questions & Contact

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