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Data submission in Europe – an EMA update

PHUSE FDA/CSS 2024

Presented by Eftychia Eirini Psarelli and Peter van Meer on 05 June 2024
Methodology Workstream, Data Analytics and Methods Task Force, EMA
Medicines Evaluation Board



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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 strong analytical skills in the area of statistical programming and data curation.

Eftychia fosters EMA activities where data standards can have an added value, particularly for clinical trial data. She is also an observer in Europe's CDISC Coordinating Committee (E3C).



Peter van Meer

Title: Senior Assessor in the Pharmacology Toxicology and Pharmacokinetics division

Organisation: Medicines Evaluation Board

About me:

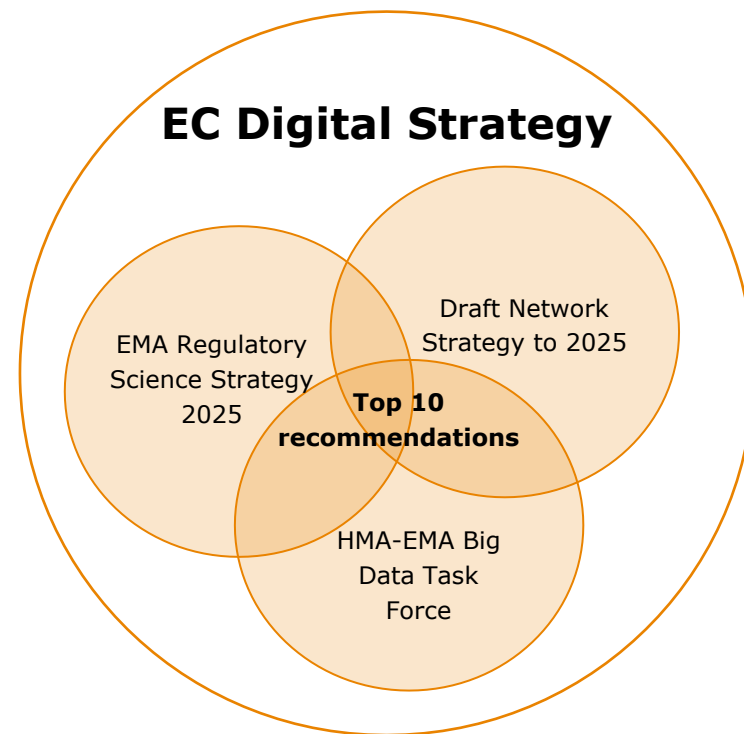
- Strong interest in regulatory science and 3Rs
 - Affiliated to Nijmegen University as a researcher, supervising 2 PhDs on 3Rs related topics
 - Member of the Dutch Regulatory Science steering group
 - Member of (various) scientific advisory boards and committees
- Member of the EMA Non-clinical Working Party
 - (co)-Chair for 2 reflection papers on NHP and COVID-19
 - ESEC member for 3Rs/non-clinical domain, OEG member, DG member,...
 - EMA SEND pilot



- Spotlight on selected EMA's activities supporting data submission
 - Individual patient data from clinical trials
 - Non-clinical data in SEND format
- Next steps and synergies with data governance & quality framework

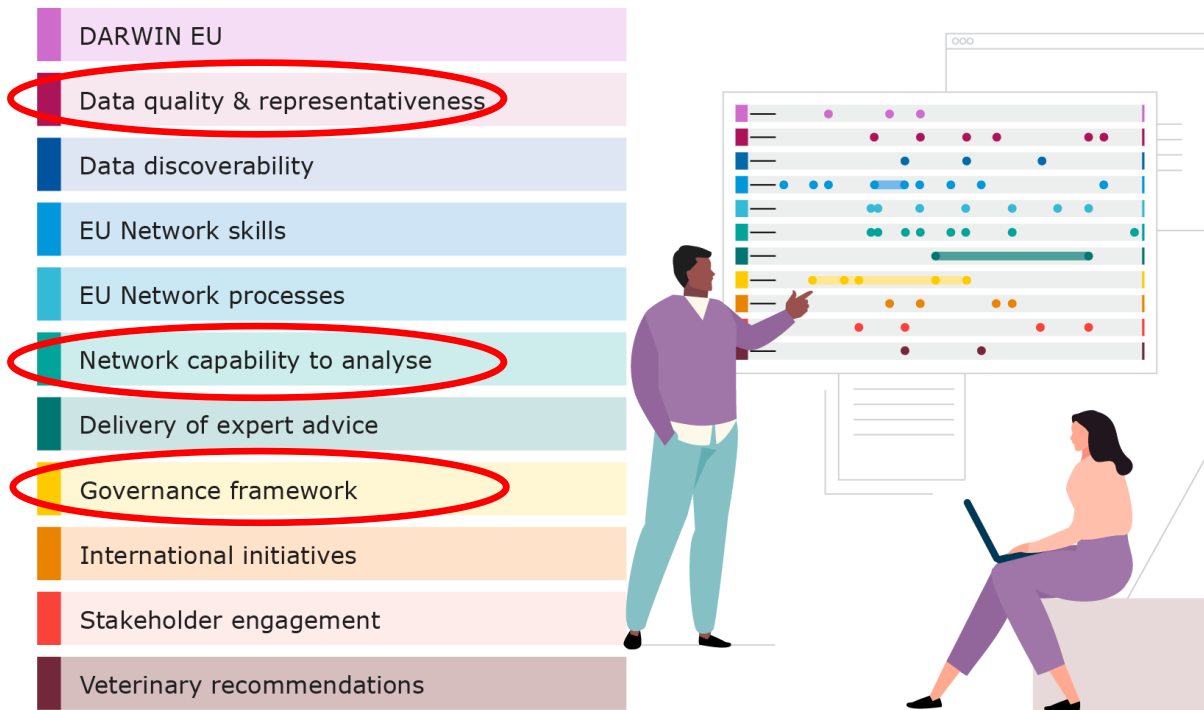


- Key initiatives referred to the Commission digital strategy “**EU health data space**” (EHDS):
 - **EU Network Strategy to 2025** (data & digital pillar)
 - **EMA Regulatory Science Strategy to 2025**
 - **Joint HMA EMA Big Data Task Force**; and
 - the resulting **Top-ten data recommendations**
- Synergic initiatives:
 - **Pharmaceutical strategy for Europe**
 - **European Health Union**

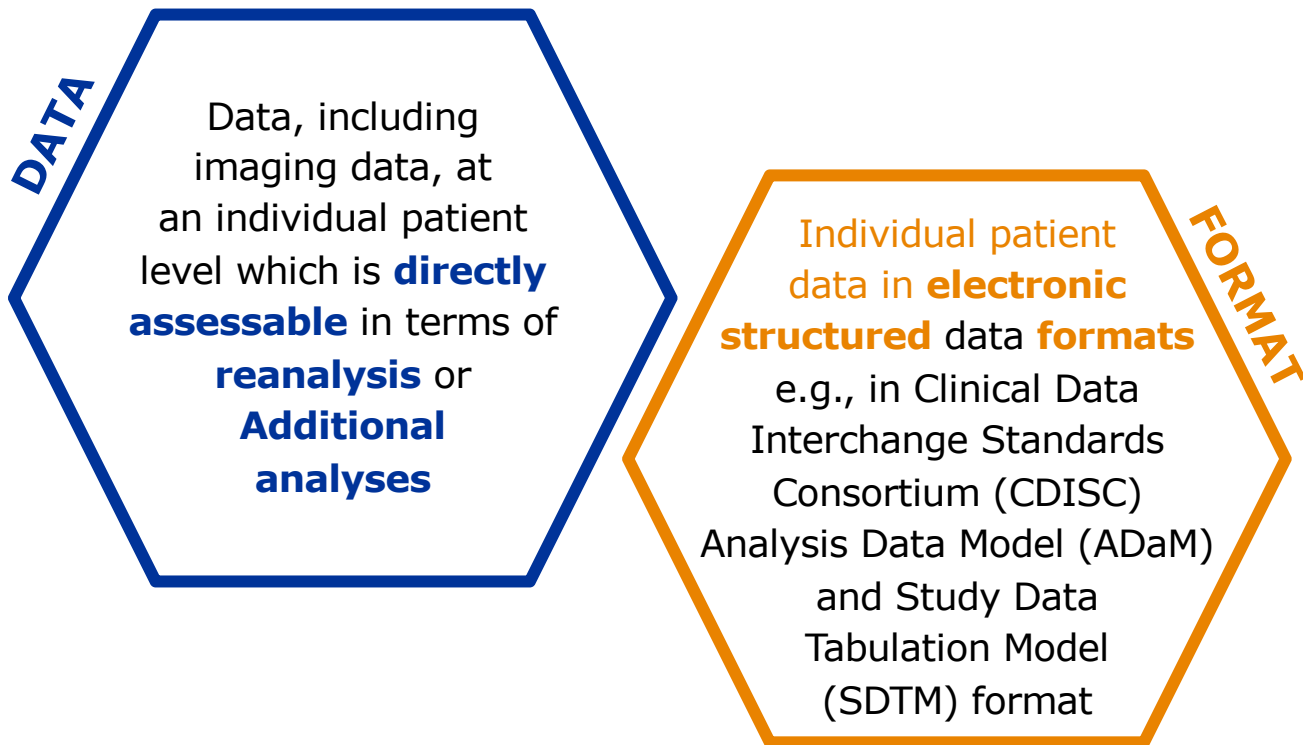


Vision: innovate to turn data into decisions on medicines that create a healthier world

Framework - to enable use of data and facilitate its integration into regulatory decision making



Submission of individual patient data from clinical trials





Aim

- Determine **regulatory benefit of access to raw data**, resulting in recommendations to EMA's **Committee for Medicinal Products for Human Use** (CHMP)
- Support **EU Regulatory Network** to understand and **take informed decision** on the place of analysis of **raw data for future regulatory submissions**



How

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

-  • **Timeline:** Approx. **10 regulatory procedures over two years** from September 2022; **8 procedures included** so far
-  • **Scope:** **Initial Marketing Authorisation Applications (iMAAs)** and **post-authorisation applications.**
-  • **Participation:** Procedures will be selected based on **voluntary participation of CHMP Rapporteur teams** and **companies**
-  • **Usage:** Analysis of clinical data to inform assessment of underlying dossier. Information on analysis methods and results will be **shared with company**. Companies may be asked to **replicate analyses**
-  • **Resources:** Three **resourcing scenarios for data analysis** will be explored: the CHMP Rapporteur team, EMA staff or EMA contractors

- Raw data received continues to **comply 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



Register your interest to participate in the pilot with a specific procedure – only **2 spaces** left:

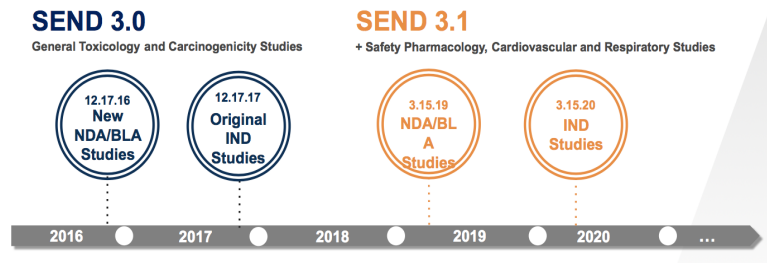
rawdatapilot@europa.eu

Interim pilot report to be publicly available in Q3 2024

Submission of non-clinical data in SEND format

A proof-of-concept study, initiated in 2024

- **Standards for Exchange of Non-clinical Data**
- Initiated by FDA to improve **predictability, consistency & efficiency** of review process
- **Required** by FDA since December 2016
 - All general toxicology and carcinogenicity studies started on or after December 17, 2016 are required to be submitted using SEND 3.0
 - Non-clinical studies for New drug Application/Abbreviated New Drug Application and certain Biologics License Applications/Investigational New Drug Application submissions, that were initiated on or after March 15 2020, must comply with SEND 3.1
- **Until 2023, processes and tools at EMA were not facilitating submission**
 - SEND has been highlighted as an important tool in EMA's regulatory science strategy 2020-2025
 - In 2020 a working group consisting of non-clinical assessors from several National Competent Authorities was formed with the goal of evaluating the potential benefits and limitations of implementing SEND visualisation in the regulatory review process resulting into recommendations



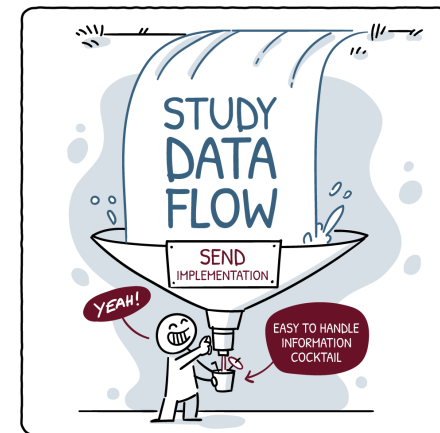
- Working group of 5 NCAs

Jakob Paur and Günter Waxenecker	AGES (AT)
Sonja Beken and Violaine Francois	FAGG-AFMPS (BE)
Susanne Brendler-Schwaab, Henning Brohmann, Bodo Haas and Bettina Lange,	BfArM (DE)
Peter van Meer and Peter Theunissen	CBG (NL)
Tania Cavaliero, Elisabeth Klenke, Anja Langenkamp, Hasan Mohajeri, Tatjana Petkovic, Eva Rached and Daniel Roth	Swissmedic (CH)

- Anonymised datasets provided by **EFPIA** and **Instem**. Not used in new/running procedures
- Pilot with a run time of 6 months was intended to:
 - Gain basic experience with SEND and visualisation with novel tooling
 - Identify use cases in day-to-day assessment
 - Gain insight in general considerations of SEND in regulatory assessment

- In its current form, **SEND compliant data can be useful in routine assessments**
- SEND could improve the **quality and efficiency** of assessment
- SEND can be particularly useful in
 - **Any procedure** where data is complex and requires visualisation/independent analysis
 - Procedures where rapid regulatory input is needed (based on incomplete study programs) such as **Rolling review, accelerated procedures, PRIME)**
 - **Regulatory Science** projects or read across to facilitate policy and/or guideline recommendations

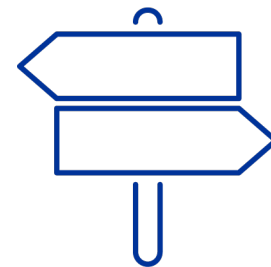
- Proof-of-concept study with a run time of 1 year to evaluate if availability of non-clinical information in SEND format will improve **quality, consistency** and **efficiency** of assessments
- Expected benefits
 - Improved and more consistent assessment **quality**
 - More **science driven** & less **data driven** questions to Applicant
 - **Fewer non-clinical rounds** and/or **faster completion** of the review of the non-clinical dossier
- Applicants are encouraged to submit their (already available) non-clinical SEND data packages, in addition to the electronic common technical document format, as part of their eCTD MAA submission



For additional information you can reach out to:
SEND@ema.europa.eu

What's next?

- **Submission of 'raw data'**
 - Decision on IPD submission requirements expected in late 2024/early 2025
 - No experience yet in receipt of non-interventional studies and applicable data standards
 - Quality and manufacturing structured data
- **Data Quality framework**
 - Work in progress for delivering a Real-World Data specific chapter of the published Data Quality Framework for medicines regulation (estimated to conclude towards the end of 2024)
 - Further prioritisation for other use cases (e.g., clinical trials) to be carried out in Q2 2024
- **Governance framework**
 - European Medicines Regulatory Network Data strategy will be published end of 2024; focus on data management and data governance
 - Continue supporting European Health Data Space (EHDS) in establishing the value of an infrastructure and data ecosystem for the reuse of health data





Big Data



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Any questions?

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