EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Artificial Intelligence in Medicines Regulation

ENCePP Plenary – 18 November 2021

Presentation: Luis Pinheiro
Additional thanks to: Peter Arlett, Ralf Herold, Gianmario Candore

An agency of the European Union

Content

- Promise of AI and Requirements
- AI activities at European Medicines Regulatory Network (EMRN)
- AI EMA Cross-Agency groups
- AI and DARWIN EU
- Delivering on AI
- AI topics at the Horizon Europe Health Cluster

AI in Healthcare | The Promise

Greater efficiency

- Automate processes
- Address scalability issues

Reduce error

- Facilitate access to information
- Reduce human cognitive load

Expose data

- Transform text data into structured data
- Reduce dimensionality of data
- Imputation of missing data

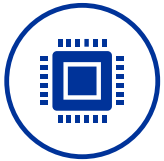
Expand insights

- Probabilistic phenotyping
- Clinical prediction modelling
- Confounding adjustment
- Heterogeneity of treatment effects

AI in Healthcare | Requirements

Skills

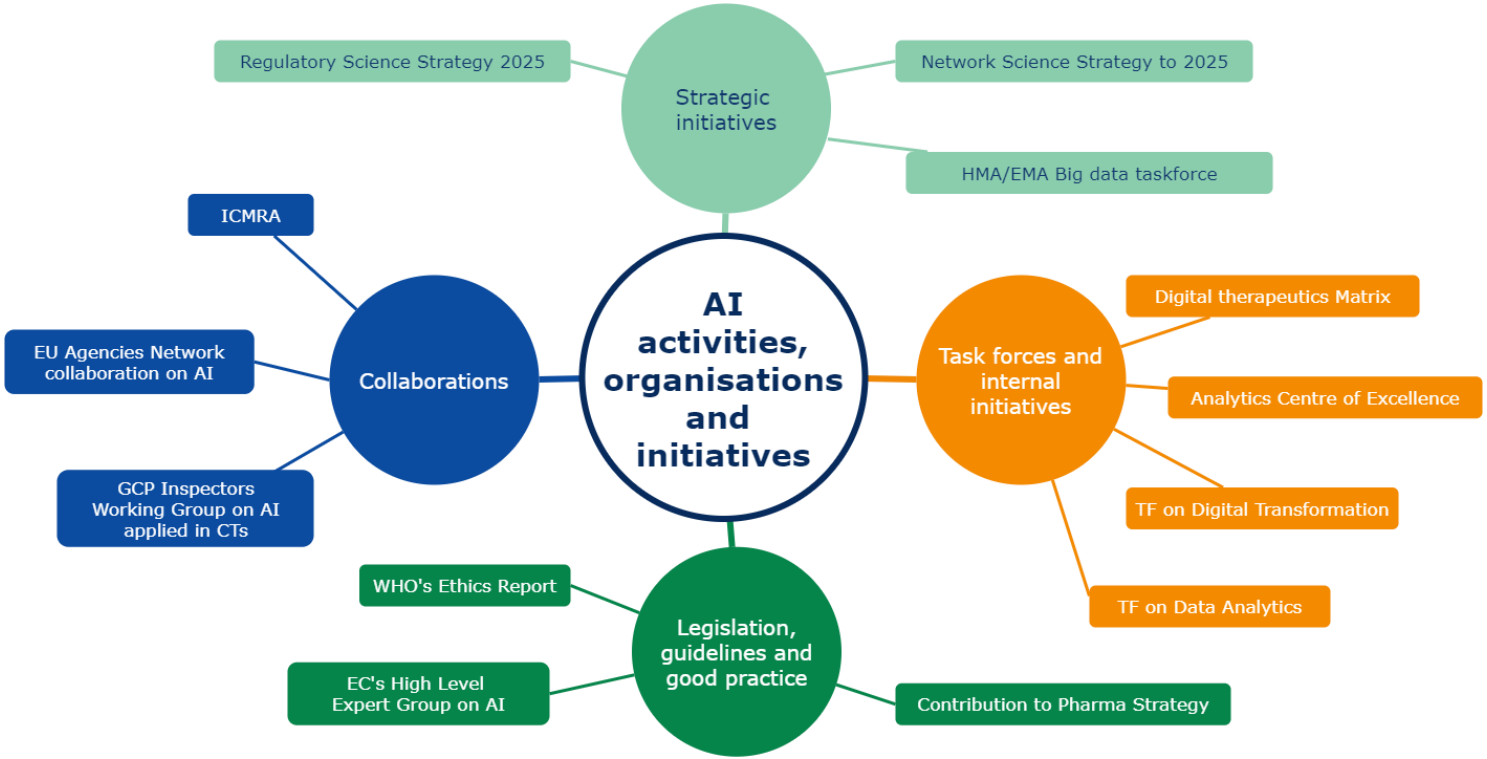
Data



Technology

Oversight

AI at EMRN | Snapshot of initiatives



Planning | Prioritisation of AI recommendations (Workshop on AI)

Strategic initiatives

- HMA/EMA Big Data Taskforce
- Regulatory Science Strategy 2025
- European Medicines Agencies Network Strategy 2025

AI recommendations

- Promote experimentation
- Learning & skills
- Methods & guidelines
- Governance
- Initiatives
- Partnerships & collabs

Stakeholder input in Workshop

- **Priorities**
- Methods & Guidelines
- Partnerships
- Learnings & skills

Mapped EMRN activities

- **Big Data Steering Group**
  - AI Guidance Q4 2022
  - Follow up AI Workshop 2023
  - Data science curriculum
- **EU NTC Digital Academy**

AI at EMRN | Activity examples

Process Analytics

- System to support the validation of variations
- Personal Data Recognition
- Document Comparison – compare leaflet and labelling documents
- Literature monitoring

Regulatory submissions

- Statistical adjustment on deep learning prognosis covariates obtained from histological slides
- Stand-alone software for automated design of nanomedicine drug delivery systems

Healthcare data analytics

- Assigning genotype of patient based on adverse reactions
- Social media monitoring for attitudes toward vaccine authorizations
- TTS case adjudication

External collaboration (incl. legislation)

- ICMRA
- WHO AI Ethics Report
- EC Legislation

AI at EMRN | Example of Healthcare Analytics

- A particular genotype can increase the probability of causing a combination of a set of ill-defined adverse reactions (i.e., a syndrome) to a class of medicines
- There are tens of thousands of reactions for that class of medicines in a global pharmacovigilance database
- Defining public health impact:
  - How can we tell *how many* had the susceptible genotype?
    - Consider that prior knowledge of that genotype will affect the probability of treatment.

An Application of Machine Learning in Pharmacovigilance: Estimating Likely Patient Genotype From Phenotypical Manifestations of Fluoropyrimidine Toxicity

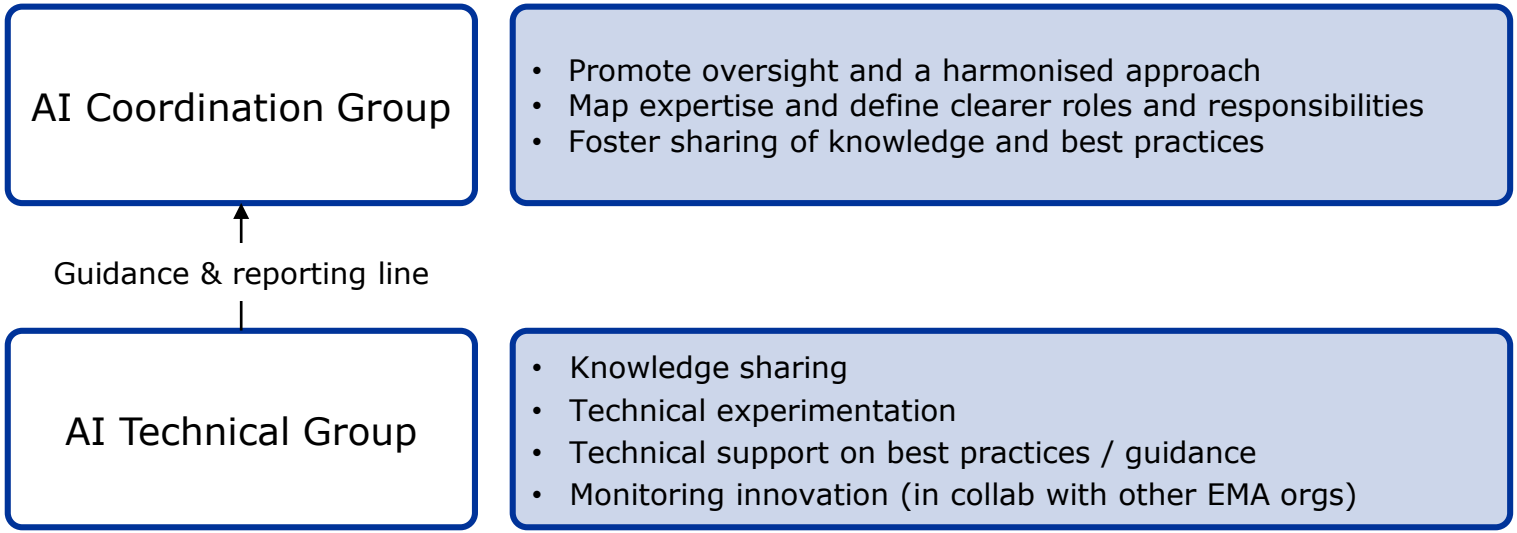
Luis Correia Pinheiro[1,*], Julie Durand[1] and Jean-Michel Dogné[2,3]

Dihydropyrimidine dehydrogenase (DPD)-deficient patients might only become aware of their genotype after exposure to dihydropyrimidines, if testing is performed. Case reports to pharmacovigilance databases might only contain phenotypical manifestations of DPD, without information on the genotype. This poses a difficulty in estimating the cases due to DPD. Auto machine learning models were developed to train patterns of phenotypical manifestations of toxicity, which were then used as a surrogate to estimate the number of cases of DPD-related toxicity. Results indicate that between 8,878 (7.0%) and 16,549 (13.1%) patients have a profile similar to DPD deficient status. Results of the analysis of variable importance match the known end-organ damage of DPD-related toxicity, however, accuracies in the range of 90% suggest presence of overfitting, thus, results need to be interpreted carefully. This study shows the potential for use of machine learning in the regulatory context but additional studies are required to better understand regulatory applicability.

AI at EMRN | Examples of AI presented to EMRN

Clinical Use Cases	• to select patients / enrich trial • to determine tumour volume and response • to generate a covariate for adjusting, for more precisely estimating treatment effects • to guide melatonin administration • to manage patients in trial with decentral elements • to analyse real-world data • for clinical treatment management • for candidate selection, lead optimisation
Automation	• to automatically adjudicate adverse events • to structure text information

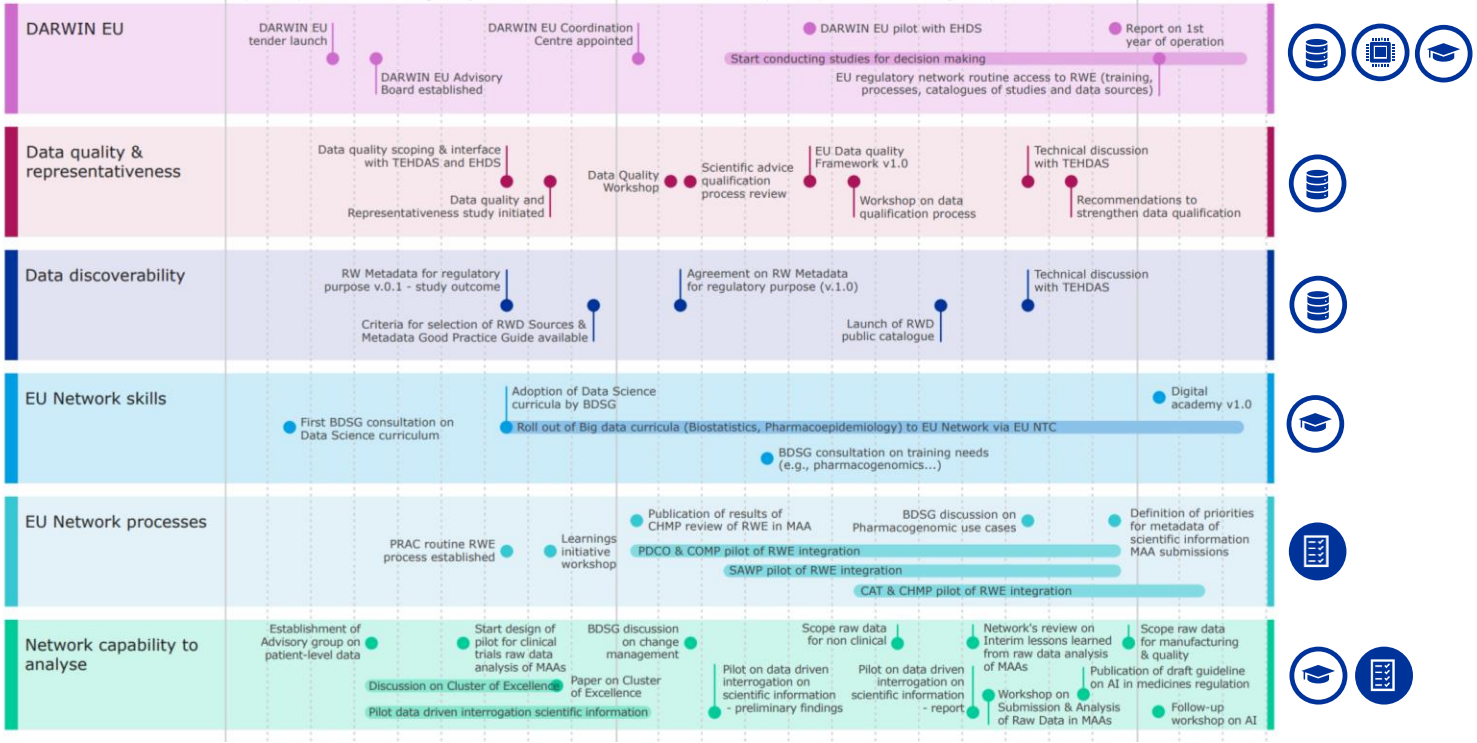
AI at EMA | Cross-agency groups



AI and DARWIN EU

- DARWIN Methodological research needs:
  - Evidentiary value
  - Real world data use in clinical trials
  - Data quality and representativeness
  - *Natural Language Processing*
  - *Artificial Intelligence*

BDSG deliverables | Mapped to AI requirements



Horizon Europe | Health cluster

- HORIZON-HLTH-2021-DISEASE-04-04: Clinical validation of artificial intelligence (AI) solutions for treatment and care
- HORIZON-HLTH-2021-CARE-05-02: Data-driven decision-support tools for better health care delivery and policy-making with a focus on cancer
- HORIZON-HLTH-2022-STAYHLTH-01-04-two-stage: Trustworthy artificial intelligence (AI) tools to predict the risk of chronic non-communicable diseases and/or their progression
- HORIZON-HLTH-2022-TOOL-11-02: New methods for the effective use of real-world data and/or synthetic data in regulatory decision-making and/or in health technology assessment

Any questions?

Further information

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