
# Joint HMA/EMA Workshop on Artificial Intelligence in Medicines Regulation

19 & 20 April 2021

Workshop Report

EMA/292319/2021
25 May 2021

# Workshop Report: Joint HMA/EMA Workshop on Artificial Intelligence in Medicines Regulation

19 and 20 April 2021

## Introduction and motivation

The Joint HMA/EMA Big Data Taskforce, the Regulatory Science Strategy to 2025 and the European Medicines Agencies Network strategy to 2025 have all produced recommendations on leveraging Artificial Intelligence (AI) and new digital technologies to improve efficiency in processes and increase insights into data.

While these initiatives addressed AI, they were not specific to AI, and there is a need to compile AI-specific recommendations and to prioritise, thereby supporting multiannual work planning within the regulatory network.

In this context, the Joint HMA/EMA workshop on AI in medicines regulation had three aims: i) to inform on state-of-the-art of AI applications in Medicines and Medicine Regulation, taking stock of innovation that has occurred since the publication of the recommendations, ii) Engage stakeholders and iii) Collect views of stakeholders on the prioritization of AI specific recommendations.

A broad range of stakeholders were invited to participate, including Pharmaceutical Industry, MedTech, Academia, Healthcare professionals, Researchers, Patients, the EU-Innovation Network, Consumers, Inspectors, and (General) Industry.

The workshop was divided into two days, with the first day focusing on presentations of the state-of-the art AI applications in medicines regulation and initiatives by regulatory authorities, industry and research organisations on AI, and the second day presenting the existing recommendations followed by a round-table discussion where stakeholders could highlight their top priorities and explain the rationale from the list of recommendations.

## Sessions

***Scene setting: AI – a paradigm-shifting technology in healthcare***

***Moderator: Nikolai Brun***

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Prof. Andre Dekker, Maastricht University, discussed the use of AI to improve patients' lives using the prediction of the survival of Non-Small Cell Lung Cancer patients as an example. Prof. Andre highlighted the importance of FAIR data (Findable, Accessible, Interoperable and Reusable) to make best use of data for public health.

In the following talk, Prof. Peter Rijnbeek, Erasmus MC, discussed the use of common data models (CDM) to facilitate the development and external validation of clinical prediction models across multiple electronic health records databases. He then discussed additional work within the OHDSI community to create a prediction model library and share model performance information. He stressed that models are not universal and validation and continuous monitoring of model performance is paramount.

Prof. Liesbet Geris, Universities of Liege and KUL, presented on Digital Twins – the direct use of individual specific models for the prevention, prediction, screening, diagnosis and treatment of a disease, as well as the evaluation, optimization, selection and personalisation of intervention options.

The following talk, by Prof. Atul Butte, University of California, San Francisco, presented a series of examples of the use of AI across the lifecycle of medicinal products, and stressed the importance of (deep) learning healthcare systems where after authorisation of a product, real-world data is used to understand which populations benefit the most from the medicine, in a continuous cycle. He also expressed the view that, in the future, at the point of care, a new role of algorithm stewardship for AI and Machine Learning (ML) technologies, will be required.

***Applications of AI in Medicines and Medicines Regulation***

***Moderator: Zaide Frias***

Lucie Gatepaille, WHO Uppsala Monitoring Centre (UMC), presented the research initiatives that use machine learning at the UMC, in particular: clustering methods to identify clinically coherent sets of reports and new data-driven representations of drugs and disorders.

Joaquim Berenguer Jornet and Florence Butlen-Ducuing (both EMA), presented the AI and Digitalisation activities at EMA, namely the work conducted in the Analytical Centre of Excellence, the ML initiatives in Healthcare data analytics and the challenges of regulating AI in medicines.

Khair El Zarrad, FDA, discussed AI in Therapeutic Development at FDA. Khair presented an overview of AI that has actually been used, from Early Development, to Clinical Development and Post-marketing and discussed the challenges and opportunities of AI using RWD. He also addressed the use of AI during Public Health Emergencies.

Wolfgang Lauer, BfArM, presented on the BfArM perspective on AI in Medical Devices and Digital Healthcare Applications. Wolfgang walked through the initiatives of BfArM on Digital Medical Devices, contextualised the topic by addressing reliability and regulatory challenges and introduced DiGA (Digital Health Applications) and related procedure.

Boris Braylyan, Pfizer, shared four case studies on the use of AI within Pfizer, specifically on Data reconciliation, Regulatory Portfolio Planning, Pharmacovigilance and Statistical Table Quality control, sharing lessons learnt and value of these initiatives.

***AI Transformation in Medicines Regulation: recommendations for action***

***Moderator: Jesper Kjaer***

This session was reserved for the presentation of the HMA/EMA strategic initiatives (Jesper Kjaer, DKMA) and presenting the key recommendations from the Big Data Taskforce (Gianmario Candore, EMA), ICMRA AI recommendations (Agnes Saint-Raymond, EMA) and presenting the Big Data Training

Survey (Jörg Zinserling, BfArM). These recommendations formed the basis of the discussion in the round table.

***Round table discussion***

***Moderator: Anthony Humphreys***

Stakeholders from Pharmaceutical Industry (Kelly Zou, Viatris), MedTech (Danny van Roijen, COCIR), Academia (Prof Mark Lawler), Healthcare professionals (Ioana Agache, EACCI), Researchers (Prof Peter Rijnbeek), Patients (Marilena Vrana, European Heart Network), the EU-Innovation Network (Larry O'Dwyer, HMA), Consumers (Jelena Malinina, BEUC), Inspectors (Lisbeth Bregnhøj, DKMA), and (General) Industry (Douglas Gregory, BMS, Digital Europe) contributed to the round table.

Stakeholders were asked to identify the top three priorities from the list of compiled recommendations (Annex I) extracted from the three strategic initiatives of EMA/HMA as well as the ICMRA AI recommendations. The most frequently highlighted priorities by the stakeholders were:

- To Develop a framework to assess and validate AI,
- Build a framework that supports the development of guidelines, and
- Build Partnerships with Academic and Research Centres and Collaborate with international partners.

After the round-table discussion, and informed by it, the audience was given an opportunity to also provide their top three priorities via an online survey tool. This provided a list of three top priorities, pooled across the different stakeholders:

- Developing a framework to access and validate AI,
- Build a framework that supports the development of guidelines, and
- Upskilling EMA and EU Regulatory Network.

# Summary and take-home message

During this two-day workshop, several innovative uses of Artificial Intelligence and Machine Learning were presented, highlighting once more that AI holds the promise of improving the efficiency of processes and boosting knowledge discovery from healthcare data.

Stakeholders indicated where they feel the European Regulatory network should place their priorities, namely on developing a framework to access and validate AI and a framework that supports the development of guidelines. They also offered a view on how to achieve this, namely by building partnerships, with academia and research centres and across international institutions, but also via upskilling of staff across the regulatory network.

# Annex I – List of compiled recommendations

Address Ethical Aspects of AI

Build a framework that supports the development of guidelines

Build partnerships with Academia and Research centres

Create and Maintain a multistakeholder forum

Develop a framework to assess and validate AI

Develop Capacity

EMA Expert Group

Engage with Experts

Establish framework for early engagement with potential end-users of AI

Experimentation with AI/Sandbox

Influence research priorities for funders

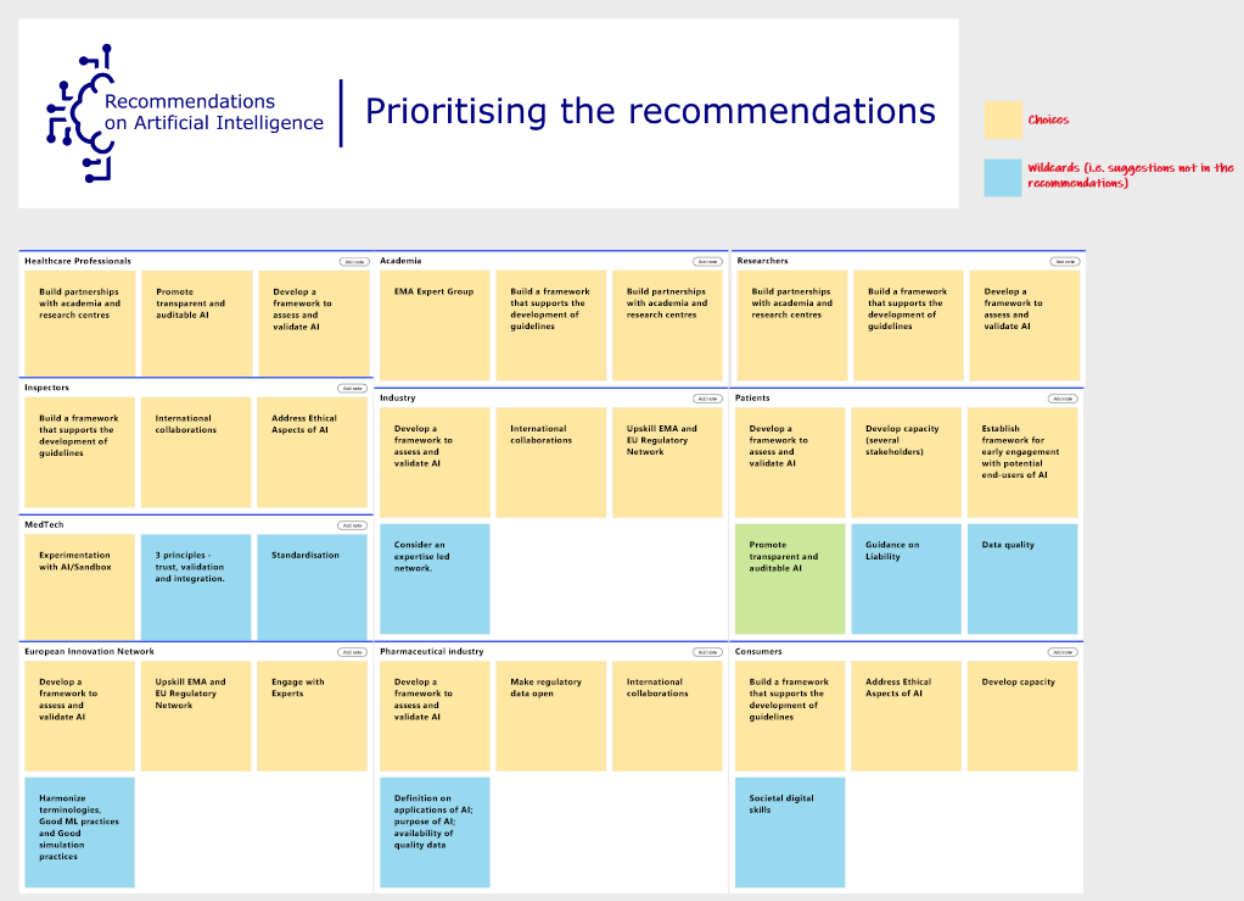
International collaborations

Make regulatory data open

Promote transparent and auditable AI

Upskill EMA and EU Regulatory network

# Annex II – Whiteboard



# Annex III – Agenda

15 April 2021
EMA/176509/2021

# Agenda – Joint HMA/EMA Workshop on Artificial Intelligence in Medicines Regulation - 19-20 April 2021 (Virtual)

## Day 1 - 19 April 2021 (15:00-18:50 CET)

### Introduction

| | | |
|---|---|---|
| *14:45-15:00* | ***Joining and technical checks*** | *15'* |
| | **Welcome to the workshop** | |
| | Peter Arlett, EMA | |
| 15:00-15:05 | **Opening remarks from the EMA Executive Director** | 5' |
| | Emer Cooke, Executive Director, EMA | |
| 15:05:15:10 | **Opening remarks from the HMA Chairperson** | 5' |
| | Karl Broich, Chairperson, BFARM, HMA | |
| 15:10-15:20 | **European Commission policy initiatives in AI** | 10' |
| | Andrzej Rys, Director - Health Systems, Medical Products and Innovation, DG SANTE | |

### Scene setting: AI – a paradigm-shifting technology in healthcare

Moderator: Nikolai Brun, DKMA

| | | |
|---|---|---|
| 15:20-15:40 | **AI to improve the lives of patients** | 15' |
| | Andre Dekker, Maastricht University | |
| | **Discussion** | 5' |
| 15:40-16:00 | **Putting machine learning into real-world practice: patient-level prediction development and validation in observational data** | 15' |

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| | | |
|---|---|---|
| | Peter Rijnbeek, Erasmus MC | 5’ |
| | **Discussion** | |
| 16:00-16:20 | **AI, Digital Twins and the promise of personalised medicine** | 15’ |
| | Liesbet Geris, Universities of Liège and KUL | |
| | **Discussion** | 5’ |
| 16:20-16:50 | **Translating a Trillion Points of Data into Real World Evidence and Enabled Intelligence for Medicine** | 20’ |
| | Atul Butte, USCF | 10’ |
| | **Discussion** | |

## Applications of AI in Medicines and Medicines Regulation

Moderator: Zaide Frias, EMA

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|---|---|---|
| 16:50-17:10 | **Novel methods in pharmacovigilance: use cases in VigiBase** | 20’ |
| | Lucie Gattepaille, WHO-UMC | |
| 17:10-17:30 | **AI and Digitalisation at EMA** | 20’ |
| | Joaquim Berenguer Jornet & Florence Butlen-Ducuing, EMA | |
| 17:30-17:50 | **AI in Therapeutic Development – A Policy Perspective** | 20’ |
| | Khair El Zarrad, FDA | |
| 17:50-18:10 | **AI in Medical Devices and Digital Healthcare Applications – the BfArM perspective** | 20’ |
| | Wolfgang Lauer, BFARM | |
| 18:10-18:30 | **Company experience of using AI to aid drug development** | 20’ |
| | Boris Braylyan, Pfizer | |
| 18:30-18:50 | **Discussion and end of day 1** | 20’ |

# Day 2 - 20 April 2021 (15:00-18:00 CET)

## Introduction to second day

| | | |
|---|---|---|
| *14:45-15:00* | ***Joining and technical checks*** | *15’* |
| 15:00-15:05 | **Opening remarks** | 5’ |
| | Peter Arlett, EMA | |

## AI Transformation in Medicines Regulation: recommendations for action

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|---|---|---|
| Moderator: Jesper Kjaer, DKMA | | |
| 15:05-15:25 | **European medicines agencies network strategy to 2025 - Strategy for Digital transformation**<br>Jesper Kjaer, DKMA | 20’ |
| 15:25-15:45 | **Big Data Taskforce Recommendations and Regulatory Science Strategy on AI**<br>Gianmario Candore, EMA | 20’ |
| 15:45-15:55 | **ICMRA AI Recommendations**<br>Agnes Saint-Raymond, EMA | 10’ |
| 15:55-16:05 | **Big Data Training Survey**<br>Jörg Zinserling, BFARM | 10’ |

| | | |
|---|---|---|
| 16:05-16:20 | **Break** | 15’ |

## Discussion on Recommendations

Moderator: Anthony Humphreys, EMA

Rapporteur: Luis Pinheiro, EMA

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|---|---|---|
| 16:20-17:45 | **Round table discussion**<br>• Inspectors - Lisbeth Bregnhøj, DKMA<br>• Researchers - Peter Rijnbeek, Erasmus MC<br>• Academia - Mark Lawler, Queen’s University Belfast, FEAM<br>• Consumers - Jelena Malinina, BEUC<br>• MedTech - Danny van Roijen, COCIR<br>• Patients Organisation - Marilena Vrana, European Heart Network<br>• Healthcare professional Organisation - Ioana Agache, EACCI<br>• Pharmaceutical Industry - Kelly Zou, Viatris<br>• Industry - Douglas Gregory, BMS, Digital Europe<br>• European Innovation Network - Larry O’Dwyer, HMA | 85’ |

## Summary of the workshop and conclusion

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|---|---|---|
| 17:45-18:00 | **Concluding remarks**<br>Nikolai Brun, DKMA | 15’ |

## Abbreviations

BFARM – Bundesinstitut für Arzneimittel und Medizinprodukte – Federal Institute for Drugs and Medical Devices

BEUC - The European Consumer Organisation

BMS – Bristol Myers Squibb

COCIR – European Coordination Committee of the Radiological, Electromedical and Healthcare IT Industry

DKMA – Danish Medicines Agency

EAACI - European Academy of Allergy and Clinical Immunology

EHN – European Heart Network

EMA – European Medicines Agency

FDA – Food and Drug Administration, United States

FEAM – Federation of European Academies of Medicine

HMA – Heads of Medicines Agency

UCSF – University of California San Francisco

WHO-UMC – Uppsala Monitoring Centre - World Health Organization Collaborating Centre for International Drug Monitoring

## List of documents and links

### Documents with recommendations

Joint HMA/EMA Big Data Taskforce

EMA Regulatory Science Strategy to 2025

European medicines agencies network strategy to 2025

### Links to organisations

International Coalition of Medicines Regulatory Authorities

### Documents of National Competent Authorities

Questions to critical GxP AI/ML applications