Understanding AI/ML in the Drug Development Lifecycle

Virtual Meeting
December 13, 2022
12:30pm – 4:30pm ET

Meeting Objective: Artificial Intelligence (AI), including machine learning (ML), is becoming more integrated in all phases of drug development— from drug discovery and clinical research to post-market safety surveillance. This workshop will focus on AI/ML innovations in different phases of drug development, with an emphasis on those areas that have the greatest need for regulatory clarity. Discussion will be rooted in specific examples from various phases in the drug development process.

12:30pm **Welcome, Overview, and Introductions**

Marianne Hamilton Lopez, Duke-Margolis Center for Health Policy

12:40pm **Opening Remarks**

M. Khair ElZarrad, U.S. Food and Drug Administration

12:50pm **Overview of AI/ML in Drug Development**

Tala Fakhouri, U.S. Food and Drug Administration

Open Discussion
Moderator: Marianne Hamilton Lopez, Duke-Margolis Center for Health Policy

Discussion Questions:

1. *How is AI/ML anticipated to be used in the short term (2-5 years)?*
2. *In what areas do you expect to see "the next stage" of development in the long term (next 5-7 years?)*

1:20pm **Session 1: Understanding and Evaluating Model Performance**
Moderator: Christina Silcox, Duke-Margolis Center for Health Policy

Objective: During this session, stakeholders will highlight current use cases and evolving practices to develop, evaluate, monitor, and improve the use of AI/ML in different stages of the drug development process. Participants will then discuss which specific tool characteristics and approaches for validation are appropriate for which contexts of use and discuss approaches to document the performance of AI/ML-enabled tools.

Initial Remarks

- Karandeep Singh, University of Michigan

Initial Reactant

- Chris McCurdy, Amazon Web Services

Open Discussion

Discussion Questions:

1. *How do different contexts of use change the approach to designing and selecting AI-enabled tools and assessing their performance?*
2. *How can pre-specification be used to ensure the safe and effective use of AI/ML in drug development? How are control changes captured and monitored?*
3. *What are some examples of when you have had to balance performance and explainability? Are there contexts of use where this issue is more common?*

2:20pm **Break**

2:30pm **Session 2: Data-Related Challenges**
Moderator: Marianne Hamilton Lopez, Duke-Margolis Center for Health Policy

Objective: Discussants will speak about common challenges and mitigation strategies to issues such as data availability, generalizability, and privacy. Participants will discuss practices that developers, manufacturers, and other stakeholders are currently using to ensure the integrity of data used to build AI/ML tools, and to address issues such as bias and missingness.

Initial Remarks
- Alastair Denniston, University of Birmingham

Initial Reactants
- Asieh Golozar, Odysseus Data Services, Inc
- Shameer Khader, Sanofi

Open Discussion

Discussion Questions:

1. *What challenges are you finding in the availability and quality of the data you need to use for training, testing, and operationalizing AI/ML in drug development?*
2. *What practices are developers, manufacturers, and other stakeholders currently using to ensure the integrity of data used to build AI/ML tools? To address issues such as bias and missingness?*
3. *What practices and documentation are being used to inform and record data source selection and inclusion/exclusion criteria?*
4. *What are some promising practices used by stakeholders to help ensure data privacy and security?*

3:30pm **Session 3: Governance, Accountability, & Transparency – Regulatory Implications**
Moderator: Christina Silcox, Duke-Margolis Center for Health Policy

Objective: In this session, stakeholders will discuss regulatory implications and challenges of using AI/ML in the drug development process. Participants will discuss which use cases of AI/ML in drug development need additional regulatory clarity, and will also tie in examples and key takeaways from the previous sessions before opening the floor to wider discussion.

Initial Remarks

- Charles Fisher, Unlearn.AI
- Mike Krams, Exscientia

Open Discussion

Discussion Questions:

1. *Are there use cases where following emerging GMLP is more challenging? Are there gaps where more consensus guidelines are needed?*
2. *What are the main barriers or facilitators of transparency with AI/ML used during the drug development process?*
3. *What are the benefits and challenges in using routinely collected operational and outcome data to monitor AI/ML performance in order to facilitate accountability and transparency?*
4. *When and how do stakeholders use meaningful human involvement to mitigate risk in the use of AI/ML in drug development? What are key considerations for ensuring that products in development have opportunities for "humans in the loop"?*

4:30pm **Closing Remarks and Adjournment**

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Glossary

Algorithm

A process or set of rules, whether created by machines or humans, to be followed in calculation or other problem-solving operations. One or more algorithms are the basis for all AI-enabled tools. (ANSI/CES)

Artificial intelligence

A general term addressing machine behavior and function that exhibits the intelligence and behavior of humans (Duke-Margolis)

- **Machine Learning**

  algorithms that use data to create relationships without being explicitly programmed.

- **Rules-Based:**

  algorithms programed to use human-derived (and generally clinically accepted) rules to guide decision-making.

AI-enabled Tool

A finished AI-enabled software product that is ready to use - including one or more AI-enabled algorithms as well as software to connect with data sources and interact with the user.

Biased Algorithm

When an algorithm demonstrates significantly different performance in a subgroup of the population of interest:

- Demographic (racial, ethnicity, age, sex, gender, etc.)
- Socioeconomic (income, insurance status, etc.)
- Geographic (rural vs urban)
- Health system (community hospital, academic health center)
- Comorbidities

(Duke-Margolis)

Black Box

This term refers to users not being privy to how an algorithm works (although the developers may know and are concealing it as a trade secret). With machine learning, a "black box" algorithm may not be able to be explained, and even the developers don't know. (Duke-Margolis)

Continuous Learning

Training that leads to change of a [machine learning tool] with each exposure to data that takes place on an ongoing basis during the operation phase of [the tool's] life cycle. (IMDRF)

Explainability

Explainability (also called explicability) is defined as concept in which a human can comprehend or understand how an AI system or application was to result in a specific outcome or recommendation. (CTA-2089)

Operational data

The input data used to come to an output/prediction for a tool in actual use (e.g., a patient's EHR and sensor data used to determine a risk score for a patient) (ANSI))

Reliability

Property of consistent intended behavior and results. (ISO/IEC DIS 22989) (IMDRF)

Retraining

Updating a previously trained algorithm through additional training with new data specific to a particular context of use

Semi-Supervised Machine Learning

Machine learning algorithms that leverage both unsupervised and supervised techniques during training. (IMDRF)

Supervised Machine Learning

Machine learning that makes use of labelled data during training (IMDRF)

Testing data

The data used to test algorithmic performance after a system is trained. (IMDRF)

Training

The process intended to establish or to improve the parameters of a ML model, built by inputting training data into a selected ML learning algorithm and specifying optimization parameters.

Training data

Data used to initially train the algorithm. Learning algorithms use the data to find relationships between the data and the label/annotation (supervised machine learning) in order to make predictions. (Duke-Margolis)

Transparency

Available information about the AI-enabled tool. This must include intended use, user, and operational data requirements. It could also include information about the training data, learning algorithm, optimization parameters, testing data, testing results (including subgroup performance), an explanation of how the tool works, and other information.

Unsupervised Machine Learning

Machine learning that only makes use of unlabeled data during training (IMDRF)

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