KYRIAKIDES GEORGOPOULOS
LAW FIRM

**LIFE SCIENCES & HEALTHCARE**

# Reflection Paper on the use of Artificial Intelligence in the medicinal products lifecycle

August 29, 2023

# Reflection Paper on the use of Artificial Intelligence in the medicinal products lifecycle

BY IRENE KYRIAKIDES, VICTORIA MERTIKOPOULOU, AITHRA-VALENTINA ANTONIADOU

On July 19th, 2023, EMA published a draft reflection paper on the use of Artificial Intelligence (AI) in the medicinal product lifecycle, inviting all interested stakeholders to comment on the draft reflection paper up until December 31st, 2023. This reflection paper focuses on the use of AI and Machine Learning (ML) in the lifecycle (development, authorization, post-authorization) of medicinal products, describing the current experience of EMA, which should be combined with the European legal framework on AI, data protection and medicinal products. The considerations included in this reflection paper are summarized as follows:

- Drug discovery: AI in drug discovery is considered to be low-risk since non-optimal performance mainly affects sponsors.

- Non-clinical development: Improving performance in data analysis and using AI/ML modelling approaches to reduce and refine the use of animals.

- Good clinical practice (GCP): The requirements provided for in the ICH E6 guideline for GCP or VICH GL9 Good clinical practices (veterinary) would apply to the use of AI and/or ML in clinical trials.

- Use of medical devices and in vitro diagnostics in clinical trials: AI and/or ML systems used for clinical management of an individual patient may fall under MDR or IVDR.

- Data analysis and inference: AI and/or ML models used for data transformation or analysis in clinical trials could be considered as part of the statistical analysis and, hence, should follow applicable guidelines as regards statistical principles for clinical trials and should include analysis of the impact on downstream statistical inference.

- Precision medicine: AI and/or ML can be used to individualize treatment following indicative parameters: disease characteristics, patient genotype, wide-band biomarker panels and clinical parameters. AI and/or ML referring to the summary of product characteristics may also be part of the individualization of the treatment.

- Product information: AI applications for drafting, compiling, translating or reviewing medicinal product information documents should be used under close human supervision to ensure that all model-generated text is both factually and syntactically correct prior to regulatory review.

- Manufacturing: The use of AI and/or ML in the manufacturing of medicinal products

will be increased and any model development, performance assessment and life-cycle management should adhere to the quality risk management principles, taking into account patients' safety, data integrity and product quality.

- Post-authorization phase: AI and/or ML tools may support post-authorization (efficacy and safety or surveillance studies) and pharmacovigilance activities *via* a flexible approach to AI/ML modelling.

- Regulatory interactions: There is no clear applicable guidance, although regulatory impact, risk analysis of all AI/ML and regulatory interactions are expected.

- Data acquisition and augmentation: AI/ML models are data-driven and, hence, vulnerable to the integration of human bias into models. A balanced training dataset is needed and augmentation techniques should be applied to expand the training dataset.

- Training, validation and test data: In ML validation refers to the data used to inform on the selection of model structure and hyperparameter tuning. Once this process is completed, the performance of the model is evaluated using the hold-out test data set. In case the test performance is unsatisfactory, further model development is needed and the current test data set becomes a second-stage validation data set.

- Model development: Developing practices towards a model of generalizability and robustness, describing clearly the intended use of such model to allow a validity assessment of the feature engineering and preventing overfitting as regards validation and test datasets.

- Performance assessment: choosing the metrics for performance assessment, so as to include parameters that are insensitive to class imbalances and describe the full confusion matrix.

- Interpretability and explainability: Transparent models with underlying general rationale and detailed information on model architecture, hyperparameter tuning, training metrics, validation and test results, and a pre-defined monitoring and risk management plan for mitigating non-transparency issues should be used.

- Model deployment: Deployment of AI/ML models should be aligned with a risk-based approach described for model development.

- Governance: Internal policies and SOPs as regards good practice principles on data and algorithm governance should be extended so as to refer to all data, models and algorithms used for AI/ML throughout the medicinal product lifecycle.

- Data protection: It is the applicant's or MAH's responsibility to ensure that all personal data, including those indirectly held within AI/ML models, are stored and processed in compliance with the applicable legislation. All data processing activities should comply with the principles of lawfulness, fairness and transparency, purpose limitation, data minimization, accuracy, storage limitation, integrity and confidentiality, accountability and also with the rights of data subjects as well as data protection by design and default.

- Integrity aspects: Integrity preservation measures should be adopted before transferring any model to a less secure environment.

- Ethical aspects and trustworthy AI: The following ethical principles for AI, as defined in the guidelines for trustworthy AI and incorporated in the Assessment List for Trustworthy Artificial Intelligence for self-assessment (ALTAI), to all phases of the lifecycle of medicinal products for human and veterinary medicines:
  - Human agency and oversight
  - Technical robustness and safety
  - Privacy and data governance
  - Transparency
  - Accountability
  - Societal and environmental well-being
  - Diversity, non-discrimination, and fairness

## Conclusion

The quickly developing AI and ML potentials are expected to significantly enhance and facilitate all phases of the medicinal products and veterinary medicines lifecycles. On such basis, the newly raised risks should be mitigated, so as to ensure the integrity of clinical study results and patients' safety.

# Contact Us


Irene Kyriakides
**PARTNER**
*i.kyriakides@kglawfirm.g*

Victoria Mertikopoulou
**PARTNER**
*v.mertikopoulou@kglawfirm.gr*


*Follow Us*


**ATHENS OFFICE**

28, Dimitriou Soutsou Str.,
115 21 Athens

T +30 210 817 1500
F +30 210 685 6657-8
E kg.law@kglawfirm.gr

**THESSALONIKI OFFICE**

31, Politechniou Str.,
551 34 Thessaloniki

T +30 2310 441 552
E kg.law@kglawfirm.gr


*www.kglawfirm.gr*