AI in Healthcare & Drug Development – EU Perspectives

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What we will cover

- EU AI Act Overview
- Intersections between AI Act & GDPR
- Breaking down the AI Act
  - Medical Devices and IVD as High-Risk AI Systems
- AI Act Research Exemption
- Equivalent Guardrails for exempted AI?
  - Clinical Trials Regulation
  - ICH Guidelines
  - EMA Guidance
  - GDPR
  - Supplementary national laws

Note: This presentation is not intended as legal advice.

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Overview and Intersections

EU AI Act Overview

- It’s a Regulation, not a Directive
  - Direct law in EU Member States
  - Intended to create high level of harmonization
- Provides for massive fines (up to 7% global turnover)
- Has extra-territorial effect
- AI systems are classed by level & nature of risks
- Obligations linked to risk classification
- Strong focus on governance and documentation
- New regulators established at EU and Member State level
- Phased implementation over 2-year period

GDPR & AI Act Intersections

Some **common principles and elements**:

- Touchstone: EU Charter of Fundamental Rights
- Risk-based regulation with eye to outcomes
- **Privacy by design/AI protections by design**
  - Documented risk assessments before the data processing starts, with updates as needed
  - Limitations on significant automated decision-making
  - Training data and deployed AI Systems need to accommodate exercise of data subject rights
    - E.g., transparency, consent (sometimes), deletion, correction
- Extra protections for sensitive personal data
- Accountability (“show your work”)

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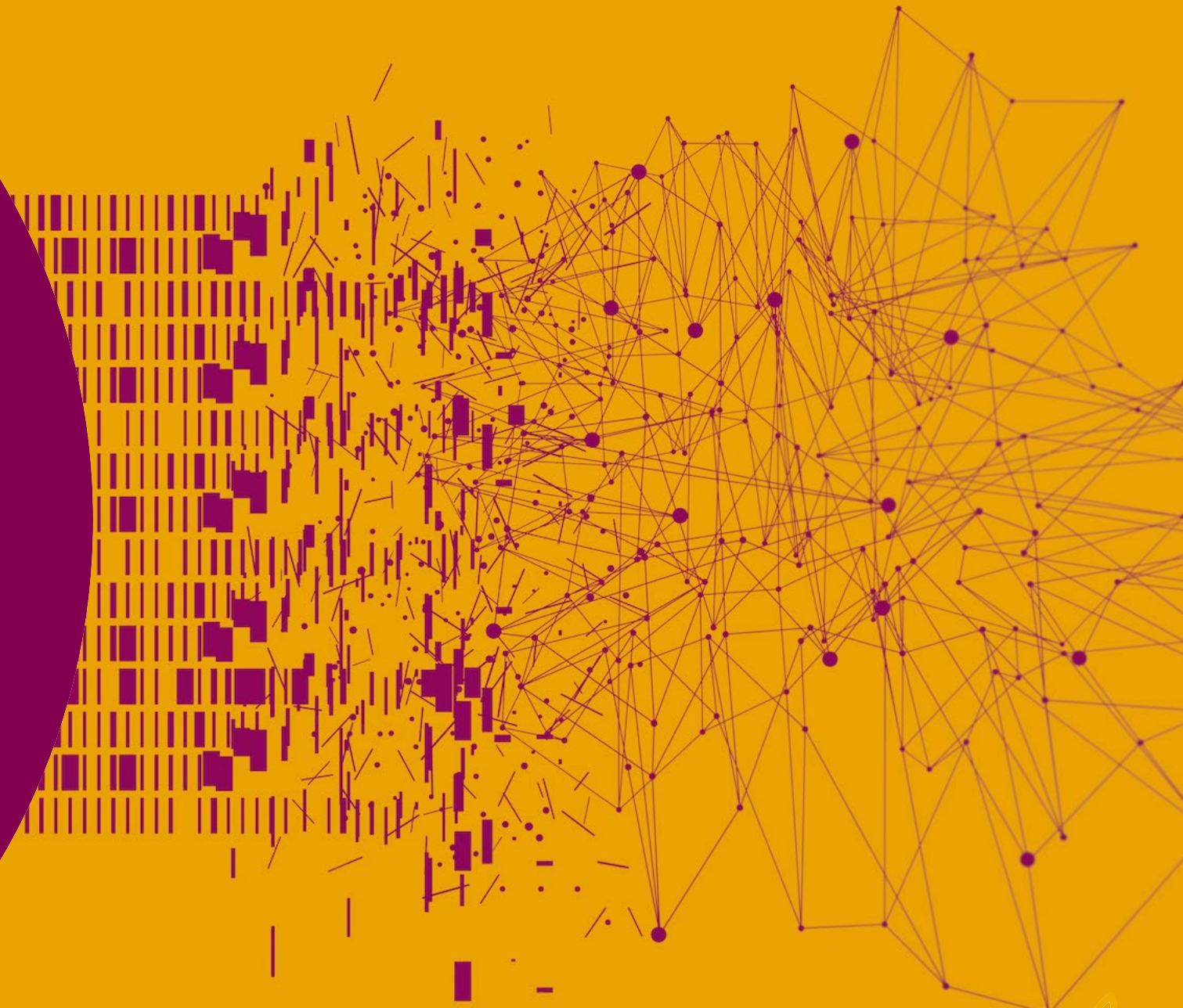
Breaking down the European Union's AI Act



Key Categories

Prohibited AI Practices

High-risk AI Systems

AI Systems subject to Transparency Requirements

General Purpose AI Models with Systemic Risks

Other General Purpose AI Models

Research Exemption

Prohibited AI Practices

- Certain AI “practices” are prohibited because they conflict with EU Fundamental Rights:
  - Subliminal or purposefully manipulative or deceptive techniques intended to materially distort people’s behaviour/decisions
  - Exploiting certain vulnerabilities with the objective or effect of materially distorting a person’s or group’s behaviour creating risk of significant harm
  - “Social scoring” leading to unfair detrimental treatment
  - Predictive policing (profiling to determine whether you are likely to commit a crime)
  - Untargeted scraping of facial images to build facial recognition systems
  - Inference of emotion in workplace or education
  - Biometric categorisation to infer sensitive characteristics
  - Real-time remote biometric ID systems for law enforcement (with exceptions)

High-risk AI Systems – Annex I

How does an AI system get to be a High-risk AI System?

Either:

- Fall under Art. 6(1)(a) and (b):
  - The AI system is a product, or a safety component of a product, that is regulated by EU legislation listed in Annex 1, and
  - a third-party conformity assessment is required to put the safety component/system itself on the market in EU.
    - Annex I includes the Medical Devices Regulation (Regulation (EU) 2017/745) and the *In Vitro* Diagnostics Regulation (Regulation (EU) 2017/746)
- Or land in Annex III (unless specified exceptions apply)
  - *See next slide for Annex III*

High-risk Systems listed in Annex III

- Certain biometric systems
- Safety components for critical infrastructure
- Certain uses in education
- Employment recruitment/selection/decision-making
- Access to essential private or public services/benefits (including public healthcare services; health insurance; emergency medical services)
- Certain law enforcement activities
- Certain migration, asylum and border control activities
- Certain activities for the administration of justice and democratic processes:
  - One for the lawyers in the audience: AI systems for doing legal research/analysis that may be relied upon by judicial authority
  - AI used to influence voting behaviour or outcome of an election/referendum or

Requirements for High-risk AI Systems

- Risk management system
- Quality criteria for training, validation and training data
- Quality management system
- Technical documentation
- Automated event logging for system monitoring
- Transparency information and instructions for deployers
- Human oversight to detect, prevent and minimise risk
- Measurable levels of accuracy, robustness and cybersecurity (against yet to-be-developed benchmarks)
- Conformity assessments and CE marking
- Providers not established in EU must appoint a local representative
- Annex III High-risk AI Systems must be registered in EU databases
- And other requirements for providers, deployers and distributors

AI Systems subject to transparency requirements

- Chapter IV (Transparency Obligations for Providers and Deployers of Certain AI Systems) applies to specific AI use-cases:
  - AI systems designed for direct interaction need to be identified as AI systems unless that's obvious
  - AI-generated synthetic content needs to be labelled as such in a machine-readable format
  - Deployers of emotion recognition systems or biometric categorisation systems need to tell users that they are in operation (and GDPR applies)
  - Deep fakes must be labelled as artificially generated or manipulated
  - Text on matters of public interest (e.g., news) that has been generated or manipulated with AI must be labelled, unless the output is subject to human review or editorial control and a natural or legal person is responsible for the publication of the content.
- For High-Risk AI Systems, these requirements are in addition to the requirements for High-Risk AI Systems.

General-Purpose AI Models

A “general-purpose AI model” is a model that:

- Is trained on a large amount of data using self-supervision at scale
- Displays significant generality
- Can perform a wide range of tasks, and
- Can be integrated into a variety of downstream systems or applications

Requirements:

- Technical documentation of training, testing etc.*
- Provision of documentation to providers who will incorporate the model into their AI systems*
- Copyright compliance policy
- Publicly available summary of training content
- Appointment of authorised representative if not established in EU

**limited exception for open-source models that do not present a systemic risk*

General-Purpose AI Models with Systemic Risk

A general-purpose AI model with system risk is one that:

- Has “high impact capabilities” (e.g., based on computation power for training) *or*
- Has been identified as such by a Commission official act or by the scientific panel created by the AI Act

Additional requirements:

- Model evaluation to identify and mitigate risks
- Assessment and mitigation of systemic risks
- Tracking and reporting serious incidents to AI Office and potentially national authorities
- Adequate cybersecurity

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AI Act Research Exemption

AI Act Research Exemption

- **Article 2.6**: **This Regulation does not apply to AI systems or AI models, including their output, specifically developed and put into service for the sole purpose of scientific research and development.**
- **Recital 25**: This Regulation should support innovation, should respect freedom of science, and should not undermine research and development activity. It is therefore necessary to exclude from its scope AI systems and models specifically developed and put into service for the sole purpose of scientific research and development . . . .

Caveat: Sole Purpose

- Also in Recital 25:

  Furthermore, without prejudice to the exclusion of AI systems specifically developed and put into service for the sole purpose of scientific research and development, ***any other AI system that may be used for the conduct of any research and development activity should remain subject to the provisions of this Regulation****.*

- So if researchers want to use an AI system that has not been *solely* developed and used for scientific R&D, that system is subject to the AI Act.
- This could catch any AI system that is being developed both for research and potential commercial applications, such as a companion diagnostic.

Industry comment on AI Act

EFPIA Statement on the use of AI in the medicinal product lifecycle in the context of the AI Act:

1. The EU AI Act exemption for AI dedicated to scientific research

. . . . AI systems and models specifically developed and put into service for the sole purpose of scientific research and development are excluded from [the AI Act's] scope (as described in Recital 25, Articles 2.6 and 2.8). EFPIA considers that this exemption applies to AI-based drug development tools used in the research and development of medicines because the sole use of these tools is in the R&D of medicines development.

2. The majority of AI uses in the development of medicines cannot qualify as high-risk AI under the current EU AI Act

If the exemption were not to apply, it is important to note that the majority of uses of AI in medicine research and development typically involves AI enabled software that is not regulated under any of the legal frameworks outlined in Annex I (including those for medical devices) nor are they featured under Annex III high risk uses. Therefore, they cannot legally qualify as high risk under the AI Act.

https://efpia.eu/news-events/the-efpia-view/statements-press-releases/efpia-statement-on-the-use-of-ai-in-the-medicinal-product-lifecycle-in-the-context-of-the-ai-act/ Visited 6 June 2024; emphasis added.

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Equivalent Guardrails?

Looking beyond the AI Act

- **More from AI Act Recital 25:** In any event, any research and development activity should be carried out in accordance with **recognised ethical and professional standards for scientific research and** should be conducted in accordance with **applicable Union law**.
- Such as ???
  - Clinical Trials Regulation (Regulation (EU) No 536/2014)
  - ICH Guidelines, particularly on GCP (being updated)
  - European Medicines Agency (EMA) Guidance
  - GDPR
  - Supplementary national data protection & health laws

Clinical Trials Regulation

- The Clinical Trials Regulation is a comprehensive law governing all clinical studies conducted in the EU
- Transparency: High standard for participant information and consent to participate in study
- Conditions on data re-use: Sponsor may ask the participant to consent to the use of data for scientific research outside the scope of the protocol (usually called “future research”) (CTR Art. 28(2))
  - Consent to future research is freely revocable
  - Usually understood to mean that the lawful basis for processing for future research must be consent (although future guidance on “ethical consent” vs “consent as lawful basis” may challenge that)
  - The processing remains subject to GDPR

ICH Guidelines

- ICH Guideline on good clinical practice (GCP) E6 (R2)
  - currently in force
  - being updated to address developments in technology and newer approaches to conducting clinical studies
- New: ICH E6 (R3) (consultation draft)
  - Detailed requirements for “Computerized Systems”
  - Quality of data outputs must be ensured by design, testing/validation and audits
  - Extensive record-keeping requirements (including audit trails)
  - Security requirements
  - Incidents with potential impact on quality of data outputs must be recorded and reported
- New ICH E6(R3) Annex-2 (draft not yet published) anticipated to cover decentralised clinical trials and use of AI

EMA AI Guidance

- European Medicines Agency (EMA) published a consultation draft “Reflection paper on the use of Artificial Intelligence (AI) in the medicinal product lifecycle”
  - Available at https://www.ema.europa.eu/en/news/reflection-paper-use-artificial-intelligence-lifecycle-medicines
  - Consultation closed 31 December 2023; final draft pending
  - Likely to form basis for formal guidance
- Key points:
  - Supports risk-based approach to AI
  - Marketing authorisation applicant/holder is responsible for ensuring that the AI tools that it uses are **fit for purpose and meet ethical, technical, scientific and regulatory standards per GxP and EMA scientific guidelines** – which **may be stricter** than standard practice in the field of data science.

EMA "Reflections"

To highlight just a few important EMA "reflections":

- **Explainability**: Models generated for trials are considered part of the clinical trial data or trial dossier and must be made available for comprehensive assessment as part of the marketing authorisation application.
- **Documentation/Controls**: AI/ML models used for transformation or analysis of data within clinical trial must be included in the trial's statistical analysis plan (and subject to related controls).
- **Regulatory Input:** AI used in late-stage pivotal trials cannot be modified "on the fly" without first discussing with the regulators.
- **Transparency:** EMA encourages models to be published in an open repository prior to use in a pivotal trial.
- **Heightened scrutiny for Precision Medicine:** If AI used to individualise treatment (patient selection, dosing, etc.) and that forms part of the marketing authorisation application, the AI element becomes subject to medicines regulation.

National Laws & Frameworks

- GDPR permits the Member States to legislate further in certain areas including health (Rec. 10; Art. 10(4))
- Medical confidentiality laws should be considered
- DPA-approved frameworks for processing data in connection with clinical studies should be considered
  - Examples:
    - France, Reference Methodology 001 (MR001)
    - Spain, Code of Conduct Regulating the Processing of Personal Data in Clinical Trials and Other Clinical Research and Pharmacovigilance Activities

Q&A