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The Role of Real-World Evidence and Artificial Intelligence in Accelerated Approval / Assessment in Oncology

Compliance & Regulatory Perspective

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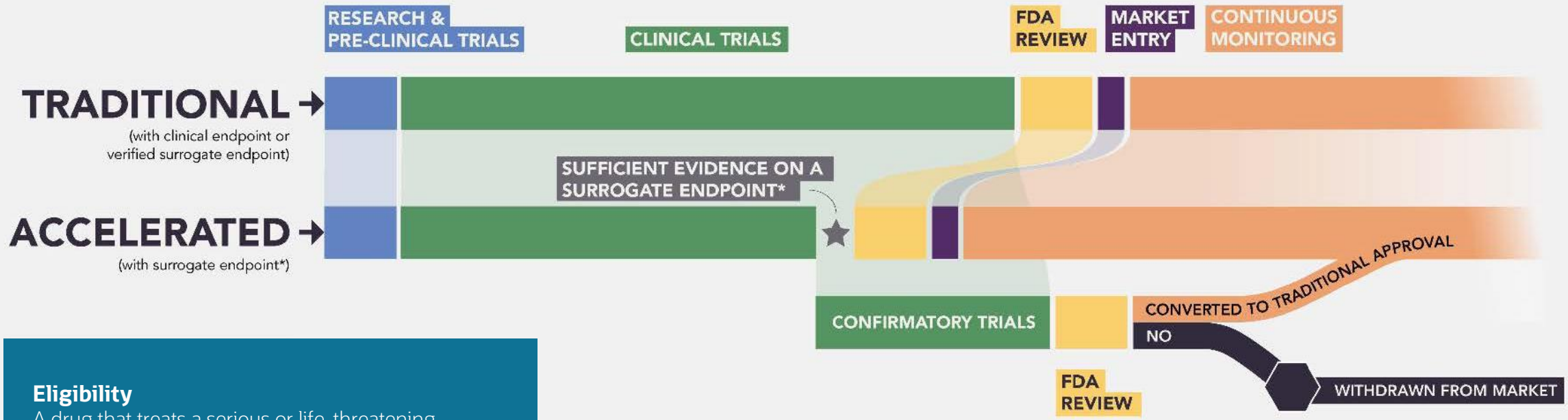
Approval pathways for drugs & biologics



Eligibility
A drug that treats a serious or life-threatening disease, taking into account unmet medical need. The drug is studied using a surrogate endpoint, which in this case, is a marker (such as tumor shrinkage) that is considered reasonably likely to predict a clinical benefit (such as increased overall survival).

Ref: Reagan-Udall Foundation for the FDA (2022)

Requirements for FDA Accelerated Approval

Surrogate Endpoints
Robust dataset

Confirmatory trials
Clinical benefit

Labelling statement
Surrogate vs clinical

Promotional materials
Special review

AA may be withdrawn
If fail to verify clinical benefit

Ref: Reagan-Udall Foundation for the FDA (2022)

FDA Accelerated Approval regulatory trend

Data needed to support AA

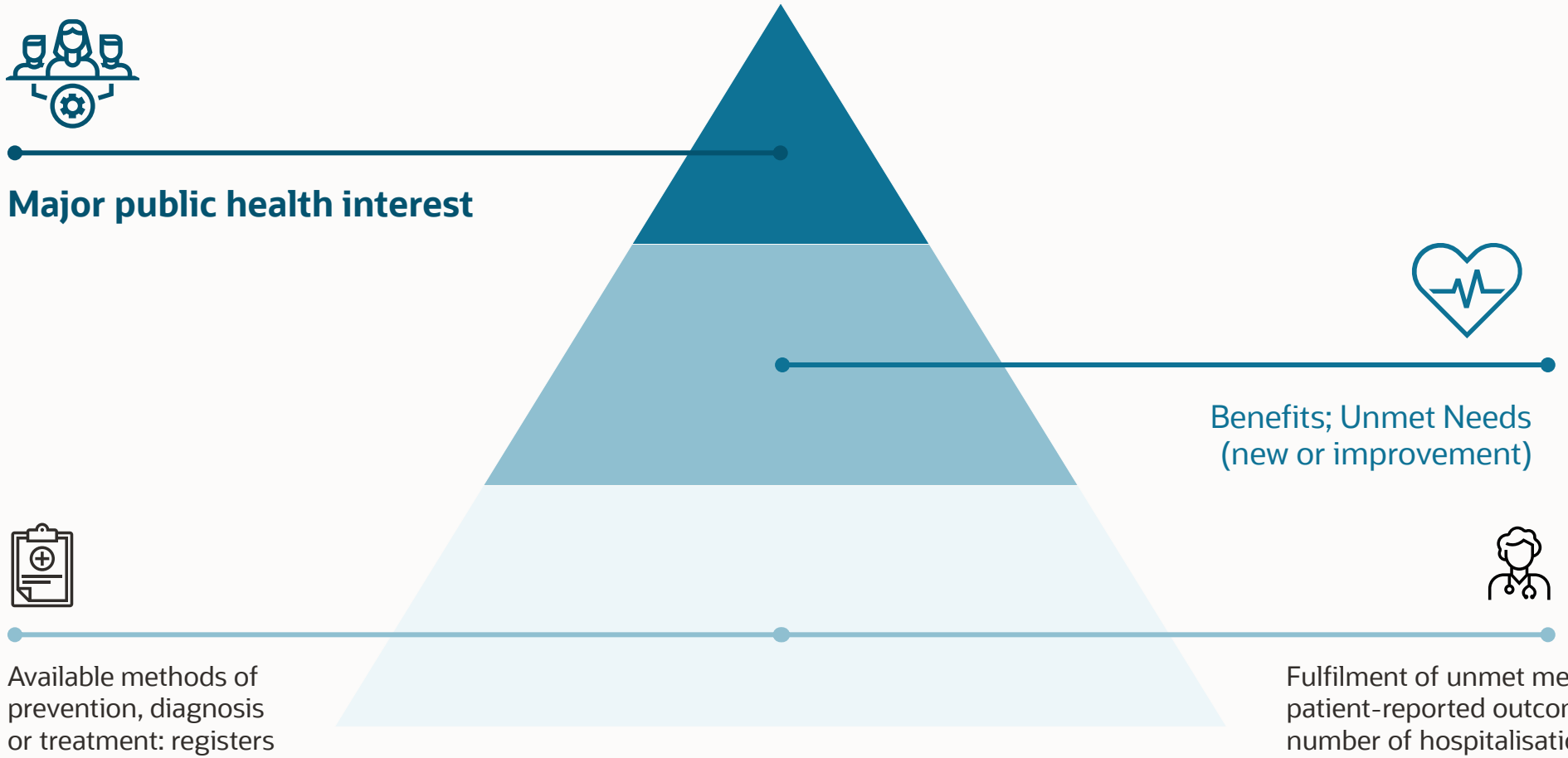
RCT as the preferred approach

Single arm trials for AA

Prolonged duration on the market without confirmatory studies

Ref: Ongoing Cancer Accelerated Approvals (Sep 2009 to Jun 2024); Oncology/Cancer Hematologic Malignancies Approval Notifications (Oct 2018 to Jun 2024)

To be considered in the EMA's Accelerated Assessment framework



Ref: https://www.ema.europa.eu/en/human-regulatory-overview/marketing-authorisation/accelerated-assessment

The role of Artificial Intelligence (AI)

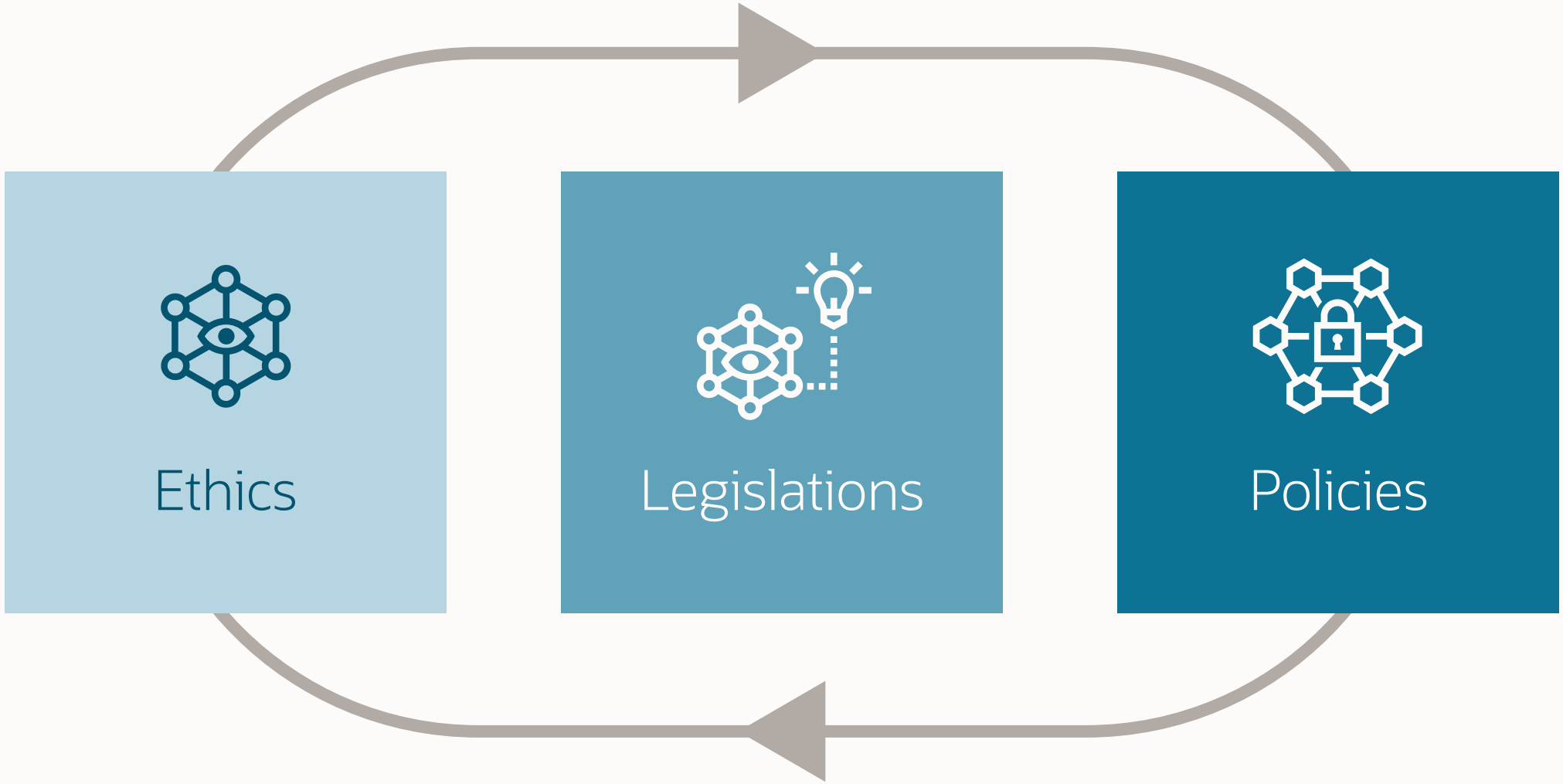
images generated by MidJourney

What HEOR practitioners MUST KNOW

There is a **huge wave of AI related legislations** coming in 2024

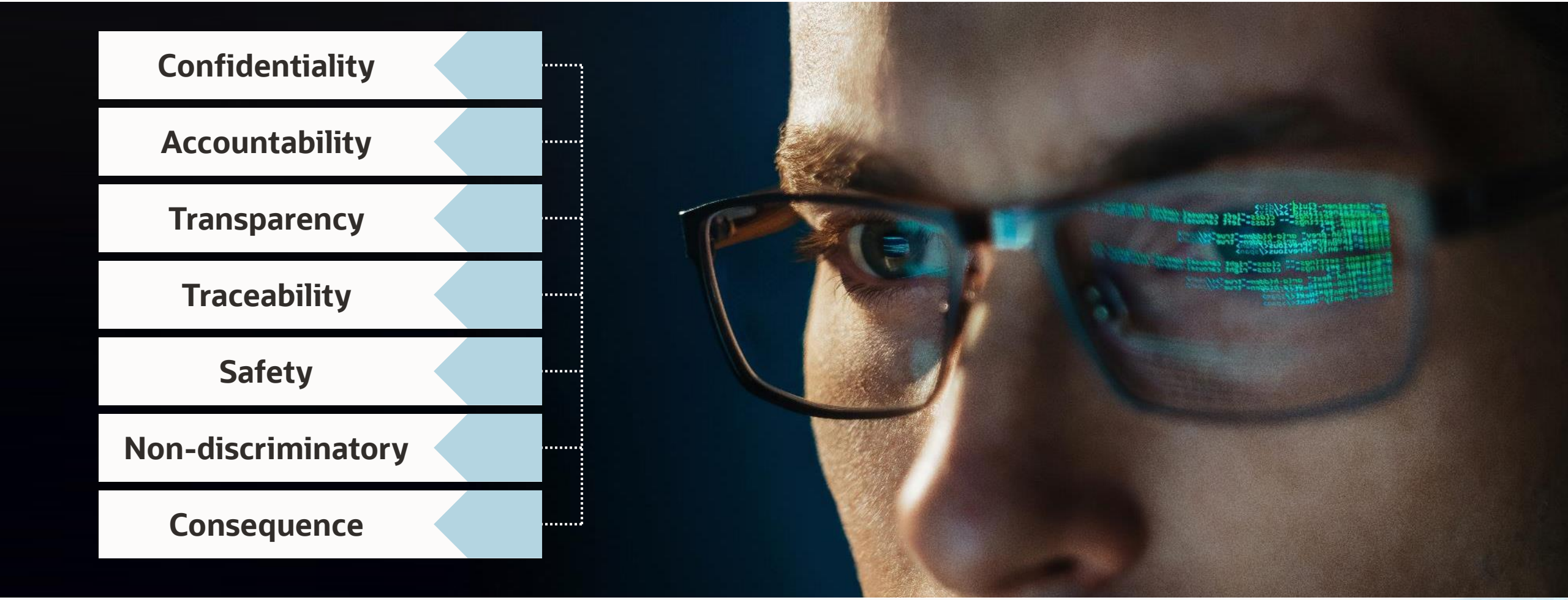
YOU (designer, user) are responsible, not the AI.

The role of AI



Principles

- Confidentiality
- Accountability
- Transparency
- Traceability
- Safety
- Non-discriminatory
- Consequence



EU AI ACT

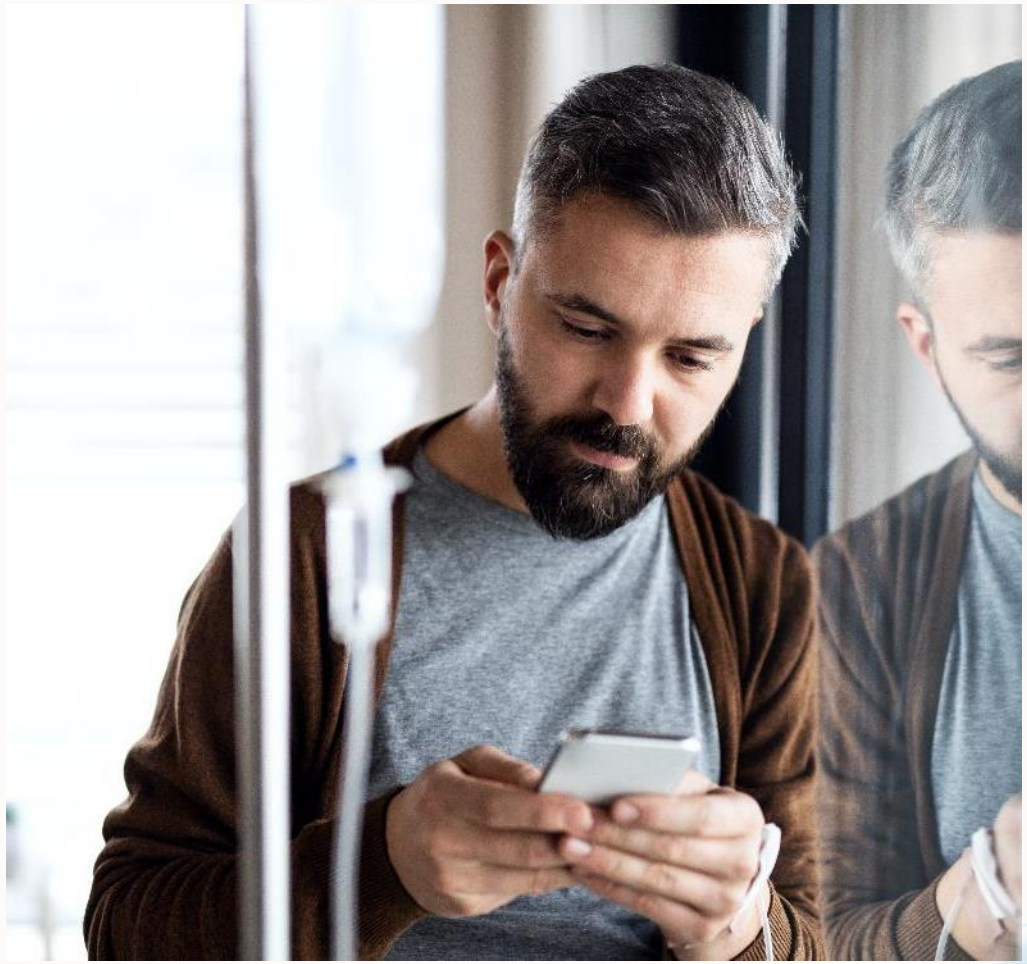
The scope of the EU AI Act – A risk-based approach

Prohibited AI Practices (Systems that contravene the values of the EU by violating fundamental rights are prohibited)

High Risk (Systems including Biometric identification, management of critical infrastructure, employee management, law enforcement…)

Limited Risk (Systems that interact with human, detect emotions or association based on biometric data…)

Minimal Risk Systems (Voluntary creation and enforcement of a code of conduct that may include commitments)



Polling Question 1 –
ChatGPT belongs to which category?

A.
Prohibited AI Practices

B.
High Risk

C.
Limited Risk

D.
Minimal Risk

Polling Question 2 –
Use of AI in medical research?

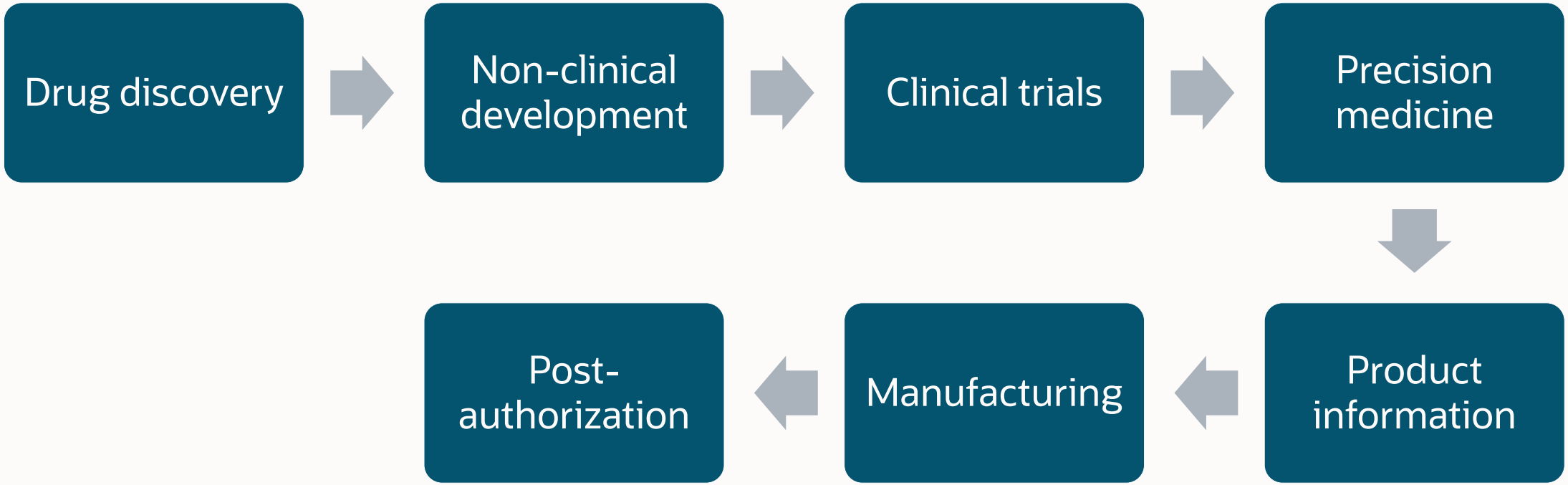
A.
Prohibited AI Practices

B.
High Risk

C.
Limited Risk

D.
Minimal Risk

EMA on the use of AI in medicinal product lifecycle



Ref: EMA Reflection paper on the use of Artificial Intelligence (AI) in the medicinal product lifecycle - https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-use-artificial-intelligence-ai-medicinal-product-lifecycle_en.pdf

Real World Evidence (RWE)

Regulatory RWE requirements & challenges for Accelerated Assessment and Approval

- To address evidentiary gaps
- Better integration of RWD/RWE
- Readiness to address
- Supplementing RCT

Ultra-rare indication / Lack of standard of care

- Heterogeneous data sources
- Lack of global collaboration
- Different levels of quality
- Various governance models for data sharing and access

The Data Quality Framework
by Towards the European Health Data Space (TEHDAS)

Ref: Multi-stakeholder workshop on Real World Data (RWD) quality and Real World Evidence (RWE) use" 26-27 June 2023, hybrid meeting, EMA, Amsterdam held by HMA and EMA: https://www.ema.europa.eu/en/documents/report/report-multi-stakeholder-workshop-real-world-data-rwd-quality-and-real-world-evidence-rwe-use_en.pdf
The Data Quality Framework: https://www.ema.europa.eu/system/files/documents/regulatory-procedural-guideline/data-quality-framework-eu-medicines-regulation_en_1.pdf

Opportunities to use RWD with or without AI in future AAs in oncology

- Indication - rare diseases including oncology and special populations such as paediatrics
- Regulatory decision-making

Figure 1: Use case objectives and categories in which RWE can support regulatory decision-making

Use case objective	Support the planning and validity of applicant studies	Understand the clinical context	Investigate associations and impact
Use case category	Design and feasibility of planned studies	Disease epidemiology	Safety studies
		Clinical management	Effectiveness studies
	Representativeness and validity of completed studies	Drug utilisation	Impact of regulatory actions

(ref: HMA/EMA Real-world evidence provided by EMA - Support for regulatory decision-making: https://www.ema.europa.eu/en/documents/other/guide-real-world-evidence-provided-ema-support-regulatory-decision-making_en.pdf) - Note that this is in the context of RWE provided by the EMA.

Case study: RWE used to support a supplemental NDA (New Drug Application) for Ibrance® (male breast cancer)

- FDA approval in 2019 of a supplemental NDA for Ibrance (palbociclib) for men with advanced or metastatic breast cancer based predominately on RWD
  - Original indication was granted under the AA by the FDA
  - The approval was based on data from electronic health records and post-marketing reports of the real-world use of Ibrance in male patients sourced from three databases:
    - Pfizer's global safety database
    - HER (Tumor Response)
    - Claims Data (Duration of Therapy)

Ref: https://www.pfizer.com/news/press-release/press-release-detail/ibrance_palbociclib_receives_fda_regular_approval_and_expanded_indication_for_first_line_hr_her2_metastatic_breast_cancer

Thank you

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