Regulations on AI research in Europe.

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Artificial Intelligence in Cardiovascular Magnetic Resonance Imaging

May, 6th, 2022

SCMR
Society for Cardiovascular Magnetic Resonance

EACVI
European Association of Cardiovascular Imaging
European Society of Cardiology

Declaration of interest

- **Consultancies:**

Blue Earth Diagnostics, CuriumPharma, General Electric Medical System, Naogen, NovoNordisk, Pfizer.

AI is a medical software

The European high-level expert group provides the following definition for AI:

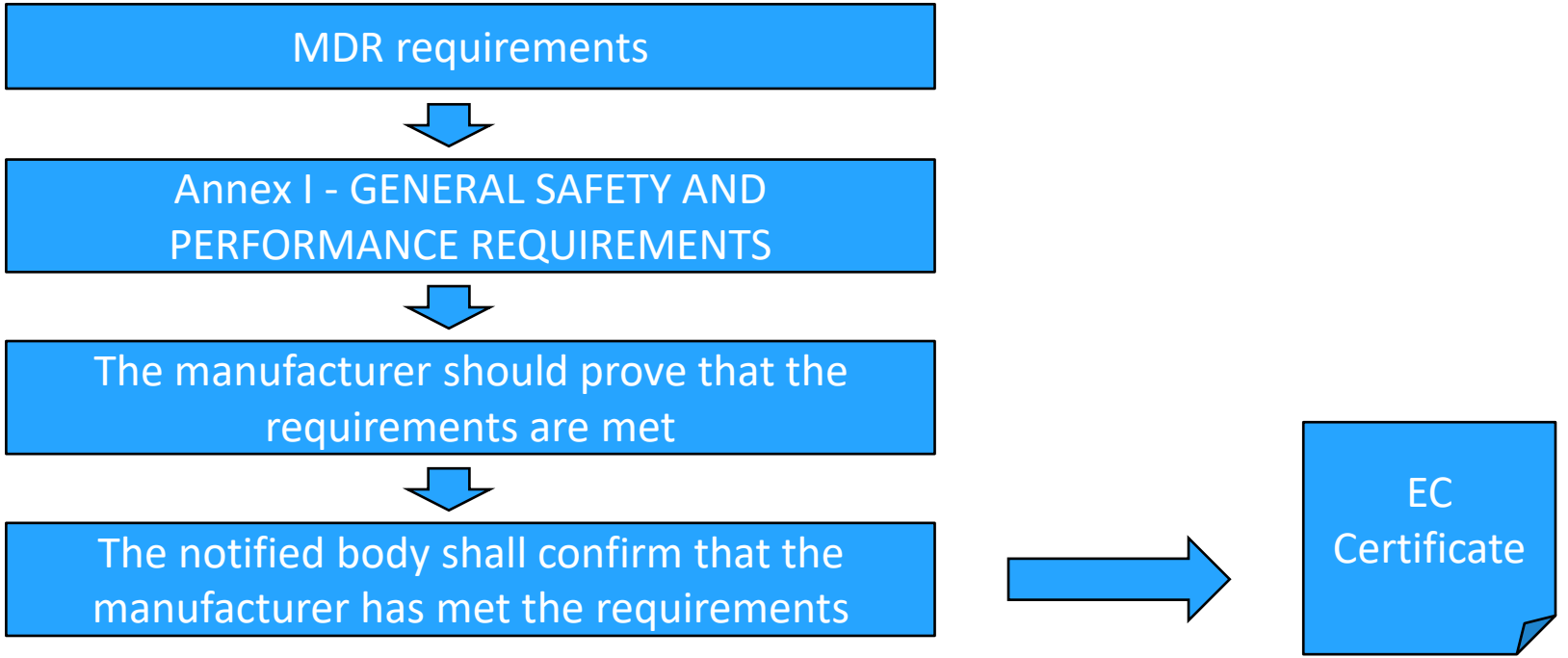
« AI are **software** designed by humans that, given a complex goal, act in the physical or digital space by perceiving their environment through data acquisition, interpreting the collected structured or unstructured data, reasoning on the knowledge, or processing the information from these data and deciding the best action(s) to achieve the targeted goal. »

- COCIR supports that **regular applications of AI in Healthcare** could be adequately regulated using **MDR and GDPR,** with the most advanced applications of AI requiring an update of the current regulation.

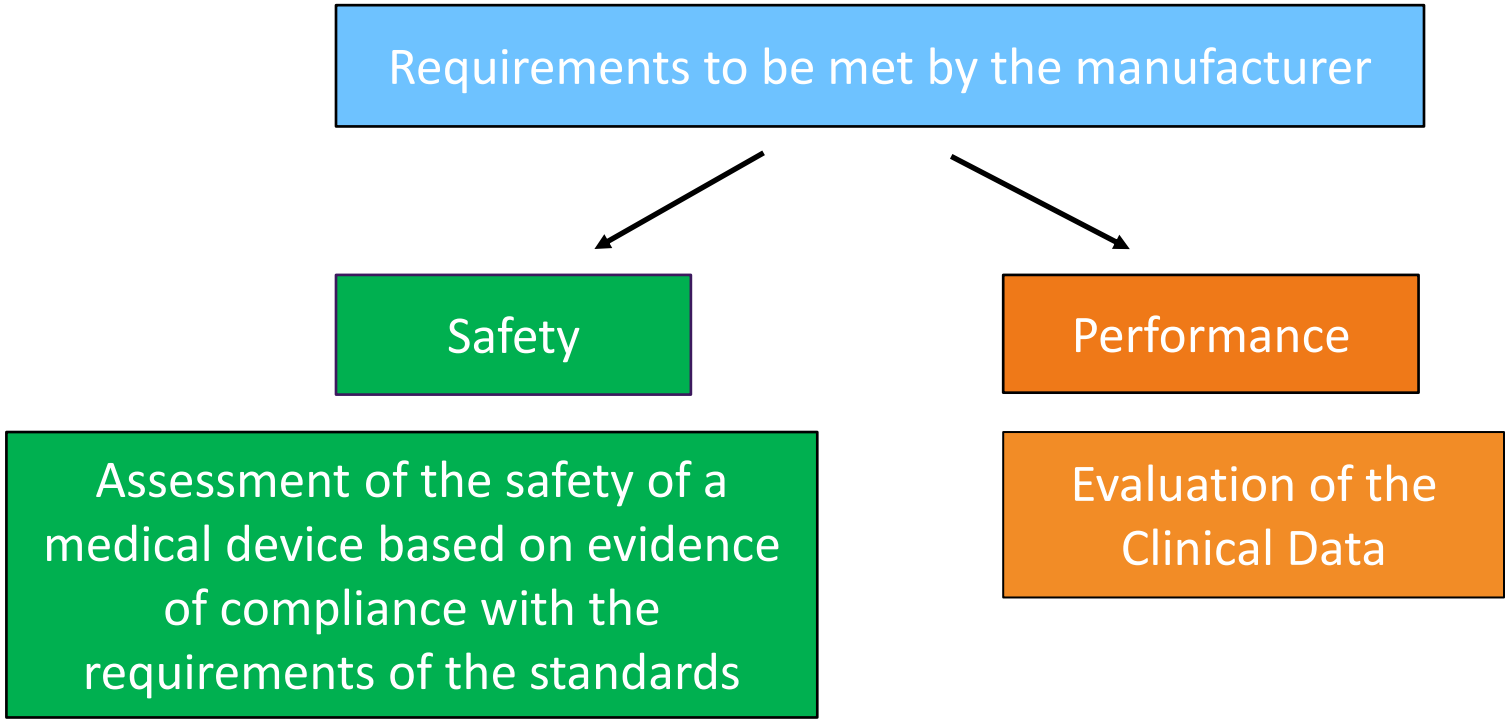
- The EU is currently finalizing a **new regulation** aimed at covering general aspects of AI, which will provide a framework **for advanced applications of AI**.

Regulation of medical software in the EU

- Medical software are classified as medical devices and approved in the EU following the Medical Device Regulation (MDR).



Annex 1: general safety and performance requirements



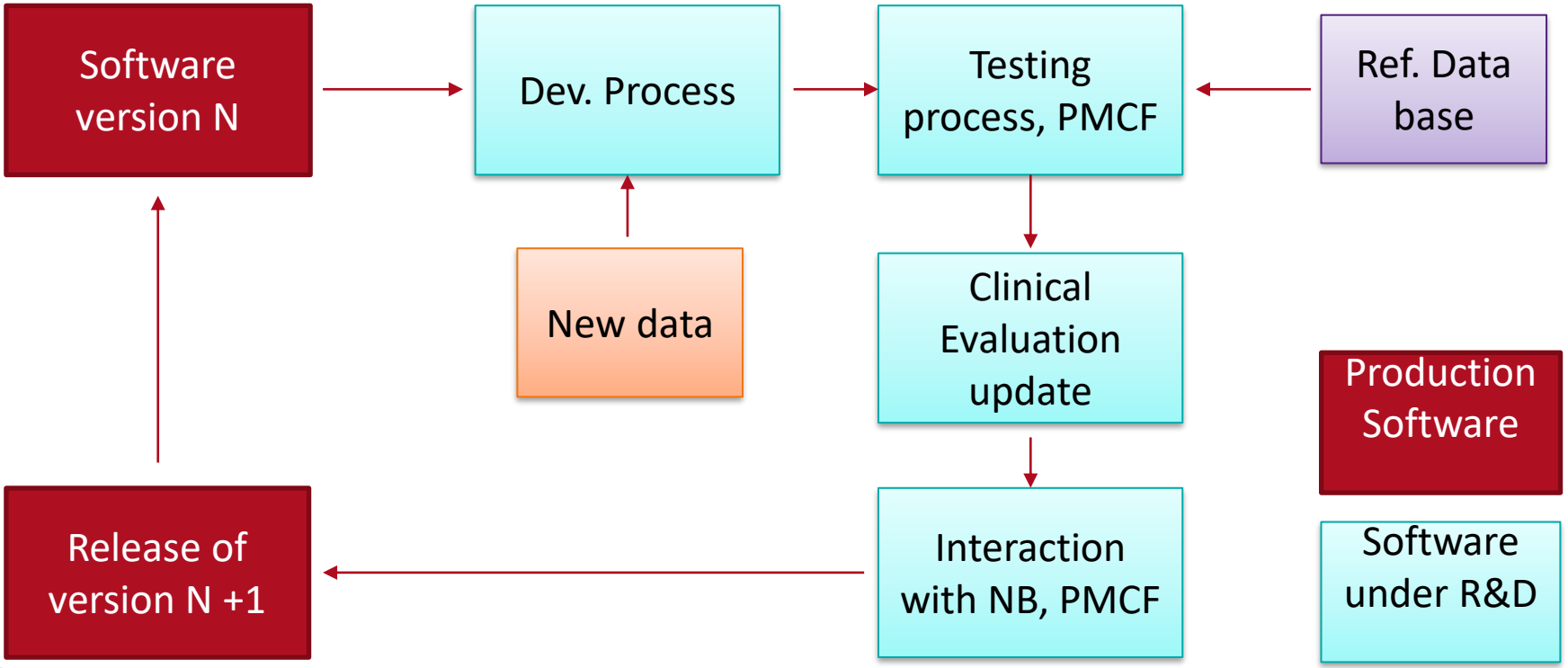
Harmonized standards

- Devices should be in **conformity with the relevant harmonized standards**, or the relevant parts of those standards published in the Official Journal of the European Union.

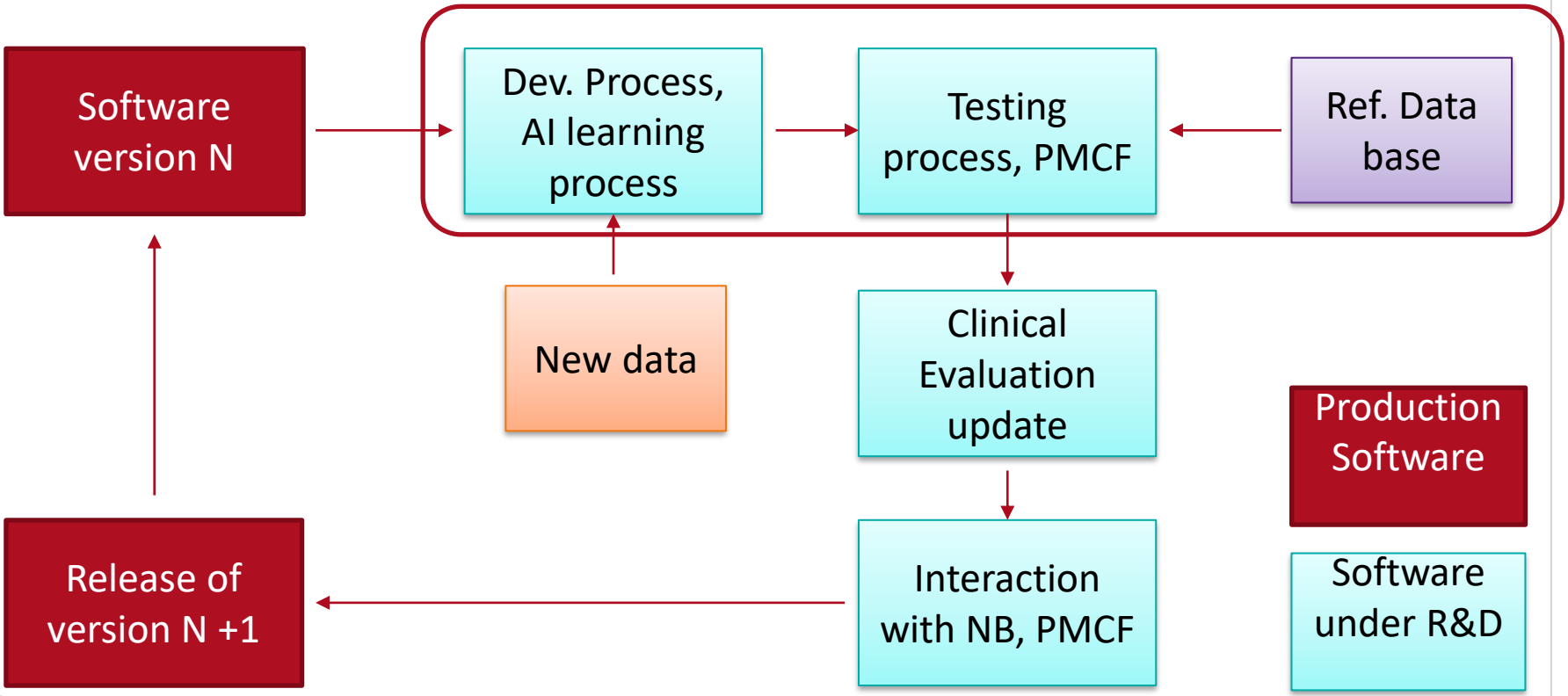
- The main standard for medical software is : EN IEC 62304 medical device software – software life cycle processes (EU & FDA).

- Most standards focus on safety (repeatability, reliability, cyber-security) of medical software and not on how to evaluate the diagnostic performance.

Software life cycle processes



Specificities of AI

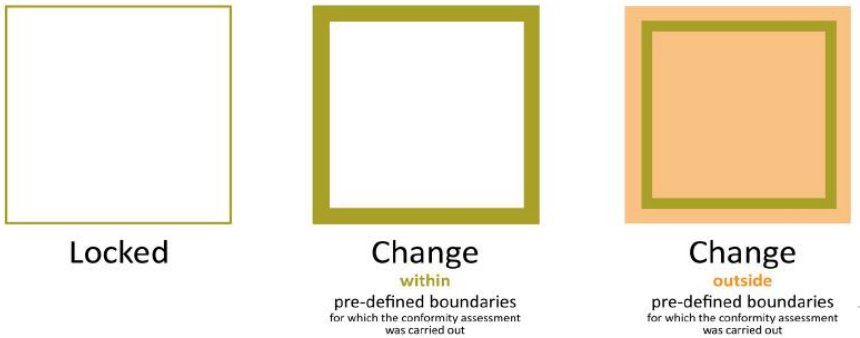


Machine learning approaches with AI

Under EU MDR and EU IVDR, **manufacturers could place devices on the market comprising locked AI or AI that changes within pre-defined boundaries** for which a conformity assessment was carried out.

Currently, **the EU MDR and EU IVDR do not allow manufacturers to place devices on the market comprising AI that changes outside of pre-defined boundaries**.

1. LOCKED	2. CHANGE BY USER	3. DISCRETE CHANGE THROUGH LEARNING	4. CONTINUOUS CHANGE THROUGH LEARNING
May learn in the field, usually through "offline learning" with feedback being analyzed at the manufacturer site	May learn in the field, usually through "offline learning" with feedback being analyzed at the manufacturer site	Learns in the field	Learns in the field
Does not change during use	User can select an appropriate working point	Update of the model with explicit/distinct update by manufacturer or user	Update of the model without explicit manufacturer or user interaction



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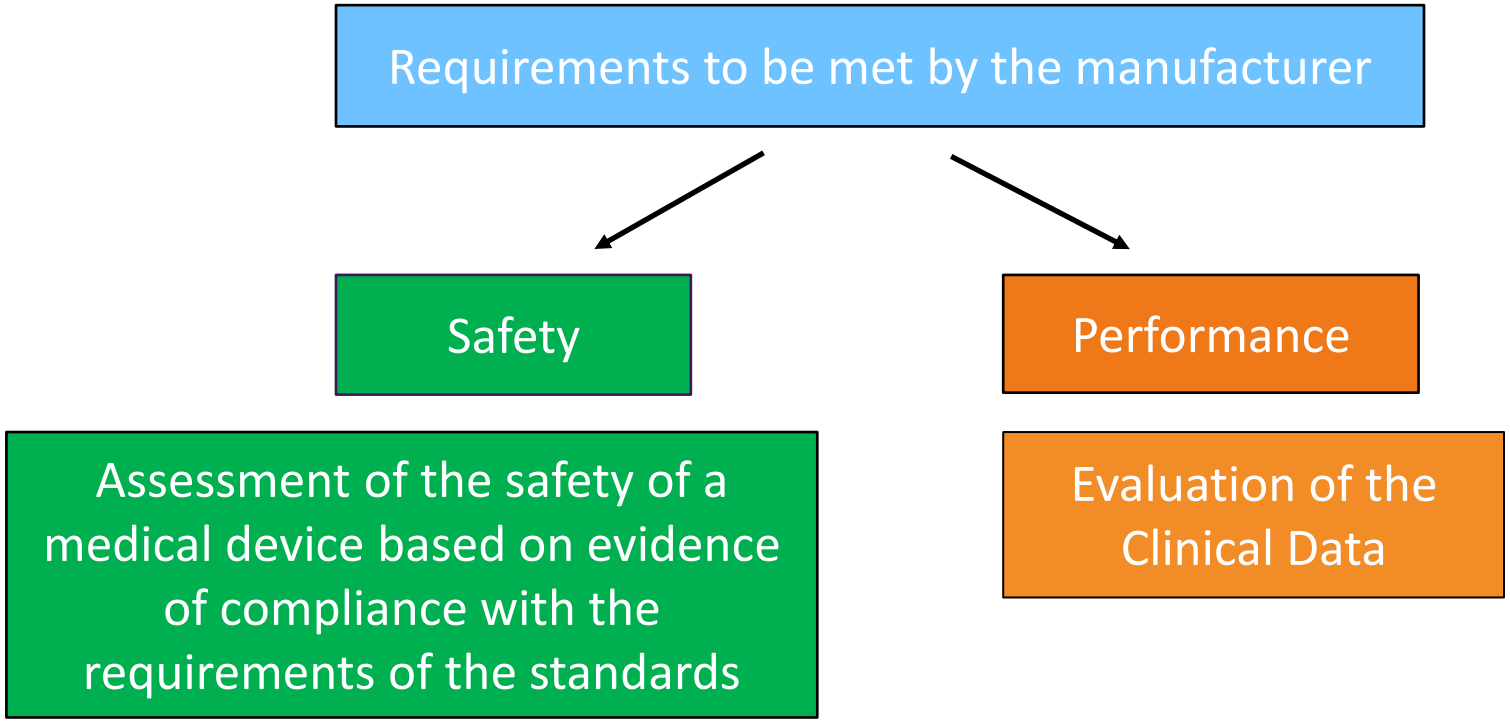


MDR classification of risks associated to medical devices

Classification of medical devices depends on the intended use and patient condition
=> Room for interpretation depending on the choice of intended use.

State of Healthcare situation or patient condition		**High** Treat or diagnose	**Medium** Drives clinical management	**Low** Informs clinical management (everything else)
	Critical situation or patient condition	Class III	Class IIb	Class IIa
	Serious situation or patient condition	Class IIb	Class IIa	Class IIa
	Non-serious situation or patient condition	Class IIa	Class IIa	Class IIa

Guidance on Qualification and Classification of Software in Regulation (EU) 2017/745 – MDR and Regulation (EU) 2017/746 – IVDR

MDR : clinical evaluation

Three components of clinical evaluation for medical software :

- **Valid clinical association** as an indicator level of clinical acceptance and how much meaning and confidence can be assigned to the clinical significance of software output in the intended healthcare situation.

- **Analytical validation** provides confirmed evidence that, the software is correctly constructed with reliable input data and generates output data with **appropriate level of accuracy, repeatability and reproducibility** and demonstrates that the software meets the specifications conformed to user needs and intended uses.

- **Clinical Validation** is evaluated based on its **ability to yield clinically meaningful output for the intended use**, as well as for the healthcare situation.

MDR : clinical evaluation

- **Clinical Evaluation Plan :** define the criteria applied to generate the necessary **clinical evidence** based on the characteristics of the medical software.

- **Clinical Evaluation Report :** identify relevant **data on performance and/or safety of the device and any unaddressed issues or gaps in the data**, analyse available data and its relevance to demonstrating conformity with General Safety and Performance Requirements (GSPRs).

- The clinical evaluation shall be updated and documented throughout the life cycle of the medical software concerned with data obtained from **implementation of a Post Market Clinical Follow-up/Post Market Performance Follow-up** plan.

Implementing AI approaches in the MDR

- Regular AI applications in Healthcare may be included in the current MDR pending few restrictions.

- New regulation is required for the most advanced applications of AI. This could be done by updating the standard for medical software IEC 6230415 :

- Require manufacturers to **define an Algorithm Change Protocol for AI-based device** that change through learning during runtime.

- **Describe AI attributes in the user documentation** (human oversight or control, provide a description of change dynamics and change boundaries)

- Consider a **design capable of storing discrete states of a learned model and capable of returning to a previously stored state** in order to reproduce results.

- Update the technical documentation and perform a new conformity assessment **in case of significant changes** to the pre-determined Algorithm Change Protocol.

Public consultation on the AI White Paper

Final report

European Commission

SCMR Society for Cardiovascular Magnetic Resonance

EACVI European Association of Cardiovascular Imaging

Main concerns regarding AI

90% AI may breach fundamental rights

87% Use of AI may lead to discriminatory outcomes

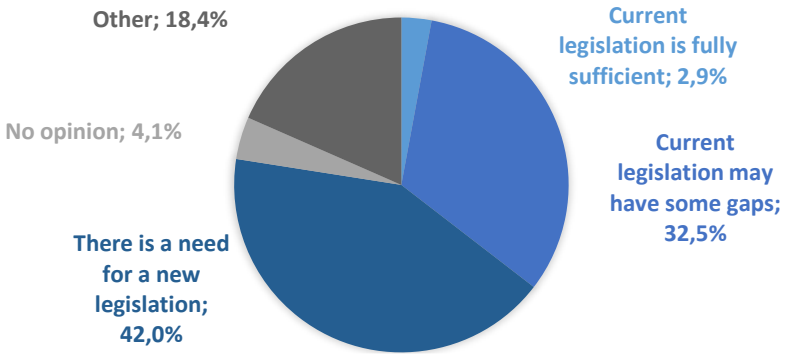
82% AI may endanger safety

78% AI may take actions whose rationale cannot be explained

70% AI is not always accurate

68% AI may make it more difficult to obtain compensation

New regulation focused on AI is wished



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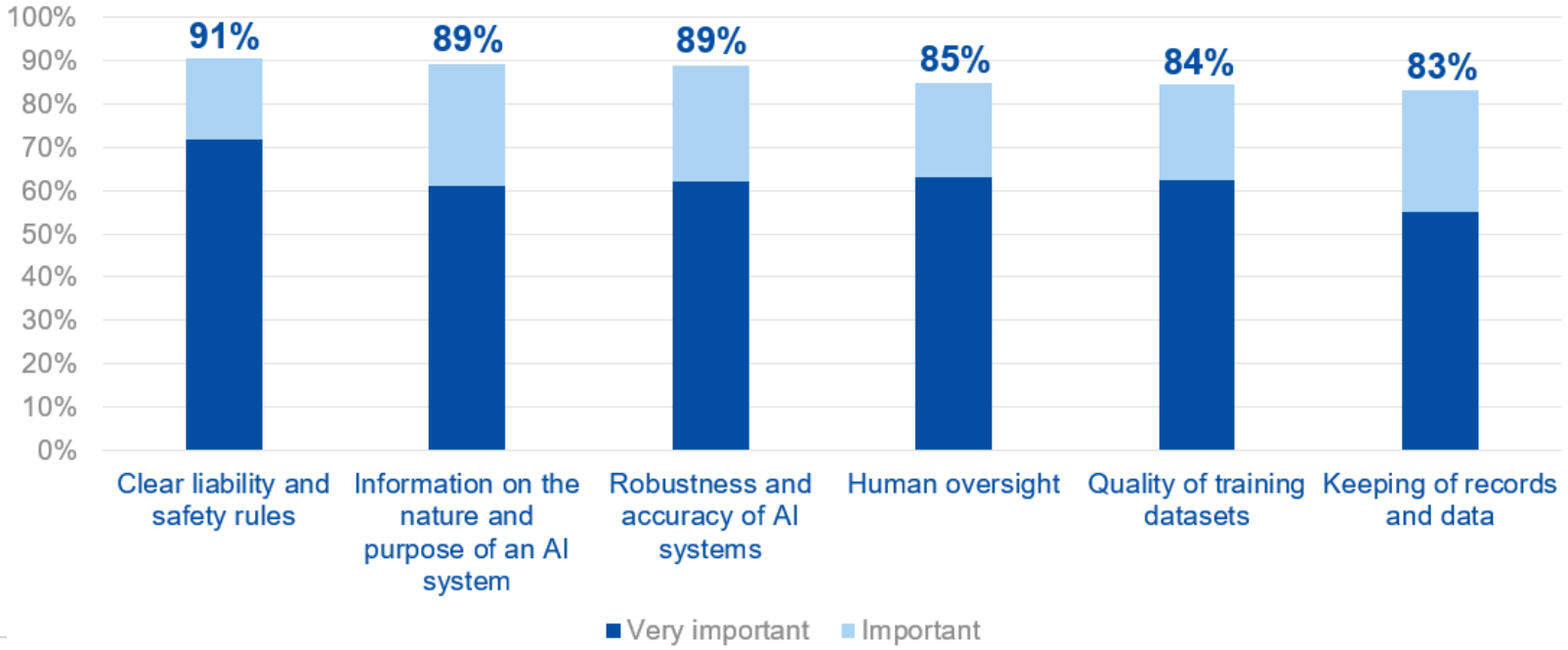
Suggested mandatory requirements for AI



Laying down the Artificial Intelligence Act

- The purpose of this Regulation is to improve the functioning of the internal market by laying down a **uniform legal framework** in particular for the development, marketing and use of AI in conformity with Union values.

- In order to ensure a **consistent and high level of protection of public interests** as regards health, safety and fundamental rights, common normative standards **for all high-risk AI systems** should be established.

- The proposals identify and categorize four levels of AI risk: unacceptable risk, high risk, limited risk and minimal risk.

- Healthcare AI applications would generally fall into the high-risk category.

Laying down the Artificial Intelligence Act

High-risk applications of AI would need to fulfill the following criteria to achieve regulatory approval:

- **High quality of the datasets** feeding the system to reduce risks and discriminatory outcomes
- **High level of robustness, security and accuracy**

- **Detailed documentation** providing all information necessary on the system and its purpose, for authorities to assess its compliance
- Logging of activity to **ensure traceability of results**
- **Clear and adequate information** to the user

- **Adequate risk assessment and mitigation systems**
- Appropriate human oversight measures to reduce risk

Ensur robustness and limit bias of AI

- The **technical robustness is a key requirement** for high-risk AI systems. They should **perform consistently throughout their lifecycle and be resilient** against risks connected to the limitations of the system (e.g. errors, faults, inconsistencies, unexpected situations).

- Training data sets used to develop AI should be well described and accessible to the users to **minimize bias**.

=> The European health data space will facilitate non-discriminatory **access to health data and the training of artificial intelligence algorithms on those datasets**.

=> Suggestion of setting up AI Testing and Experimentation Facilities (TEFs) bringing together academics and the industry.

Transparency of AI applications

- To address the opacity that may make certain AI systems incomprehensible to or too complex for natural persons, **a certain degree of transparency should be required** for high-risk AI systems.

- High-risk AI systems should be designed and developed in such a way that **natural persons can oversee their functioning**.

=> Requirements to have **logging capabilities** (traceability & auditability) in AI to be able to identify bias or error.

=> Provide clinicians with **instructions for use** and **information on capabilities and limitations** of the system

=> Patient should be informed of the use of AI for their clinical management.

Liability of AI applications

Legal system needs to make a decision how to strike the **balance between safety and regulatory burden**.

Risk-based differentiation based on the gravity of the initial risk that is the reason to introduce legislation, the burden implied by the measure taken, and considerations of practicality, clarity and certainty of the law (**proportionnality**)

The **autonomy and opacity** of AI-system may render it difficult to get compensation under existing liability regimes.

⇒ Requirements to have **logging capabilities** (traceability & auditability) in AI to be able to identify the origin of the bias or error.

⇒ Liability of clinicians using AI applications in case of errors or bias ?

Conclusions

- AI applications in Healthcare could be regulated with MDR pending additional regulation covering the most advanced applications of AI.
- The AI Act is currently in the EU legislative process and will provide new general regulations for AI that may impact the regulation of Healthcare applications.
- A good alignement of the MDR and the future AI Act is key to prevent further increasing legislative complexity and legal uncertainty for AI applications in Europe.
- Clinicians need to get involved in proposing guidance on how to evaluate AI in healthcare, identify possible bias, stratify risks and organize post-market surveillance.

Acknowledgements

ESC Regulatory Affairs Committee

Alan Fraser

Piotr Szymanski

Maria-Luisa Ranconi, Patricia Munoz, Ilaria Leggeri.

ESC / EACVI Task Force on the Regulatory Governance of Cardiovascular Imaging

Chiara Bucciarelli-Ducci

Maka Cikes

Industry

Nicole Denjoy (COCIR)

Kornel Lukaszczyk (TUV Nord)

Zuzanna Kwade (MD-CORE), Koen Cobbaert (Philips)

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