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Integrating patients' Fundamental Rights in the Use of Artificial Intelligence enabled Medical Devices (AI-MD) in clinical research: the example of the HT-Advance European project (GA n°101095407)

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Pauline Rateau, Gauthier Chassang, Emmanuelle Rial-Sebbag

UMR 1295 CERPOP, Inserm, University of Toulouse III - Paul Sabatier ;Genotoul Societal Platform « Ethics and Biosciences », GIS Genotoul

References

The HT-Advance project in brief

A clinical investigation that aims to personalise the management of arterial hypertension through clinical trials using **machine-learning techniques and multi-omics data** to enable early diagnostic and therapeutic response predictions for preventing the associated risk factors and facilitating **professional medical decision-making**.
The project is articulated around **3 randomized clinical trials**. These use-cases allow to examinate the complexity of the applicable legal and ethical framework for this type of research.

In this poster

We identify how the project's activities **interrogates both legal and ethical values of the EU** which refers to different fundamental rights protected under the Charter of Fundamental Rights of the EU **and regulatory framework applicable to a European project**.

The 3 clinical trials in HT-Advance

HT-ENDO
Aims to determine the diagnostic performance of a new diagnostic biomarker developed through machine learning

HT-PREDICT
Aims to identify a biomarker predicting the response and side effects to hypertensive treatment

HT-TREAT
Aims to establish performance of MOMICS signatures as treatment response prediction tool in clinical hypertension

Which are the rights protected by the Charter of Fundamental Rights of the EU addressed in HT-Advance ?

HT-Advance activities

Driven by Art.35.Health care *as the project aims to reduce mortality from hypertension through improved medical decision-making*

Personal data processing

Art.1 HUMAN DIGNITY: inalienable right underpining all fundamental rights.

The development and use of AI driven technologies is likely to broadly affect it.

Therefore, it should be considered how to practice **informed consent**, to ensure **transparency** of the processing methods and of the results to be used by health professionals.

Involvement of human beings

Art.7.Privacy. Protection of private life through protection of personal data due to the **existing high risk of data re-identification** ; specific protection provided for by the **GDPR.**
Art.8.Data protection. At the **core of fundamental rights** when it comes to AI and sensitive (health/genetic) personal data processing

⇒ Principles of the GDPR: **mandatory legal basis for lawful processing, data minimisation, quality** and **protection** by design and default (safeguarding data protection at early stage of the design of the AIS and throughout the processing **with adapted organisational and technical measures** like pseudonymisation or anonymisation).

Art.20.Equality. Directly related to the **principle of non-discrimination**, leading to a **risk of unfair treatment** of patients.
Art.21. Non-discrimination. Processing sensitive data (health/genomic) may lead to discrimination among patients in clinical trials due to considered features/methodology or exacerbate existing discrimination.

⇒ Requires to **minimise/prevent potential bias in AI model**.

Art.47.Access to justice. Right to effective judicial protection including then the **question of responsibility**

⇒ **EC proposal of AI liability directive** of 28 sept 2022 in case of **harm caused by AIS** => Harmonised legal framework for victims, specific to damages caused by AIS, **presumption of causality.**

⇒ EC proposal for an amendment of the **directive on liability for defective products** as AIS-enabled medical devices are considered high risked.

AI model and device development

The design and development of AI systems should consider the patients' fundamental rights through a **multidisciplinary risk-based approach** and **human-centered governance** as misuse of AI could affect several general rights at the same time which are specified and reinforced by several EU acts.

Consideration of fundamental rights within the legal framework applicable to HT-Advance

AI Act
Purpose: **Harmonised framework** for high-risk AI systems which shall comply with **human rights by design**
Relevant rules:
- **Art.6(1)(a)** classifies **AIS being Medical Devices or Software as high-risk** with regard to potential adverse impacts on health, safety or fundamental rights ;
- **Art 9(2)(a)** requires for providers the identification and analysis of AIS risks **during its whole lifecycle ;**
- **Art 13** requires transparency from providers regarding **information** related to potential risks on fundamental rights ;
- **Art 29 requires information from deployers** to providers regarding **breaches to fundamental rights**
- **Art 27 requires deployers to perform a Fundamental Rights Impact Assessment**

GDPR
Purpose: Deals with **privacy and data protection by design**
Relevant rules:
- **Art 35: Data Protection Impact Assessment** as currently carried out in HT-Advance
- **Art 5:** core of data protection principles

⇒ lawfulness, fairness, transparency, data minimisation, integrity and confidentiality.
- **Chap.V** on data transfers

In vitro Diagnostic Devices Regulation
Purpose:
Reaffirmation of the obligation to respect fundamental rights
Relevant rules:
Recital 68 (ref to art 8) + recital 89 (ref to **dignity, integrity, protection of personal data**)

Clinical Trials Regulation
Purpose:
Reaffirmation of the obligation to respect fundamental rights
Relevant rules:
- Recital 27, 44, 83 ;
- Notions of **consent, protection of personal data,** and **dignity** are protected

- Additional rules for AI systems in AI act and classification of MD issued from IVDR
- Purpose: CE mark

Need to consider ethical standards in HT-Advance clinical trials

- ***Ethics guidelines for trustworthy AI-*** High-Level Expert Group on Artificial Intelligence (8 april 2019)
- ***Building Trust in Human Centric Artificial Intelligence***, EC communication (8 april 2019)
- ***Ethics By Design and Ethics of Use Approaches for Artificial Intelligence***, EC (25 november 2021)
- **Assessment List for Trustworthy AI**, HLEG, 17 july 2020)
- ***Recommendation on the Ethics of Artificial Intelligence*****,** UNESCO (23 nov.2023)

Conclusion

- **European values are integrated in HT-Advance clinical trials** through the redaction of the **DPIA** (in progress) and **research protocols** by ensuring that the design and development of **the AI-MD is legally and ethically compliant**, for optimum patient protection in particular regarding fundamental rights.
- The regime applicable to this project is complex because of the **significant legal and ethical intersection** regarding AI-MD.

⇒ **Question to be addressed in HT-Advance:** How can these texts be implemented to provide the best possible ethical and legal support for scientific research?
⇒ **Authorities' guidance on regulatory and ethical governance of complex research projects is needed**.