This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 8[illegible]".

REVERT FINAL EVENT

10 December 2024

"Spazio Europa", via IV Novembre, 149, Rome, Italy

L'evento avrà luogo presso Spazio Europa, gestito dall'Ufficio del Parlamento europeo in Italia e dalla Rappresentanza in Italia della Commissione europea

REVERT

Final Meeting

2024

Pioneering Advances in Personalized Cancer Therapy

Round Table 1: Regulatory Aspects and Clinical Validation

Fiorella Guadagni
IRCCS San Raffaele
REVERT Coordinator

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Challenges faced by the REVERT Project Compliance to:

GDPR
2017/745 MDR

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EU publications

Ethics guidelines for trustworthy AI

The aim of the Guidelines is to promote Trustworthy AI. Trustworthy AI has three components, which should be met throughout the system's entire life cycle: (1) it should be lawful, complying with all applicable laws and regulations (2) it should be ethical, ensuring adherence to ethical principles and values and (3) it should be robust, both from a technical and social perspective since, even with good intentions, AI systems can cause unintentional harm. Each component in itself is necessary but not sufficient for the achievement of Trustworthy AI. Ideally, all three components work in harmony and overlap in their operation. If, in practice, tensions arise between these components, society should endeavour to align them.

Published on April 2019, Corporate author(s): Directorate-General for Communications Networks, Content and Technology (European Commission)

5.5.2017 | EN | Official Journal of the European Union | L 117/1

REGULATION (EU) 2017/745 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 5 April 2017

on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC

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AI-Technologies Challenges

Report from the World Health Organization , "*Ethics and governance of artificial intelligence for health*", 2021
To limit the risks and maximize the opportunities intrinsic to the use of AI for health, WHO provides the following principles as the basis for AI regulation and governance**.**

Six principles to ensure AI works for the public interest in all countries

1. **Protecting human autonomy**: In the context of health care, this means that **humans should remain in control of health-care systems and medical decisions;** ….

2. **Promoting human well-being and safety and the public interest.**

3. **Ensuring transparency, explainability and intelligibility.**

4. **Fostering responsibility and accountability.**

5. **Ensuring inclusiveness and equity.**

6. **Promoting AI that is responsive and sustainable.**

*These principles will guide future WHO work to support efforts to ensure that the full potential of AI for healthcare and public health will be used for the benefits of all***.**

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How these challenges have been approached in the REVERT Project

The REVERT paves the way **for building AI prediction systems** in the field of medicine, in general, and cancer treatment, in particular. Indeed, one of the significant obstacles to the wide adoption of these systems **is their opacity, which undermines clinicians' trust in AI.** **Explainable AI** is the current approach to gaining the trust of clinicians, and it is extremely promising.

Explainable AI to gaining the trust of clinicians in the use of AI algorithms for a personalised therapeutic intervention

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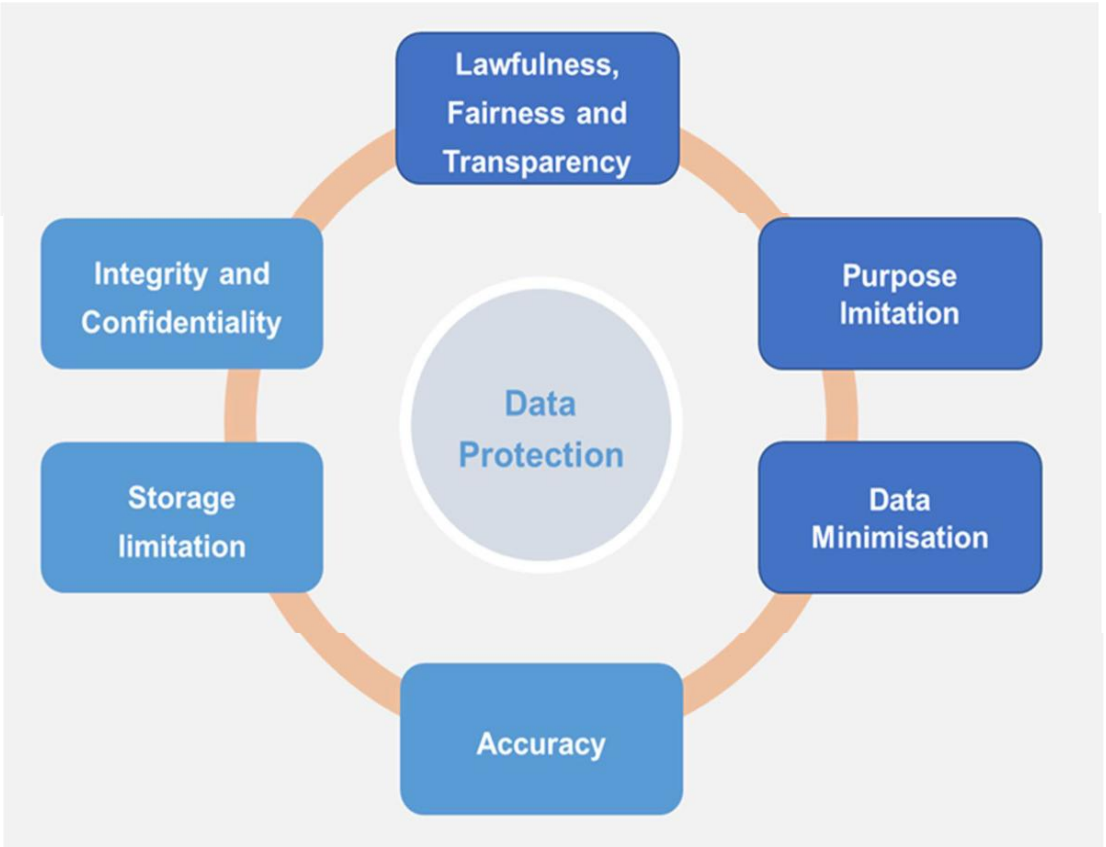
In order to address the issues relating to data protection expressively with concern to the REVERT project, **the following principles laid down in the GDPR were taken into account**

I. Pursuant to art. 5 of the GDPR, the principles governing the processing of personal data are:



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REVERT APPROACH

FIRST: RISK ASSESSMENT AND MITIGATION PLAN

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In the initial phase, a **risk assessment and mitigation plan** has been drafted, pinpointing various potential risks associated with software implementation and data management, which will be integrated into the **DMP**.

Any risks pertaining to the main IT and legal aspects will be managed as outlined in the Figure below represented i.e., will be identified, analysed, evaluated and mitigated in the best possible way as detailed in the Risk Management Plan:

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DATA MANAGEMENT PLAN

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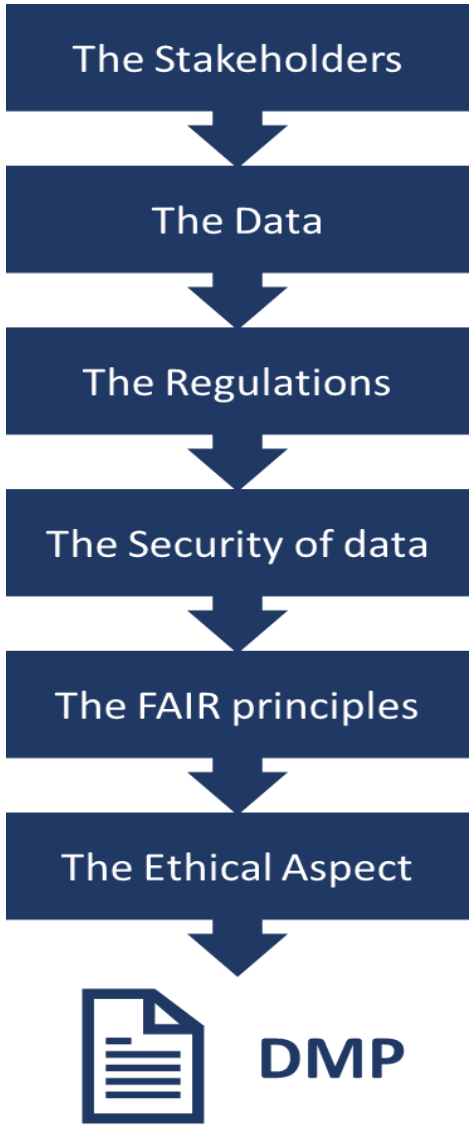

The main aspects that a DMP should consider

The Stakeholders who participate in the project and are involved in providing, manipulating or using the data

The Data that will have to be managed during the project, also considering the restrictions imposed for some types of data

The Regulations in the countries where the stakeholders operate and in those where the data will be shared

Data security, obtained through both technical and organizational measures

The FAIR Principles and their application to the project

The Ethical Aspects to consider in the execution of project activities and in the use of data

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CHOICE OF THE SERVER

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One of the first issues addressed by the REVERT project was the **choice of the server/DB** management model and the data contained in them.
The need to have machines compliant with:

1. the security requirements indicated by the GDPR and necessary for the nature of the data processed,
2. to guarantee adequate levels of security,
3. to keep management costs low
4. and to be able to make use of some features and tools,
5. have in fact shifted focus from in-house management to a cloud solution.
6. In this scenario, Amazon (AWS) was chosen among the different cloud services for multiple reasons.

AWS is Amazon's cloud platform and is perhaps the most complete and most widely used in the world, offering more than 175 comprehensive data center services globally.
AWS offers significantly more services and features within the services themselves than any other cloud provider, including computing power, storage and database infrastructures, machine learning and artificial intelligence options, data lakes, analytics and interfacing with the Internet of Things.

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PROCEDURAL APPROACH FOR DATA SHARING AND FOR BUILDING A SECURE REVERT DB

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The REVERT project aims to build a database (RDB) that collects the clinical data of patients from different biobanks located in several European countries.

Since the data of different biobanks can vary with respect to the measurement units that parameters are stored with or to the formulae with which secondary data are calculated, the **data have to be harmonized upon import** to ensure that the corresponding entries of all the records have the same meaning across all institutions that provide the samples the RDB will be built upon.

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All the processing will be executed exclusively on an AWS platform.

The only data that can be downloaded to external IT infrastructures will be the final results of the processed data.

This workflow ensures to control and trace when and by whom data have been accessed and exported. All the risks concerning IT security will be mitigated by using an Amazon cloud platform, **certified** according to GDPR and characterized by **high-level security standards**.

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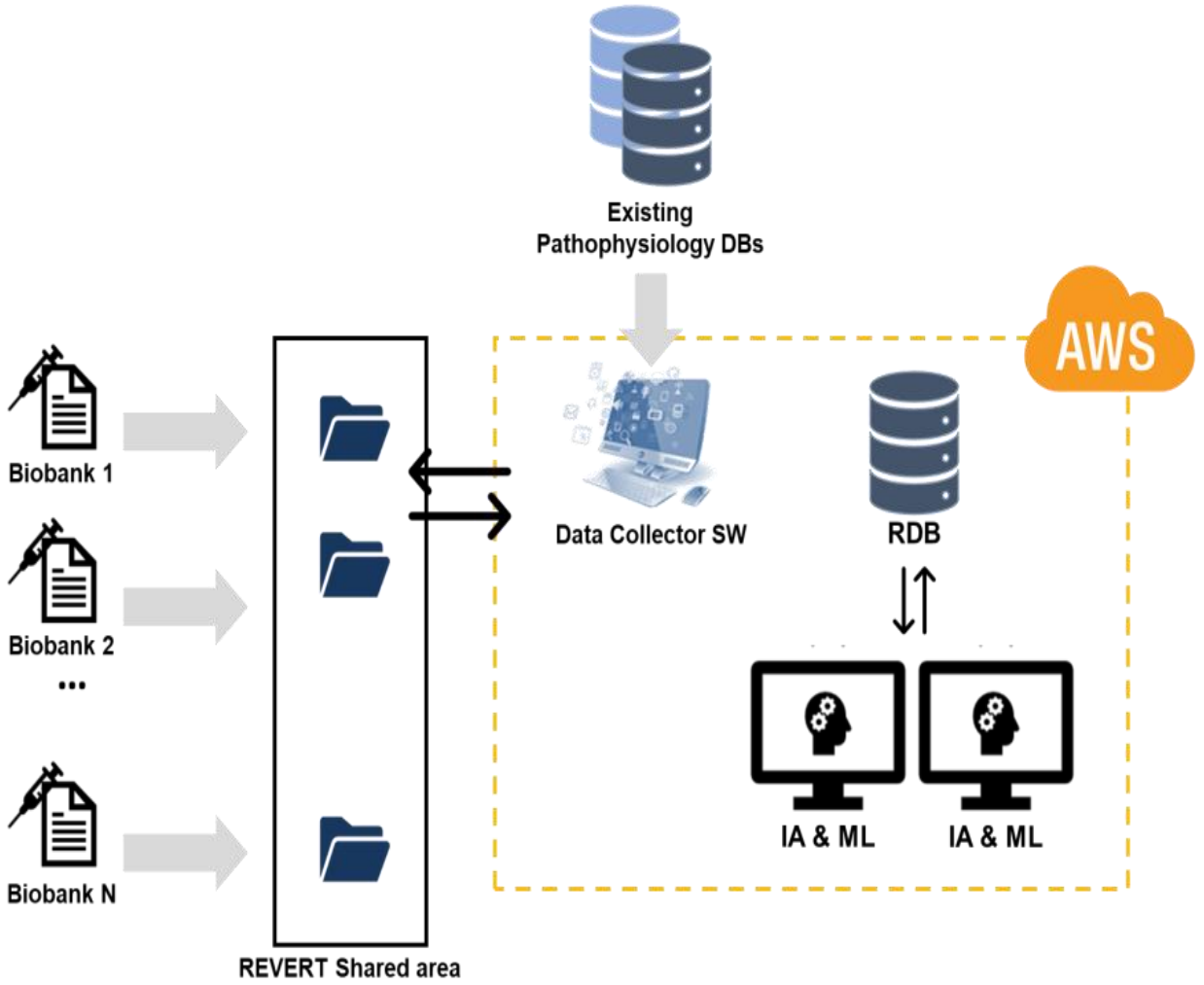
The REVERT architecture



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SECURITY MEASURES

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Security measures implemented in the REVERT project

One of the most important activities has been the risk assessment within REVERT and the definition of strategies to avoid, mitigate or remove risks.

The approach used in the REVERT project has been that of **risk assessment**, evaluated according to quality management models. As required by current regulations, all the most modern technologies has been used, based on **GDPR compliance and ISO 27001: 2013 certification**.

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ACTIONS PLANNED IN THE REVERT PROJECT

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To do this, the following activities have been planned during all the project execution:

1. **Constant vulnerability assessment**,
2. **Ensuring privacy by design at every stage** of the project
3. **Application of international security standards**
4. **Use of encryption formats** of the exchanged input and output flows
5. **Calculation of the hash of records** (exchanged, stored) to ensure that there is no corruption
6. **Mapping and risk analysis of the entire data use** cycle

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FAIR PRINCIPLES

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The FAIR principles

The nature of the data and the consent signed by the patients did not strictly allow the data to be made public.

The REVERT project, in relation to the question of keeping data open, applies the principle "as open as possible, as closed as necessary".

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DATA PROTECTION IMPACT ASSESSMENT

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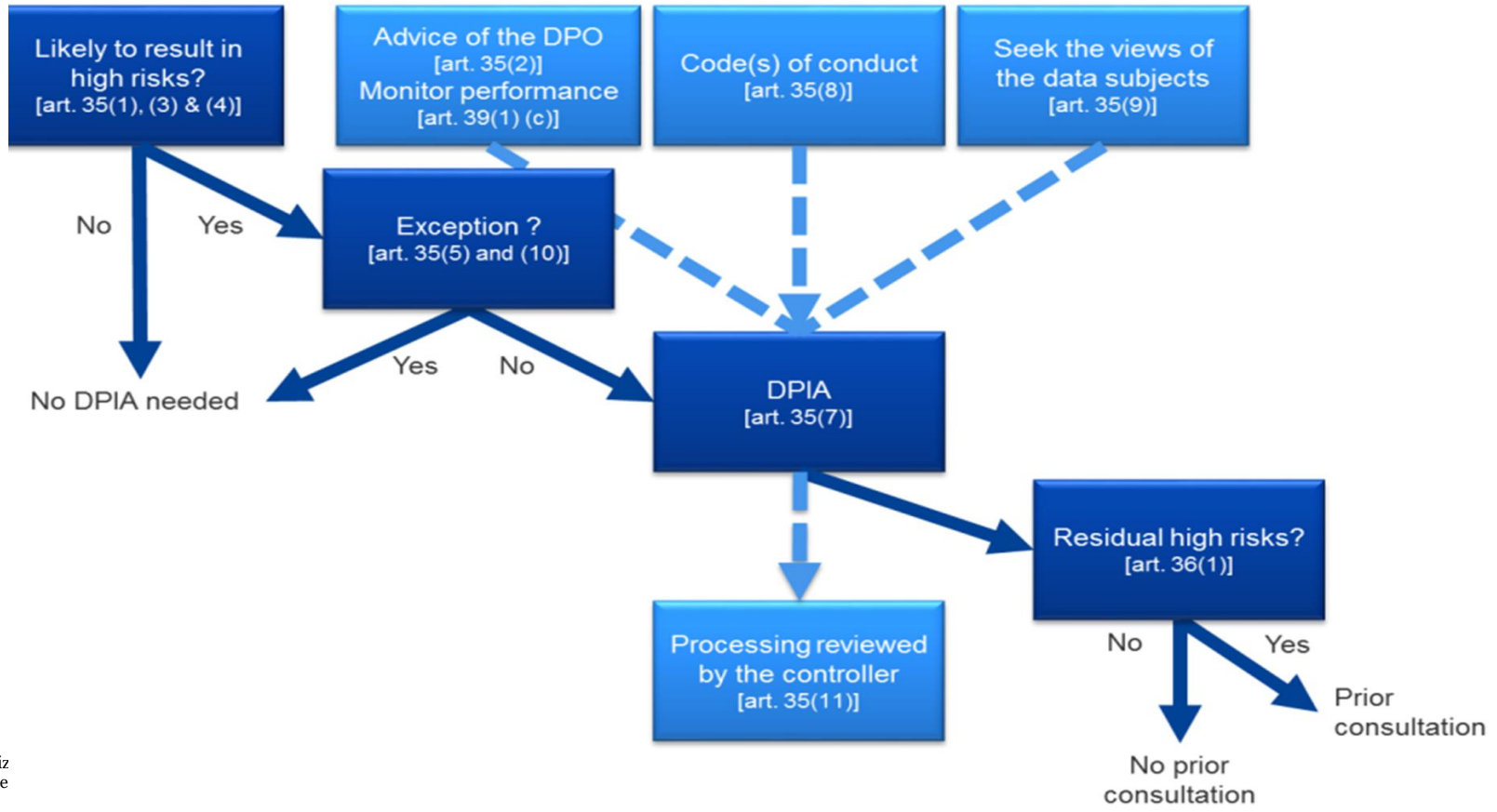
For the conduct of the DPIA, the Data Protection Officer of the Coordinator San Raffaele was consulted who –after several meetings with Partners– expressed a favourable opinion on the correctness of the conduct of the DPIA. The methodology used for the DPIA is graphically represented in the figure below.



This Horiz agree

JOINT CONTROLLER AGREEMENT

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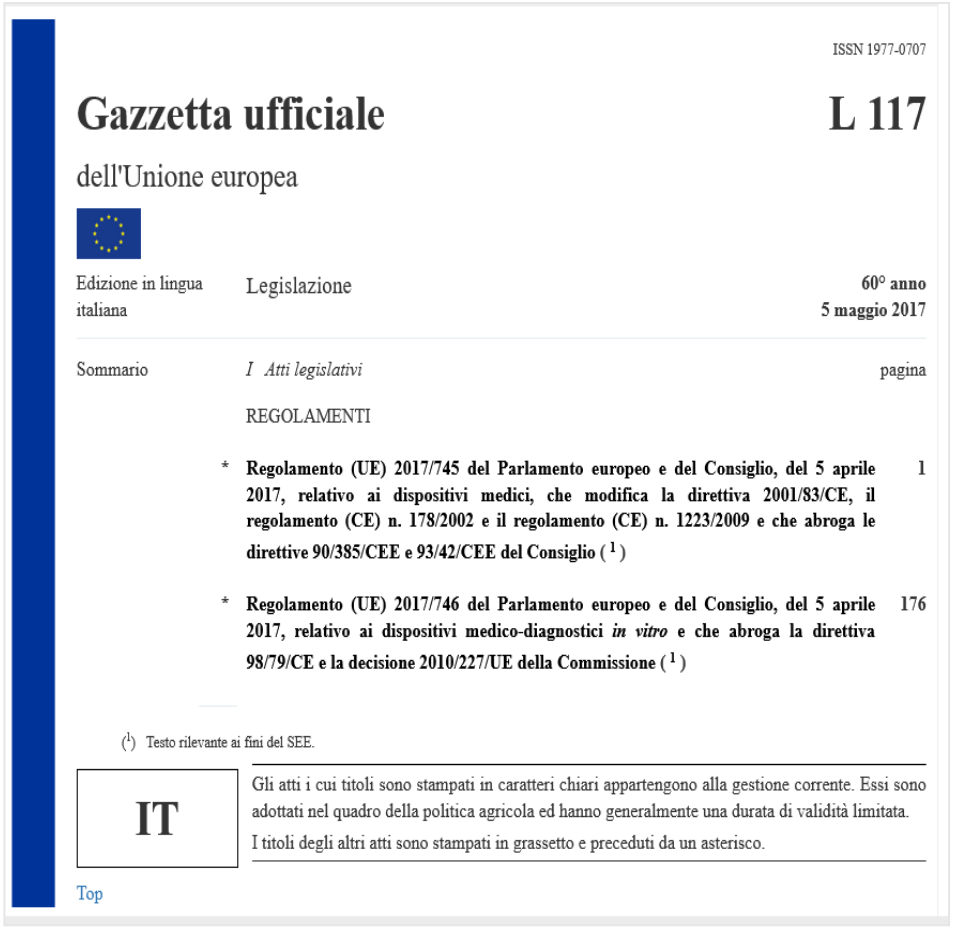

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Edizione in lingua italiana | Legislazione | 60° anno 5 maggio 2017

Sommario | *I Atti legislativi* | pagina

REGOLAMENTI

([1]) Testo rilevante ai fini del SEE.

IT

Gli atti i cui titoli sono stampati in caratteri chiari appartengono alla gestione corrente. Essi sono adottati nel quadro della politica agricola ed hanno generalmente una durata di validità limitata.

I titoli degli altri atti sono stampati in grassetto e preceduti da un asterisco.

Top

This Regulation aims to ensure the **smooth functioning of the internal market as regards medical devices**, taking as a base **a high level of protection of health for patients and users,** and taking into account the **small- and medium-sized enterprises that are active in this sector**. At the same time, this Regulation sets **high standards of quality and safety** for medical devices in order to meet common safety concerns as regards such products. Both objectives are being pursued **simultaneously and are inseparably linked** whilst one not being secondary to the other.

….. placing on the market and putting into service of medical devices … thus allowing them to benefit **from the principle of free movement of goods.** As regards Article 168(4)(c) TFEU**, this Regulation sets high standards of quality and safety for medical devices by ensuring, among other things, that data generated in clinical investigations are reliable and robust and that the safety of the subjects participating in a clinical investigation is protected**

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DECRETO LEGISLATIVO 5 agosto 2022, n. 137

Disposizioni per l'adeguamento della normativa nazionale alle disposizioni del regolamento (UE) 2017/745 del Parlamento europeo e del Consiglio, del 5 aprile 2017, relativo ai dispositivi medici, che modifica la direttiva 2001/83/CE, il regolamento (CE) n. 178/2002 e il regolamento (CE) n. 1223/2009 e che abroga le direttive 90/385/CEE e 93/42/CEE del Consiglio, nonche' per l'adeguamento alle disposizioni del regolamento (UE) 2020/561 del Parlamento europeo e del Consiglio, del 23 aprile 2020, che modifica il regolamento (UE) 2017/745 relativo ai dispositivi medici, per quanto riguarda le date di applicazione di alcune delle sue disposizioni ai sensi dell'articolo 15 della legge 22 aprile 2021, n. 53. (22G00145) (GU Serie Generale n.214 del 13-09-2022)

note: Entrata in vigore del provvedimento: 28/09/2022

L'Autorità Competente sulle indagini cliniche dei dispositivi medici è il Ministero della salute

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Art. 16 Indagini cliniche

1. Nessuna indagine clinica può essere avviata senza l'invio di idonea comunicazione al Ministero della salute e senza che siano state realizzate le condizioni previste per l'avvio dell'indagine.
2. Con decreto del Ministro della salute sono stabilite le **modalità** amministrative di pertinenza nazionale per la presentazione **della domanda di indagine clinica per i dispositivi non recanti la marcatura CE e per quelli recanti la marcatura CE** di cui all'articolo 74, paragrafo 2, del regolamento, prevedendo che nella documentazione ad essa allegata **sia ricompreso il parere favorevole espresso dal comitato etico competente**. ……

Per i dispositivi appartenenti alla classe III e per quelli invasivi appartenenti alle classi IIa oppure IIb, i richiedenti potranno iniziare le pertinenti indagini **cliniche solo dopo avere ottenuto** la relativa autorizzazione ministeriale **da rilasciarsi entro quarantacinque giorni dalla data di convalida della domanda di autorizzazione**, fatta salva la possibilità di estendere tale periodo di ulteriori venti giorni ai fini della eventuale consultazione di esperti.

Per i dispositivi oggetto di indagine della classe I o **per i dispositivi non invasivi delle classi IIa** e IIb, i richiedenti **possono iniziare l'indagine clinica trenta giorni dopo la data di convalida della domanda**, a meno che il Ministero della salute non notifichi entro tale termine che la domanda e' stata respinta per ragioni di tutela della salute pubblica, della sicurezza o della salute dei soggetti e degli utilizzatori, **purché il comitato etico competente abbia reso un parere favorevole in relazione all'indagine clinica**.

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Il Regolamento (UE) 2017/745 sui dispositivi medici (Medical Device Regulation, MDR) è direttamente applicabile in tutti gli Stati membri dell'Unione Europea.

Tuttavia, l'attuazione pratica e la sorveglianza del mercato sono gestite dalle autorità nazionali competenti di ciascuno Stato membro.

Queste autorità sono responsabili dell'applicazione del regolamento, della vigilanza sui dispositivi medici e della supervisione degli organismi notificati

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Autorità competenti in alcuni Stati membri dell'UE

✓**Italia**: Il Ministero della Salute
✓**Germania**: L'Istituto Federale per i Farmaci e i Dispositivi Medici (Bundes institut für Arzneimittel und Medizin produkte, BfArM)
✓**Francia**: L'Agenzia Nazionale per la Sicurezza dei Medicinali e dei Prodotti Sanitari (Agence Nationale de Sécurité du Médicament et des Produits de Santé, ANSM)
✓**Spagna**: L'Agenzia Spagnola dei Medicinali e dei Prodotti Sanitari (Agencia Española de Medicamentos y Productos Sanitarios, AEMPS)
✓**Paesi Bassi**: L'Ispettorato per la Sanità e la Gioventù (Inspectie Gezondheidszorg en Jeugd, IGJ)

https://health.ec.europa.eu/publications/factsheet-healthcare-professionals-and-healthcare-institutions_it

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