

Towards EHDS2 interoperability framework: An interactive EIF-based standards compliance toolkit for AI-driven projects

Rada Hussein, Amelie Gyrard, Somayeh Abedian, Philip Gribbon, Sara Alabart
Martínez

Submitted to: Journal of Medical Internet Research
on: December 09, 2024

Disclaimer: © The authors. All rights reserved. This is a privileged document currently under peer-review/community review. Authors have provided JMIR Publications with an exclusive license to publish this preprint on its website for review purposes only. While the final peer-reviewed paper may be licensed under a CC BY license on publication, at this stage authors and publisher expressly prohibit redistribution of this draft paper other than for review purposes.

Table of Contents

Original Manuscript..... 5

Supplementary Files..... 32

Figures 33

Figure 1..... 34

Figure 2..... 35

Figure 3..... 36

Figure 4..... 37

Figure 5..... 38

Figure 6..... 39

Figure 7..... 40

Figure 8..... 41

TOC/Feature image for homepages 42

TOC/Feature image for homepage 0..... 43

Towards EHDS2 interoperability framework: An interactive EIF-based standards compliance toolkit for AI-driven projects

Rada Hussein^{1*} PhD; Amelie Gyrard^{2*} PhD; Somayeh Abedian¹ PhD; Philip Gribbon^{3,4} PhD; Sara Alabart Martínez⁵ PhD

¹ Ludwig Boltzmann Institute for Digital Health and Prevention Salzburg AT

² Trialog Paris FR

³ Fraunhofer Institute for Translational Medicine and Pharmacology Frankfurt am Main DE

⁴ Fraunhofer Cluster of Excellence for Immune-Mediated Diseases (CIMD) Frankfurt DE

⁵ TIC Salut Social Foundation Barcelona ES

*these authors contributed equally

Corresponding Author:

Rada Hussein PhD

Ludwig Boltzmann Institute for Digital Health and Prevention
Lindhofstraße 22
Salzburg
AT

Abstract

The ongoing development of European Health Data Space (EHDS) for the secondary use of data (known as EHDS2) by the HealthData@EU pilot is mainly based on the Towards the European Health Data Space (TEHDAS) Joint Action (JA) results and recommendations on standards, interoperability, and governance models. The TEHDAS JA also considers the real-world expertise of existing European data-driven projects in standards implementation, interoperability, and data governance. Nevertheless, as the EHDS regulations are still evolving, relevant standards are still being developed, which presents a key challenge for these projects.

The main objective of this work is to create an interactive toolkit to collect the lessons learned from the European projects in standards and interoperability implementation to contribute to shaping the EHDS2 interoperability framework. Furthermore, the best practices of these projects and their approaches to tackling the existing gaps in standards are valuable inputs for upcoming projects and standards organizations.

In collaboration with the EC European Standardisation Booster (HSbooster.eu) initiative, we conducted several meetings and workshops among seven data-driven projects with cancer use cases (October 2023-July 2024) to explore how the projects adopt health standards and data quality frameworks. These projects are: IDERHA, EUCAIM, ASCAPE, iHelp, Bigpicture, HealthData@EU pilot, and INCISIVE project. We first created a template for the EHDS2 interoperability framework based on the new European Interoperability Framework (EIF) to collect the projects' expertise in implementing the health standards. Finally, we investigated the available resources for creating the interactive toolkit based on the new EIF model and principles.

The interactive toolkit provides a user-friendly interface of the new EIF layers and principles. The lessons learned from the seven projects in addition to the main outputs and deliverables are mapped to the different EIF layers and principles. Moreover, the recent publications on standards development and AI Act implementation were also incorporated into the toolkit as a guiding material. The toolkit provided an interactive entry module to support current and future projects in editing and printing the project interoperability framework in alignment with the EHDS2 requirements.

The best practices in standards implementation and interoperability framework of the existing projects can play a crucial role in shaping the anticipated EHDS2 interoperability framework. The current version of the toolkit is based on the results of the seven projects and the recent publications on the AI Act implementation. Other projects can also use the toolkit to share their lessons learned and best practices using the entry modules of the toolkit. Thus, the HSbooster hosts the toolkit for broader dissemination

and feedback to enhance the toolkit. In this way, we can collaborate in harmonizing the implementation of the standards across the projects and ultimately shaping the EHDS2 interoperability framework.

(JMIR Preprints 09/12/2024:69813)

DOI: <https://doi.org/10.2196/preprints.69813>

Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?

Please make my preprint PDF available to anyone at any time (recommended).

Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users.

Only make the preprint title and abstract visible.

✓ **No, I do not wish to publish my submitted manuscript as a preprint.**

2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?

✓ **Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).**

Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain visible.

Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <http://www.jmir.org>

No. Please do not make my accepted manuscript PDF available to anyone.

Original Manuscript

Towards EHDS2 interoperability framework: An interactive EIF-based standards compliance toolkit for AI-driven projects

Rada Hussein^{1,*}, Amelie Gyrard², Somayeh Abedian¹, Philip Gribbon^{3,4}, Sara Alabart Martínez⁵

¹Ludwig Boltzmann Institute for Digital Health and Prevention, Salzburg, Austria

²Trialog, Paris, France

³Fraunhofer Institute for Translational Medicine and Pharmacology (ITMP), Hamburg, Germany

⁴Fraunhofer Cluster of Excellence for Immune-Mediated Diseases (CIMD), Frankfurt, Germany

⁵TIC Salut Social Foundation (FTSS), Barcelona, Catalonia, Spain

* Corresponding author:

Rada Hussein, PhD, FIAHSI

Ludwig Boltzmann Institute for Digital Health and Prevention

Lindhofstraße 22 , 5020 Salzburg, Austria

Tel +43 (0) 57 255 82713

Email: rada.hussein@dhp.lbg.ac.at

ORCID: <https://orcid.org/0000-0003-1257-4848>

Abstract

The successful implementation of the European Health Data Space (EHDS) for the secondary use of data (known as EHDS2) hinges on overcoming significant challenges, including the proper implementation of interoperability standards, harmonization of diverse national approaches to data governance, and the integration of rapidly evolving AI technologies. This work addresses these challenges by developing an interactive toolkit that leverages insights from seven leading cancer research projects (IDERHA, EUCAIM, ASCAPE, iHelp, Bigpicture, HealthData@EU pilot, and INCISIVE) to guide in shaping the EHDS2 interoperability framework.

Building upon the foundations laid by the TEHDAS Joint Action and the new European Interoperability Framework (EIF), the toolkit incorporates several key innovative features. Firstly, it provides interactive and user-friendly entry modules to support European projects in creating their own interoperability frameworks aligned with the evolving EHDS2 requirements technical and governance requirements. Secondly, it guides projects in navigating the complex landscape of health data standards, emphasizing the need for a balanced approach to implementing the EHDS2 recommended standards for data discoverability and sharing. Thirdly, the toolkit fosters collaboration and knowledge sharing among projects by enabling them to share their experiences and best practices in implementing standards and addressing interoperability challenges. Finally, the toolkit recognizes the dynamic nature of the EHDS2 and the evolving regulatory landscape, including the impact of AI regulations and related standards. This allows for continuous adaptation and improvement, ensuring the toolkit remains relevant and useful for future projects.

In collaboration with HSbooster.eu, the toolkit will be disseminated to a wider audience of projects and experts, facilitating broader feedback and continuous improvement. This collaborative approach will foster harmonized standards implementation across projects that ultimately contribute to the development of a common EHDS2 interoperability framework.

Keywords:

Artificial Intelligence, European health data space, European interoperability framework healthcare standards.



Introduction

During the past years, the European Commission (EC) has aimed to unlock the potential of health data for providing better healthcare services and advancing research and innovation while upholding ethical and privacy principles. In 2020, the European strategy for data [1] proposed to establish common European data spaces to govern access and reuse of data from various sectors across the European Union (EU), starting with the European Health Data Space (EHDS) [2] as the first common data space across Europe. The EHDS will mainly empower individuals to take control of their health data across Europe (primary use of data, known as EHDS1), in addition to reusing the health data in research, innovation regulatory activities, and policy-making (secondary use of data, known as EHDS2) [3].

The EHDS regulation was proposed on 3 May 2022, adopted by the European Parliament on 24 April 2024 [4], and is expected to enter into force by Autumn 2024. The EHDS2 obligations will be applied around 2028, except for some data categories, such as clinical trial data and human genetic data, that are expected to be implemented by 2030.

Meanwhile, the EC is establishing the main infrastructure of the EHDS, namely MyHealth@EU (for EHDS1), based on the lessons learned from the epSOS project cross-border healthcare services, and building on the xShare initiative for data portability), and HealthData@EU pilot (for EHDS2) [2,3]. Moreover, the Towards the European Health Data Space (TEHDAS) Joint Action (JA) [5] was launched to prepare the ground for the harmonized implementation of EHDS2 in the EU member states by developing the guidelines and technical specifications for smooth access to health data.

The EHDS governance is built on the EU legal frameworks (see Figure 1), mainly, the General Data Protection Regulation (GDPR), the Data Governance Act (DGA), the Medical Devices Regulation (MDR), In Vitro Diagnostics Regulation (IVDR), the Data Act, and the Network & Information

Security (NIS2) Directive [2,6,7], in addition to the recently adopted AI Act that shapes the European approach to building trustworthy AI [8]. The EHDS complements these regulations and will provide additional tailor-made rules when needed.

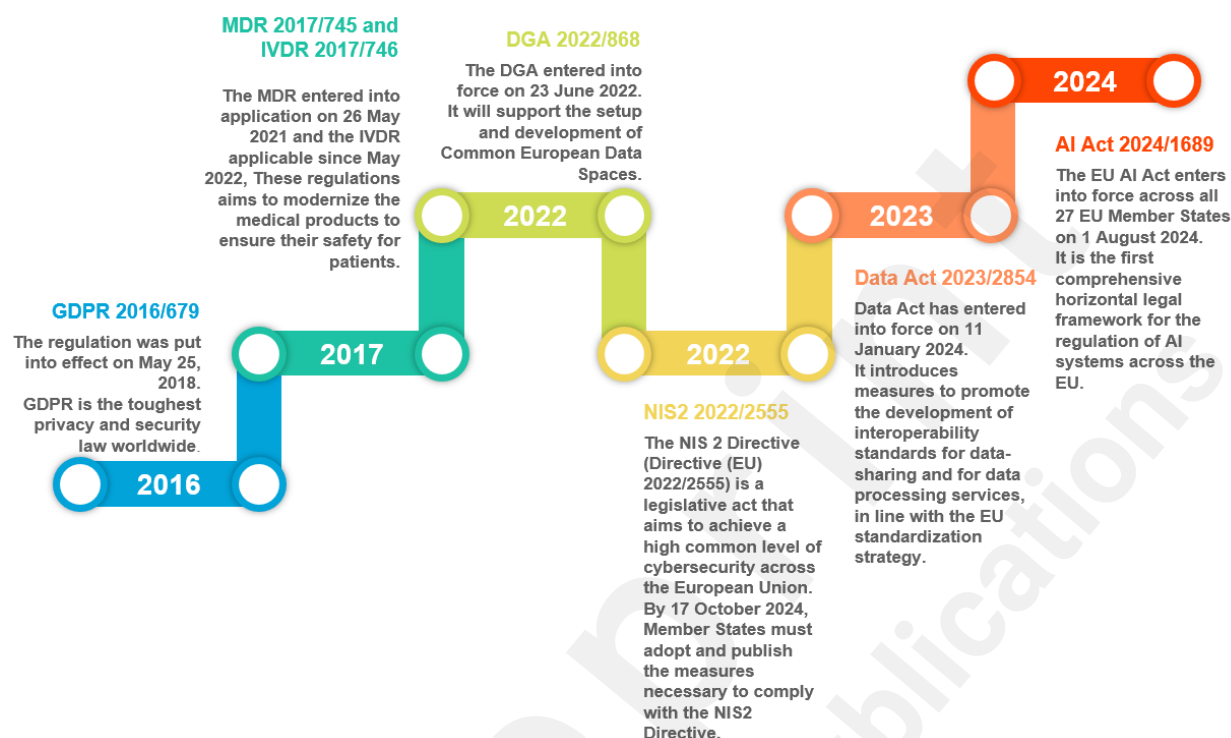


Figure 1. Timeline of the EU data regulations and frameworks shaping the EHDS

Recently, the HealthData@EU Pilot identified the common elements for health data access and data use within the legal frameworks of the participating nodes [9], namely BBMRI (European Research Infrastructure), Health Data Lab (Germany), Danish Health Data Authority (Denmark), Findata (Finland), Health Data Hub (France), Sciensano (Belgium), Norwegian Directorate of eHealth (Norway) and Croatian Institute of Public Health (Croatia). This work aimed to harmonize legal and ethical data access procedures, security requirements and GDPR citizen access rights compliance for cross-border use of data. The performed analysis reflected that nodes vary to a great extent regarding the scope of available data, the legal basis for making the data available and accessible, and responding to data misuse. There are also major differences in the degree of centralization of the decision on data access.

To harmonize the EHDS implementation across the member states, the EHDS established a new independent advisory and regulatory body, called the EHDS Board, that facilitates the exchange of information and cooperation among member states and with the EC [6], such as: coordinating the practices among Health Data Access Bodies (HDABs) in member states, exchanging best practices with the EC to support the legislation, and sharing information on EHDS2 risks and incidents.

The EC rolling plan for AI standardization (2024) highlighted the ongoing policy, legislation, ethical, and technical standardization activities [10]. The European Committee for Electrotechnical Standardization (CEN-CENELEC) created a Joint Technical Committee (JTC 21) to address AI standardization in Europe, applying both a bottom-up approach (similar to ISO/International Electrotechnical Commission (IEC) JTC 1 Subcommittees (SC) 42 “ISO/IEC JTC 1/SC 42 Artificial Intelligence”), and a top-down approach concentrating on a long-term plan for European standardization and future AI regulation. Notably, the SC 42 published standards [11] on i) Big data overview, vocabulary, reference architecture, and ii) AI covering bias in AI systems and AI-aided decision making, overview of trustworthiness in AI, assessment of the robustness of neural networks, use cases, overview of computational approaches for AI systems. The different workgroups of the SC 42 are still developing the standards on i) foundational AI standards, ii) big data ecosystem, and iii) AI trustworthiness.

The EC also established the AI watch as a hub for the Joint Research Centre’s scientific research on AI [12]. In 2023, the AI Watch published a report on the state of the art of AI's current and near-future applications in medicine, healthcare, and well-being [13]. At the implementation level, the AI for Health Imaging (AI4HI) [14] project network was launched to develop cancer imaging data repositories and AI solutions based on medical imaging to improve clinical practice. The involved projects are PRIMAGE, CHAIMELEON, EuCanImage, INCISIVE, ProCAncer-I, and RadioVal.

On the other hand, the EC adopted the new European Interoperability Framework (EIF) in 2017 [15]

to connect public administrations, businesses, and citizens across Europe [16]. The EIF conceptual model comprises four levels of interoperability namely, legal, organizational, semantic, and technical interoperability, associated with the underlying 12 principles and 47 recommendations for proper implementation. The eHealth Network refined the EIF for the eHealth domain into six layers in the Refinement of the eHealth European Interoperability Framework (ReEIF) [17]. In 2023, the INCISIVE project [18] provided its interoperability framework based on the ReEIF as recommended input for the anticipated interoperability framework for the EHDS [19]. Figure 2 depicts the four layers of the EIF and its interlinking with the ReEIF six layers and the recommended five overlapping layers by the INCISIVE project.

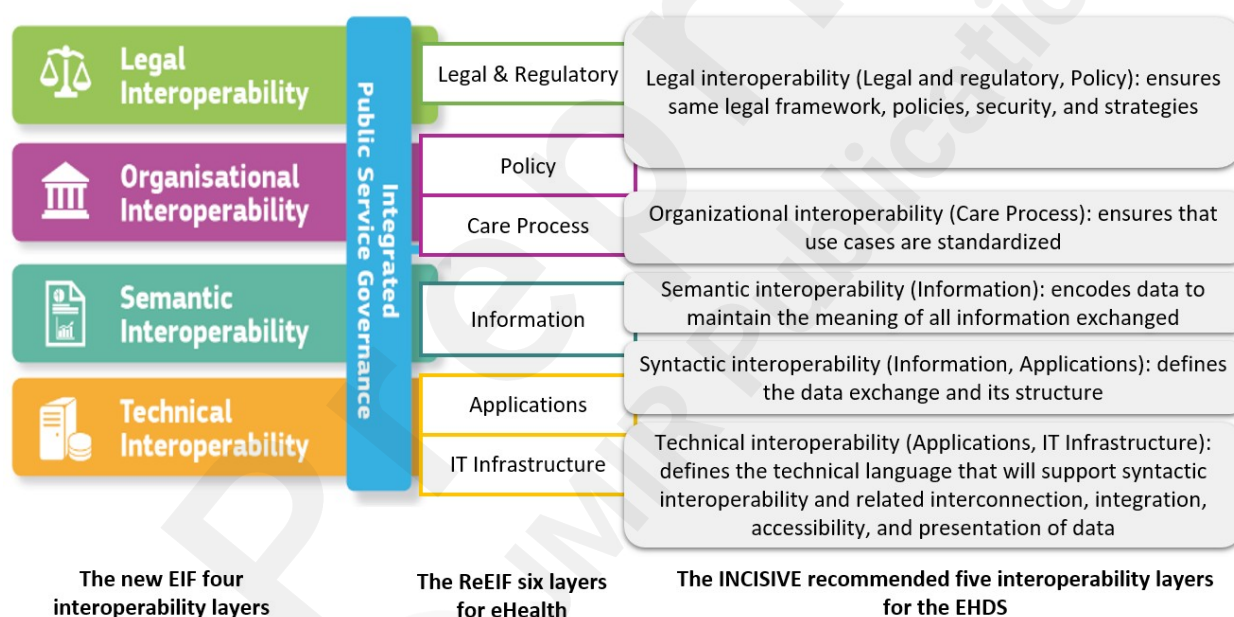


Figure 2. The interoperability layers of the EIF [15], ReEIF [17], the INCISIVE project [19]

Standards and interoperability in the European AI-driven projects

Interoperability is the cornerstone of digital medicine, especially in the AI era, which necessitates the availability of various high-quality datasets [20]. The lack of proper interoperability implementation hinders AI implementation in the real-world, as highlighted by the recent study published by the Scientific Foresight Unit of the European Parliamentary Research Service in 2022 [21]. At the

industry level, MedTech Europe and COCIR partnered to present a medical technology industry perspective on the standards, levels of interoperability, standards, profiles, and specifications relevant to digital health [22]. Furthermore, recent studies addressed the need for an interoperability framework for the EHDS that utilizes the EIF for managing specifications for interoperability [23-27] while considering the other aspects of data security, privacy, governance, and quality. The proposed interoperability framework should also be based on approved international interoperability standards for semantics and syntax, for example, the standards described and examined in [28-30].

In response to this challenge, we have created a synergy between AI-data projects with cancer use cases based [31] in October 2023, through the HSbooster.eu initiative for fostering standards in EU-funded projects. These current projects shape the EHDS implementation, e.g. the IDERHA , EUCAIM , HealthData@EU pilot , and other projects [31]. We started by creating a template for the EHDS2 interoperability framework based on the EIF. Then, we mapped the used standards in six projects with the created template [32]. We compared the health-standardized models, ontologies, and terminologies used in these projects and mapped their relevance to EHDS2 (see the supplementary material in [32]). We also examined the AI tools, techniques, and standards, as well as the federated data infrastructure in these projects.

In this work, we created an EHDS2 interoperability framework based on the EIF. We utilized the intensive expertise and lessons learned from the synergy projects in identifying the underlying interoperability standards and best practices in implementation. These standards cover health standards and Internet of Medical Things (IoMT) semantic interoperability [33] in the context of interoperability standards for health data, knowledge graphs-related technologies, Smart Applications REference ontology (SAREF), Data quality framework (DQF), Patient-Generated Health Data (PGHD), AI reasoning, federated approaches, security and privacy. This toolkit aims to support existing and future projects in creating their interoperability framework in compliance with EHDS2 governance and technical requirements.

Existing interoperability framework tools and guides

We investigated the interoperability tools and guides provided by EU-funded projects and international organizations during the past few years. Table 1 summarizes the key findings and compares these tools in terms of their compliance with the EIF and EHDS2 requirements [23].

The listed tools in Table 1 provide guidance on creating interoperability toolkits in general, while the TEHDAS and INCISIVE projects focus on EHDS2. The IHE integration profiles indicate how to define use cases in any project of clinical data interoperability and promote the coordinated use of established standards such as Digital Imaging and Communications in Medicine (DICOM®) and Health Level 7 (HL7®). Both IHE and eHAction tools mainly target EHDS1. All tools do not provide concrete guidance on how to select the proper standards for each EIF layer relevant to the EHDS2 recommended standards, for example, standards for data discoverability (meta-data standards), and other related aspects, including data quality, IoMT, PGHD, and others.

Table 1. Main recent guides and tools of the interoperability frameworks

Project/ International organization	Tool/Guide (Year)	Scope	EIF compliance	EHDS2 compliance
World Bank Group's Identification for Development (ID4D) Initiative [34]	ID4D Practitioner's Guide (2019)	To help practitioners design and implement identification (ID) systems that are inclusive and trusted—in accordance with the ten Principles on Identification for Sustainable Development and other international standards and good practices	Based on the EIF four layers	Not specifically for the health domain
eHAction JA [35]	Interoperability Guide (2020)	To support healthcare providers in planning and procuring standards-based interoperable solutions	Based on the Refined eHealth European Interoperability Framework (ReEIF)	Mainly for EHDS1
TEHDAS JA [28]	EHDS Semantic interoperability	Providing EHDS2 data life-cycle and	Based on the EIF	Target EHDS2

	framework (2022)	recommendations to enhance interoperability within the HealthData@EU		
INCISIVE project [19, 36]	Recommendations of interoperability standards (2023) INCISIVE HL7 FHIR Implementation Guide (2024)	To contribute to the EUCAIM interoperability framework, as input for the EHDS interoperability framework	Based on the ReEIF	For managing clinical data and medical images
World Health Organization (WHO) [37, 38]	Ethics and governance of AI for health (2021, 2024)	Recommendations for consideration by governments, technology companies, and healthcare providers to ensure the appropriate use of AI in health	Related to the legal interoperability layer of the EIF	Necessary for EHDS2
Integrating the Healthcare Enterprise (IHE) [39]	IHE Profiles for the exchange of documents in European eHealth Digital Services Infrastructure (eHDSI)	IHE defines Integration Profiles that use existing standards for system integration, providing effective interoperability and efficient workflow	Related to the organizational/technical interoperability layers of the EIF	Mainly EHDS1

Additionally, the recent guides of the WHO on regulatory considerations on AI for health [38], and the ethics and governance of artificial intelligence for health [37] can shape the legal, regulatory, and policy layer accompanying the adoption of the AI Act.

The EHDS2 Interoperability Framework Toolkit

The main concept of creating the toolkit is to incorporate the European guidelines, interoperability standards, and best practices of European projects in real-world implementation for shaping the EHDS2 interoperability framework (see Figure 3).

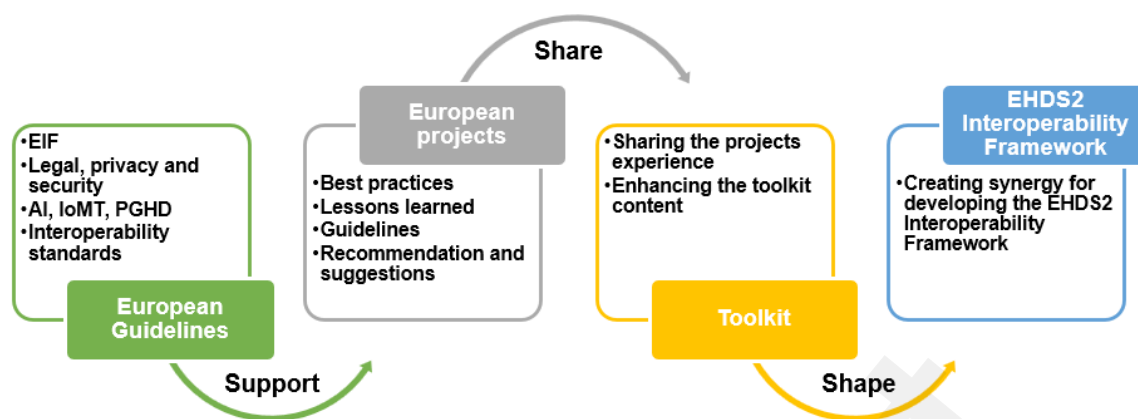


Figure 3. The EHDS2 Interoperability Framework: Concept and process of creation

Thus, the toolkit aims to provide the existing and future EU projects with an interactive and user-friendly entry interface designing, writing and printing the interoperability framework in compliance with EHDS2. It facilitates the selection of the standards for each EIF layer and provides more guidance on the proper implementation of these standards by providing best practices from other projects or international organizations (see Figure 4).

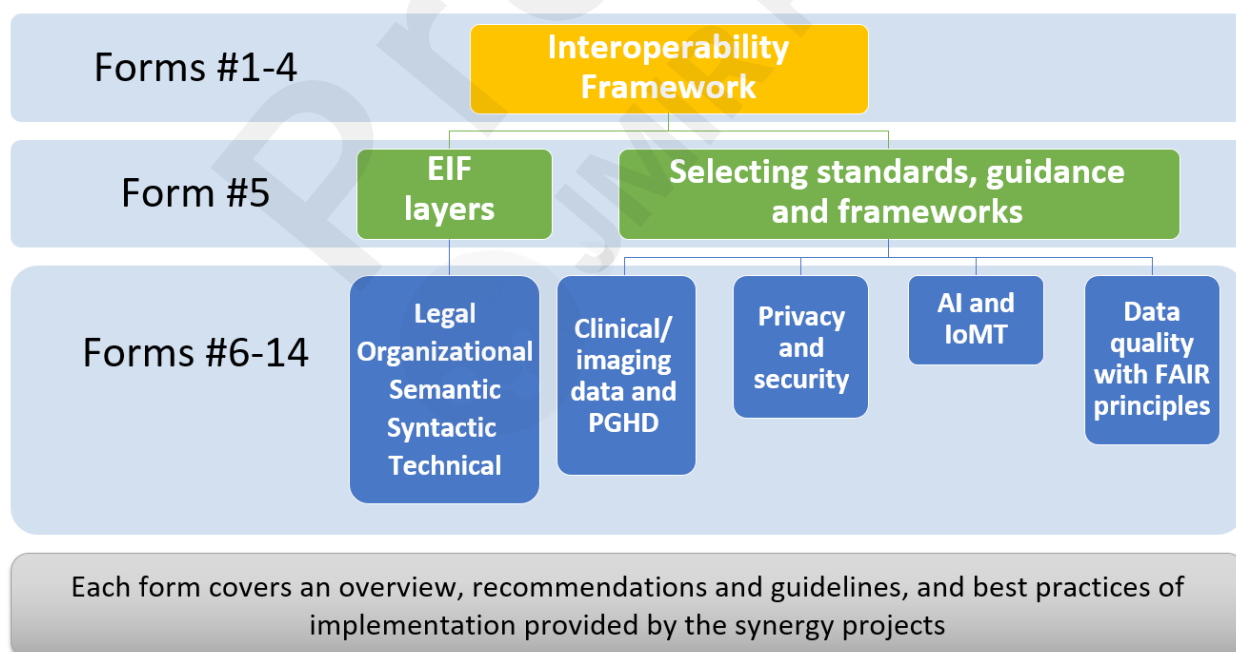


Figure 4. The toolkit of EHDS2 Interoperability Framework: Main components and sections

Standards and guidelines selection module

To design the toolkit standards and guideline modules, we first created a template for mapping the interoperability standards between TEHDAS, INCISIVE project, and the created list of implemented standards used in the HSbooster.eu synergy projects (see Table 2). We did not intend to compare the standards implemented in these projects, but rather highlight how these projects fulfill the interoperability goals and share their learned lessons. Thus, Table 2 highlights the most important standards implemented in these projects, without meaning that the other projects do not implement the proper standards.

We adopted the TEHDAS recommended categories of EHDS2 interoperability standards, as follows:

1. data discoverability: the World Wide Web Consortium (W3C) Data Catalog Vocabulary (DCAT)-Application Profile (AP), as well as the anticipated extension of DCAT-AP for health (HealthDCAT-AP) being developed by the HealthData@EU pilot,
2. enabling semantics interoperability: the Observational Medical Outcomes Partnership (OMOP)-Common Data Model (CDM)- developed by the Observational Health Data Sciences and Informatics (OHDSI), and
3. health data exchange (DICOM for imaging data and the HL7 Fast Healthcare Interoperability Resources (FHIR®) for health records).

Then, we identified the related International Organization for Standardization (ISO) standards for data quality, PGHD, AI reasoning, federated approaches, security, and privacy.

The template was refined by adding the INCISIVE standardization suggestions [19], on the following:

- Use cases and healthcare process definition
- Data exchange without losing the semantic meaning with terminologies

- Clinical documents exchange
- Medical image exchange
- Clinical data and events exchange
- Common data model to index or group data
- Standardize the database with archetypes to present data in the user interface.

Table 2. Summary of mapping the interoperability standards to the EHDS2 template based on the EIF using the TEHDAS and INCISIVE results

EIF	TEHDAS [6] Governance model of the EHDS2 of the data life-cycle	INCISIVE [19] Recommendations of interoperability standards (managing clinical data and medical images)	HSbooster.eu synergy projects [31, 32] The main health and IoMT standards*
Legal	The EHDS will build on the legal frameworks laid out by the EU regulations (see Figure 1)	Legal and security standards and Findability, Accessibility, Interoperability, and Reusability (FAIR) principles. The detailed explanation is provided in INCISIVE's Deliverable 7.3 Data donation legal framework. ISO 14971 Medical Devices Risk Management Assessment IEC 62304 Medical device software - Software life cycle processes	ISO/IEC 27001:2022- Information security, cybersecurity, and privacy protection IEEE 7000 Series- AI ethical considerations ISO/IEC 42001_2023 – AI – Management system and requirements
Organizational	Adapting the national policies in compliance with the EHDS regulations Harmonizing the EU member states health policies and the delivery of health services and medical care	The IHE integration profiles identified the care process, actors, transactions, and events.	IHE integration profiles ISO/IEC 5259-1:2024 Artificial intelligence — Data quality for analytics and machine learning (ML) ISO 9000: Data Quality Management Systems standards Data quality frameworks Data FAIRification framework
Semantic	Standards on data discoverability: (DCAT-AP) Standards that allow semantic interoperability: (OMOP-CDM)	SNOMED CT (Clinical data) LOINC (Lab data) OHDSI vocabularies	SNOMED, LOINC, ICD, RxNorm, etc. ISO 13606-Health Informatics- Electronic

			Health Record —Parts 1,2,4 (Reference model/ Archetype interchange specification / Security) ISO 11073-10101 and ISO 11073-10201- Health informatics — Device Interoperability (Point-of-care medical device communication — Domain information model/Nomenclature) ISO 23903:2021 Health informatics — Interoperability and integration reference architecture — Model and framework Standards on data discoverability: HealthDCAT-AP OMOP for enabling data analysis ISO/IEC 22989: AI concept and terminology
Syntactic	Standards that facilitate communication: FHIR (Clinical data) DICOM (Imaging data)	FHIR (All data) DICOM (Imaging data)	HL7, FHIR (Clinical data) DICOM (Imaging data) ISO/IEEE 11073-20601 and ISO/IEEE 11073-20701 (PGHD- Device Interoperability and optimized exchange protocol) EN/ISO 13606: Health Informatics- Electronic Health Record —Parts 3,5(Reference archetypes and term lists/Interface specification)
Technical	Federated peer-to-peer (P2P) network Secure processing environment	JavaScript Object Notation (JSON) or Extensible Markup Language (XML)	Semantic Web Languages such as W3C RDF, RDFS, OWL, SPARQL, JSON-LD, etc. JSON or XML (medical data) ISO accreditation for the EHDS2 secure processing environment, for example, ISO/IEC 27001 IEEE 3652.1, Guide for Architectural Framework

			and Application of Federated Machine Learning
--	--	--	---

* The complete list of standards is available in the toolkit. The table highlights the main standards used in health and IoMT

FHIR and OMOP mapping (linking the semantic layer with the syntactic layer)

Deciding between the HL7 FHIR and OMOP CDM standards can be complex, as each offers distinct advantages to different needs within healthcare systems. HL7 FHIR is particularly advantageous due to its flexibility, allowing for personalized profiles, extensions, and the use of local code systems. It enables the exchange of granular clinical data through its resource-based framework and RESTful API. This adaptability, combined with its support for incremental adoption, makes FHIR highly suitable for organizations looking to integrate real-time data exchange into their new or existing infrastructure. Additionally, its alignment with established standards like HL7 v2 and v3 reinforces its utility in a wide range of healthcare applications.

Conversely, OMOP CDM shines in facilitating research collaborations, data analysis, and evidence generation through its standardized and harmonized approach to observational healthcare data. Designed primarily to support observational research, OMOP uses OHDSI vocabularies (for this reason, OMOP is often situated as a semantic layer standard) to semantically code clinical terms instead of using CodeSystems as FHIR does, but both use the same international terminologies. While OMOP is particularly powerful for research purposes and large-scale data consumption, it may be less suitable as a messaging standard, as its implementation often requires extensions to cover all relevant healthcare domains. As such, it is more appropriate for systems focused on data analytics rather than operational data exchange.

In determining which standard to adopt, the decision depends on the intended use case. HL7 FHIR is better suited for systems that prioritize flexible, real-time clinical data exchange and customization

through extensions and local adaptations. In contrast, OMOP is ideal for those focused on research, standardized data analysis, and evidence generation across multiple healthcare organizations. Integrating both standards can offer significant benefits, promoting interoperability between clinical and research environments, and leveraging FHIR's strengths in real-time data sharing and OMOP's robust framework for data analysis and evidence generation. Fortunately, achieving interoperability between FHIR and OMOP is being carried by the HL7 and OHDSI communities. For example, the developed semantic Web-based FHIR-Ontop-OMOP system demonstrates great potential in healthcare AI applications enabled by the interoperability of FHIR and OMOP CDM [40] and the FHIR to OMOP FHIR Implementation Guide [41]. The relevant FHIR and OMOP mapping resources and implementation guide are also listed in the syntactic standards form of the toolkit to provide a proper linking of the semantic layer with the syntactic layer.

Interoperability framework entry module

We also used INCISIVE recommended methodology for the design and implementation of the interoperability framework [19], in providing the entry modules of the main components of the main interoperability framework sections: 1) needs analysis, 2) selection of data and information, 3) processes and use cases, 4) interoperability standards and implementation guides, 5) risk analysis, 6) maintenance plan, 7) specification, design and planning of interoperability phases, 8) recommendations and future actions, and 9) implementation guide publication.

Finally, we used the Fillout platform [42] in creating the interactive interface of the toolkit (see Figures 5-7). The Integration of Heterogeneous Data and Evidence towards Regulatory and HTA Acceptance (IDERHA) project in collaboration with the HSbooster.eu created the first version of the toolkit (link: <https://forms.fillout.com/t/juxLYSKmMwus>). This is a part of IDERHA's plan to align with the EHDS2 standards and interoperability requirements [43].

Interoperability Framework (Part 1/3)

What is an Interoperability Framework?
The Interoperability framework is a document that includes the analysis of the technical and functional prerequisites of a process/environment or a project, the actors and transactions of each use case involving the data use, the justification of the chosen standards, the methodology and design carried out, the interoperability risk analysis, the interoperability maintenance plan, the publication and reuse of the implementation guides and recommendations and future actions.

More info: [INCISIVE Standardization Suggestions](#)

(1) Needs Analysis
Analyze the functional, health, technical, and security needs that may change the interoperability scenario.

Needs analysis (needs and goals of the project)

Readings
van Kolfshooten H, van Oirschot J. The EU Artificial Intelligence Act (2024): Implications for healthcare. Health Policy. 2024 Nov;149:105152. doi: 10.1016/j.healthpol.2024.105152. Epub 2024 Sep 7. PMID: 39244818.

Share with us!

Please add your projects, standards, and readings

File Upload

Drag & drop a file or [browse](#)

Back

Figure 5. The interoperability toolkit: A snapshot of the entry module of the interoperability framework and how the projects can share their lessons learned

Please select the standards domain

 ☐ Legal	 ☐ Organizational	 ☐ Semantic
 ☐ Syntactic	 ☐ Technical	 ☐ Privacy
 ☐ AI and IoMT	 ☐ Quality	 ☐ FAIRness

Figure 6. The interoperability toolkit: A snapshot of the module of the standards selection

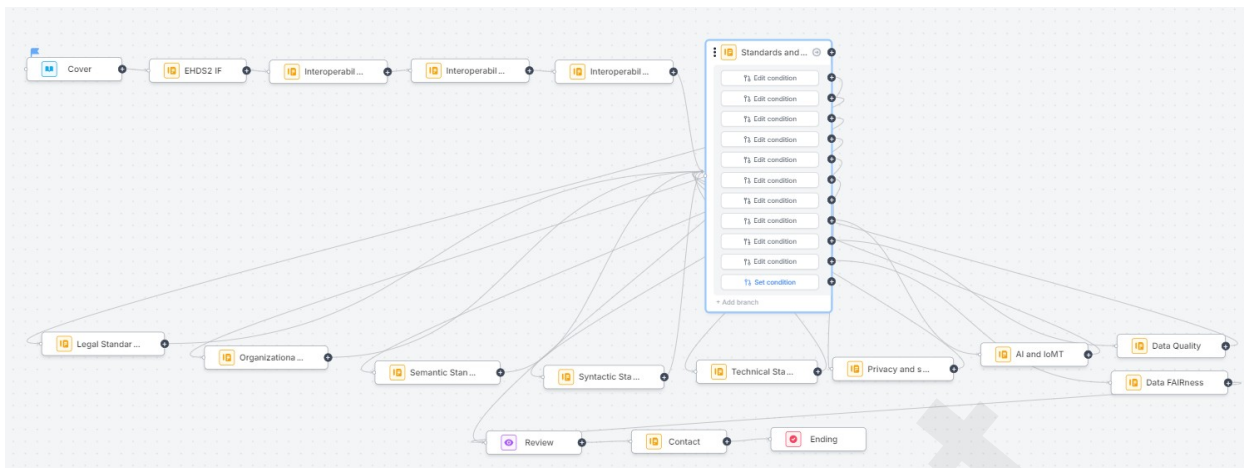


Figure 7. The logic for navigating the interoperability toolkit

Example: Identifying the AI risks and legal obligations according to the EU AI Act using the toolkit

The AI Act applies to all sectors and it does not identify certain rules for the healthcare domain. Recently, a study was published to highlight the implications of the AI Act for the healthcare sector and give a comprehensive overview of the new legal obligations for various healthcare stakeholders (technical developers, healthcare professionals, and public health authorities) [44]. We adopted this study in the toolkit as a guideline for identifying the AI risk in EU projects as a part of the risk analysis of the interoperability framework (see Figure 8).

Requirements for health-related AI systems in the EU AI Act		
	Provider obligations	Deployer obligations
Unacceptable risk	☐	☐
High-risk	☐	☐
Low-risk	☐	☐
Minimal-risk	☐	☐
General purpose	☐	☐

Reference
van Kolfschooten H, van Oirschot J. The EU Artificial Intelligence Act (2024): Implications for healthcare. *Health Policy*. 2024 Sep 7;149:105152. doi: 10.1016/j.healthpol.2024.105152. Epub ahead of print. PMID: 39244818.

Figure 8. Identifying the associated AI risk and obligations with referring to the guidance

Currently, the toolkit lists the standards and the lessons learned from synergy projects formed through the HSbooster.eu in cancer [31,32]. We also encourage other projects to share their expertise and used standards through the toolkit designated fields for input and uploading files. We enabled the Fillout settings for respondent notifications, including the link to edit submissions, to allow the respondents to revise their answers at any time. Furthermore, the automatic notification email to the respondents will contain a summary of the responses for creating the interoperability framework that can be saved or printed.

Ultimately, the toolkit can also be used at the international level for creating the EHDS2 interoperability frameworks with countries outside the European region, especially the notable

attention as an inspiring model for transatlantic collaborative health data use and AI development [45].

Conclusion and outlook

In preparation for a harmonized implementation of EHDS2, most of the funded European projects applying AI in health are planning for the proper alignment with the EHDS2 requirements in data governance and interoperability [36,43].

The described toolkit in this work will support the AI-driven project in creating the interoperability framework based on the EHDS2 governance and technical needs. We will share the toolkit with the health standards experts in TEHDAS JA and the HealthData@EU pilot to get their feedback on how to improve and maintain it. We also will share the proposed EHDS2 interoperability framework with IHE Europe to investigate the integration profiles for closing the gaps between EHDS1 and EHDS2. Moreover, we plan to conduct a workshop during the Medical Informatics Europe (MIE2025) to establish a dialogue with the health informatics community on how to utilize the toolkit as one of the inputs for the EHDS2 interoperability framework. We will also discuss the challenges of maintaining the toolkit up to date with the evolving AI standards landscape through hosting the toolkit by the HSbooster. Finally, It will be essential to assess the impact of using the toolkit to ensure that it meets its goal, and delivers the expected benefits to the health data ecosystem. This will also be accompanied by conducting a thorough review of the EHDS2 interoperability achievements and challenges across the member states driven by the real-world implementation of the EHDS.

Contributors

Conceptualization: RH, AG Methodology: SAM, SA, Writing - original draft: RH, AG, Writing - review & editing: SAM, PG. All authors provided expertise associated with their EU project, critically reviewed the manuscript and the toolkit, and made additions and edits to reach the final submitted and approved version.

Conflicts of Interest

None declared.

Abbreviations

AI: artificial intelligence

CDM: common data model

DCAT: data catalog vocabulary

DCAT-AP: DCAT Application profile for data portals in Europe

DICOM: Digital Imaging and Communications in Medicine

DQF: Data Quality Framework

EHDS: European Health Data Space

EHDS2: EHDS for secondary use of data

EIF: European Interoperability Framework

FAIR: findability, accessibility, interoperability, and reusability

FHIR: fast healthcare interoperability resource

EU: European Union

GDPR: general data protection regulation

IEC: international electrotechnical commission

IoT: Internet of things

ISO: international organization for standardization

JA: joint action

OHDSI: observational health data sciences and informatics

OMOP: observational medical outcomes partnership

PGHD: patient-generated health data

TEHDAS: Towards the European Health Data Space

Acknowledgments

Funding: A.G. declares funding from HSBOOSTER 101058391, StandICT.eu 2026 101091933. The IDERHA project is supported by the Innovative Health Initiative (IHI) Joint Undertaking (JU) under grant agreement No 101112135. The JU receives support from the European Union's Horizon Europe research and innovation programme and life science industries represented by COCIR, EFPIA / Vaccines Europe, EuropaBio and MedTech Europe. The INCISIVE project received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 952179.

References

1. Directorate-General for Communications Networks, Content and Technology. A European strategy for data | Shaping Europe's digital future [Internet]. 2024 [cited 2024 Aug 22]. Available from: <https://digital-strategy.ec.europa.eu/en/policies/strategy-data>
2. Directorate-General for Health and Food Safety. European Health Data Space - European Commission [Internet]. 2024 [cited 2024 Aug 22]. Available from: https://health.ec.europa.eu/ehealth-digital-health-and-care/european-health-data-space_en
3. Marcus JS, Martens B, Carugati C, Bucher A, Godlovitch I. The European Health Data Space [Internet]. Rochester, NY; 2022 [cited 2024 Feb 7]. Available from: <https://papers.ssrn.com/abstract=4300393>
4. Directorate-General for Communication. Commission welcomes European Parliament's adoption of the European Health Data Space and regulation on substances of human origin [Internet]. European Commission - European Commission. [cited 2024 Aug 22]. Available from: https://ec.europa.eu/commission/presscorner/detail/en/IP_24_2250
5. TEHDAS project website [Internet]. TEHDAS2 joint action. [cited 2024 Dec 2]. Available from: <https://tehdas.eu/project/>
6. TEHDAS JA. Options for governance models for the European Health Data Space [Internet]. 2023 [cited 2024 Aug 22]. Available from: <https://tehdas.eu/tehdas1/app/uploads/2023/01/tehdas-options-for-governance-models-for-the-european-health-data-space.pdf>
7. Terzis P, Santamaria Echeverria (Enrique) Oe. Interoperability and governance in the European Health Data Space regulation. *Medical Law International*. 2023 Dec;23(4):368–76.
8. Directorate-General for Communications Networks, Content and Technology. European approach to

- artificial intelligence | Shaping Europe's digital future [Internet]. 2024 [cited 2024 Aug 22]. Available from: <https://digital-strategy.ec.europa.eu/en/policies/european-approach-artificial-intelligence>
9. HealthData@EU pilot Project. HealthData@EU Pilot Identifies Common Elements for Health Data Access and Data Use within the Legal Frameworks of the Participating Nodes. 202 [cited 2025 Feb 7]. Available from: <https://ehds2pilot.eu/news/healthdataeu-pilot-identifies-common-elements-for-health-data-access-and-data-use-within-the-legal-frameworks-of-the-participating-nodes/>
 10. European Commission, European Commission Supra-national authority. Artificial Intelligence (RP2024) | Joinup [Internet]. [cited 2024 Aug 22]. Available from: <https://joinup.ec.europa.eu/collection/rolling-plan-ict-standardisation/artificial-intelligence-rp2024>
 11. ISO-IEC Joint Technical Committee. ISO/IEC JTC 1/SC 42 Artificial Intelligence [Internet]. JTC 1. [cited 2024 Aug 22]. Available from: <https://jtc1info.org/sd-2-history/jtc1-subcommittees/sc-42/>
 12. European Commission. AI Watch [Internet]. 2024 [cited 2024 Dec 9]. Available from: https://ai-watch.ec.europa.eu/index_en
 13. Joint Research Centre. Artificial intelligence for healthcare and well-being during exceptional times: A recent landscape from a European perspective [Internet]. 2023 [cited 2024 Aug 22]. Available from: <https://edupharm.pl/wp-content/uploads/2023/11/1699886368490.pdf>
 14. AI4HI | Ai for Health Imaging website [Internet]. [cited 2024 Dec 9]. Available from: <https://ai4hi.net/>
 15. European Commission website. The New European Interoperability Framework [Internet]. ISA2 - European Commission. 2017 [cited 2024 Aug 22]. Available from: https://ec.europa.eu/isa2/eif_en/
 16. Kouroubali A, Katehakis DG. The new European interoperability framework as a facilitator of digital transformation for citizen empowerment. *Journal of Biomedical Informatics*. 2019 Jun 1;94:103166.
 17. eHealth Network. Refinement of the eHealth European Interoperability Framework (ReEIF) [Internet]. 2015 [cited 2024 Aug 22]. Available from: https://health.ec.europa.eu/document/download/84839361-c768-4ad5-b7ca-e46b2123fef2_en
 18. Lazic I, Agullo F, Ausso S, Alves B, Barelle C, Berral JL, et al. The Holistic Perspective of the INCISIVE Project—Artificial Intelligence in Screening Mammography. *Applied Sciences*. 2022 Jan;12(17):8755.
 19. INCISIVE project. INCISIVE Standardization Suggestions [Internet]. 2023 Jul [cited 2024 Aug 22]. Report No.: Deliverable 3.4. Available from: https://incisive-project.eu/wp-content/uploads/2023/08/INCISIVE_D3.4_StandardizationSuggestions_v1.0_FinalVersion.pdf
 20. Lehne M, Sass J, Essenwanger A, Schepers J, Thun S. Why digital medicine depends on interoperability. *npj Digit Med*. 2019 Dec;2(1):79.
 21. European Parliamentary Research Service (EPRS) - Scientific Foresight Unit (STOA). Artificial intelligence in healthcare- Applications, risks, and ethical and societal impacts [Internet]. 2022 Jun [cited 2024 Aug 22]. Report No.: PE 729.512. Available from: [https://www.europarl.europa.eu/RegData/etudes/STUD/2022/729512/EPRS_STU\(2022\)729512_EN.pdf](https://www.europarl.europa.eu/RegData/etudes/STUD/2022/729512/EPRS_STU(2022)729512_EN.pdf)
 22. MedTech Europe and COCIR. Interoperability standards in digital health: A White Paper from the medical technology industry [Internet]. MedTech Europe. 2021 [cited 2024 Aug 22]. Available from: https://www.medtecheurope.org/wp-content/uploads/2021/10/mte_interoperability_digital_health_white-paper_06oct21.pdf
 23. Stellmach C, Muzoor MR, Thun S. Digitalization of Health Data: Interoperability of the Proposed European Health Data Space. In: Scott P, Mantas J, Benis A, Ognjanovic I, Saranto K, Ware A, et al., editors. *Studies in Health Technology and Informatics* [Internet]. IOS Press; 2022 [cited 2024 Aug 22]. Available from: <https://ebooks.iospress.nl/doi/10.3233/SHTI220922>
 24. Oemig F, Blobel B. Modeling digital health systems to foster interoperability. *Front Med*. 2022 Aug 19;9:896670.
 25. Kouroubali A, Katehakis DG. Policy and Strategy for Interoperability of Digital Health in Europe. In: Otero P, Scott P, Martin SZ, Huesing E, editors. *Studies in Health Technology and Informatics* [Internet]. IOS Press; 2022 [cited 2024 Aug 22]. Available from: <https://ebooks.iospress.nl/doi/10.3233/SHTI220209>
 26. Katehakis DG, Kouroubali A. A Framework for eHealth Interoperability Management. *JSIS* [Internet]. 2019 Dec 17 [cited 2024 Aug 22];14(5). Available from:

- <https://articlegateway.com/index.php/JSIS/article/view/2521>
27. Scheplitz T. Demonstration and Evaluation of the Digital Health Innovation Interoperability Framework. *Procedia Computer Science*. 2023;219:1404–11.
 28. TEHDAS JA. EHDS Semantic interoperability framework [Internet]. 2022 Dec [cited 2024 Aug 22]. Report No.: Deliverable 6.2. Available from: <https://tehdas.eu/app/uploads/2023/10/tehdas-recommendations-to-enhance-interoperability.pdf>
 29. Ait Abdelouahid R, Debauche O, Mahmoudi S, Marzak A. Literature Review: Clinical Data Interoperability Models. *Information*. 2023 Jun 27;14(7):364.
 30. CEN/TC 251 Health Informatics. Business plan 2023 - 2026 [Internet]. [cited 2024 Aug 22]. Available from: <https://www.ehealth-standards.eu>
 31. Gyrard A, Gribbon P, Hussein R, Abedian S, Bonmati LM, Cabornero GL, Manias G, Danciu G, Dalmiani S, Autexier S, van Nuland R, Jendrosseck M, Avramidis I, Alvarez EG. Synergies Among Health Data Projects with Cancer Use Cases Based on Health Standards. *Stud Health Technol Inform*. 2024 Aug 22;316:1292-1296. doi: 10.3233/SHTI240649. PMID: 39176618.
 32. Gyrard A, Abedian S, Gribbon P, Maniase G, van Nuland R, Zatloukal K, Nicolaeh IE, Danciu G, Nechifor SC, Marti-Bonmati L, Malloli P, Dalmiani S, Autexier S, Jendrosseck M, Avramidis I, Garcia Alvarez E, Holub P, Blanquer Esperto I, Boden A, Hussein R. Lessons Learned from European Health Data Projects with Cancer Use Cases: Implementation of Health Standards and IoT Semantic Interoperability. *J Med Internet Res*. 2025;[PMID: XXXX].
 33. Rajab RM, Abuhmida M, Wilson I, Ward RP. A Review of IoMT Security and Privacy related Frameworks. *eccws*. 2024 Jun 21;23(1):733–43.
 34. World Bank Group. ID4D Practitioner's Guide (English) [Internet]. Identification for Development Washington, D.C.; 2019 [cited 2024 Aug 22]. Report No.: 137292. Available from: <https://documents.worldbank.org/en/publication/documents-reports/documentdetail/248371559325561562/id4d-practitioner-s-guide>
 35. eHAction JA. Interoperability Guide - eHealth Action [Internet]. [cited 2024 Aug 22]. Available from: <http://ehaction.eu/interoperability-guide/>
 36. INCISIVE Project. Recommendations of interoperability standards for projects managing clinical data and medical images: the INCISIVE case [Internet]. Incisive Project. [cited 2024 Aug 22]. Available from: <https://incisive-project.eu/new/recommendations-of-interoperability-standards-for-projects-managing-clinical-data-and-medical-images-the-incisive-case/>
 37. World Health Organization (WHO). Ethics and governance of artificial intelligence for health [Internet]. 2021 [cited 2024 Aug 22]. Available from: <https://iris.who.int/bitstream/handle/10665/341996/9789240029200-eng.pdf?sequence=1>
 38. World Health Organization (WHO). Ethics and governance of artificial intelligence for health - Guidance on large multi-modal models [Internet]. 2024 [cited 2024 Aug 22]. Available from: <https://iris.who.int/bitstream/handle/10665/375579/9789240084759-eng.pdf?sequence=1>
 39. Integrating the Healthcare Enterprise (IHE). IHE IT Infrastructure White Paper: Enabling Document Sharing Health Information Exchange Using IHE Profiles [Internet]. 2024 [cited 2024 Aug 22]. Available from: <https://profiles.ihe.net/ITI/HIE-Whitepaper/#3-document-sharing-profiles>
 40. Xiao G, Pfaff E, Prud'hommeaux E, Booth D, Sharma DK, Huo N, Yu Y, Zong N, Ruddy KJ, Chute CG, Jiang G. FHIR-Ontop-OMOP: Building clinical knowledge graphs in FHIR RDF with the OMOP Common data Model. *J Biomed Inform*. 2022 Oct;134:104201. doi: 10.1016/j.jbi.2022.104201. Epub 2022 Sep 9. PMID: 36089199; PMCID: PMC9561043.
 41. HL7.FHIR.UV.VULCAN-RWD\Home - FHIR v4.0.1 [Internet]. [cited 2024 Feb 7]. Available from: <https://build.fhir.org/ig/HL7/vulcan-rwd/>
 42. Fillout | Forms that do it all [Internet]. Fillout | Forms that do it all. [cited 2024 Dec 9]. Available from: <https://www.fillout.com>
 43. Hussein R, Balaour I, Burmann A, Ćwiek-Kupczyńska H, Gadiya Y, Ghosh S, et al. Getting ready for the European Health Data Space (EHDS): IDERHA's plan to align with the latest EHDS requirements for the secondary use of health data. *Open Res Europe*. 2024 Jul 30;4:160.
 44. van Kolschooten H, van Oirschot J. The EU Artificial Intelligence Act (2024): Implications for healthcare. *Health Policy*. 2024 Sep 7;149:105152. doi: 10.1016/j.healthpol.2024.105152. Epub ahead of print. PMID: 39244818.

45. Baumgart DC. An intriguing vision for transatlantic collaborative health data use and artificial intelligence development. npj Digit Med. 2024 Jan 23;7(1):19.



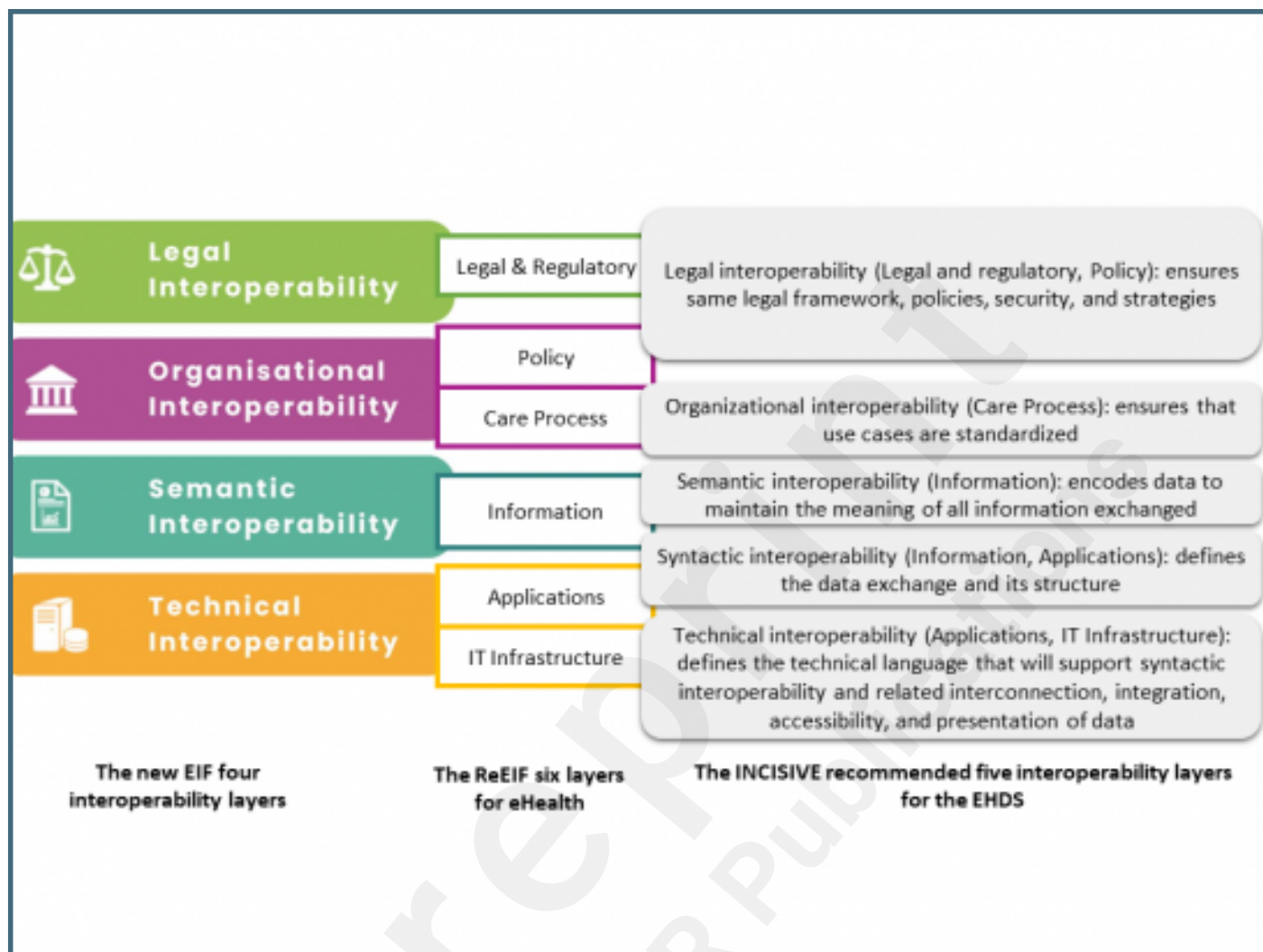
Supplementary Files

Figures

Timeline of the EU data regulations and frameworks shaping the EHDS.



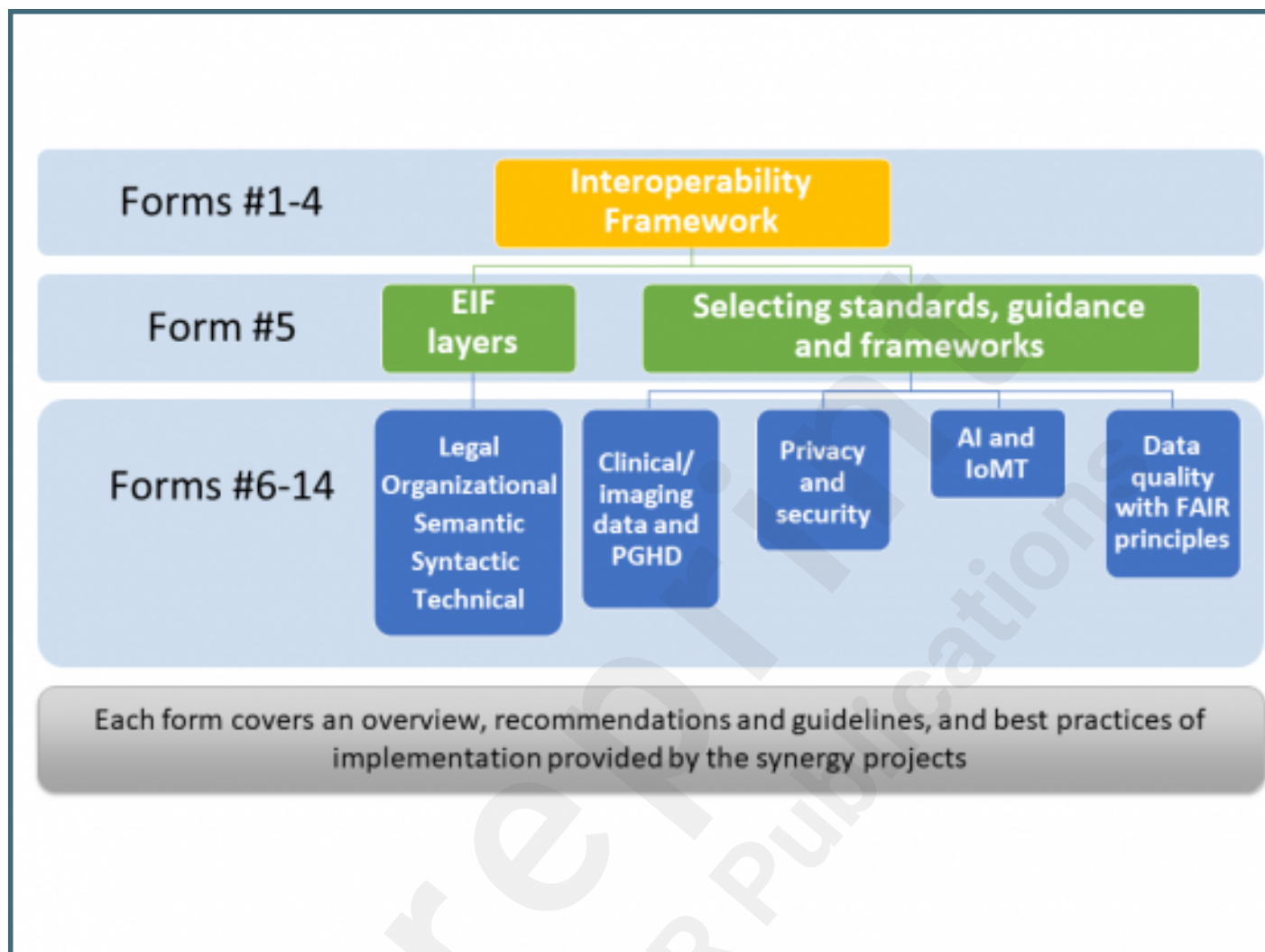
The interoperability layers of the EIF [14], ReEIF [16], the INCISIVE project [18].



The EHDS2 Interoperability Framework: Concept and process of creation.



The toolkit of EHDS2 Interoperability Framework: Main components and sections.



The interoperability toolkit: A snapshot of the entry module of the interoperability framework and how the projects can share their lessons learned.

Interoperability Framework (Part 1/3)

What is an Interoperability Framework?
The Interoperability framework is a document that includes the analysis of the technical and functional prerequisites of a process/environment or a project, the actors and transactions of each use case involving the data use, the justification of the chosen standards, the methodology and design carried out, the interoperability risk analysis, the interoperability maintenance plan, the publication and reuse of the implementation guides and recommendations and future actions.

More info: [INCISIVE Standardization Suggestions](#)

(1) Needs Analysis
Analyze the functional, health, technical, and security needs that may change the interoperability scenario.

Needs analysis (needs and goals of the project)

Readings
van Kolfaschooten H, van Oirschot J. The EU Artificial Intelligence Act (2024): Implications for healthcare. Health Policy. 2024 Nov;149:105152. doi: 10.1016/j.healthpol.2024.105152. Epub 2024 Sep 7. PMID: 39244818.

Share with us!

Please add your projects, standards, and readings

File Upload

Drag & drop a file or browse

Back

The interoperability toolkit: A snapshot of the module of the standards selection.

Standards selection

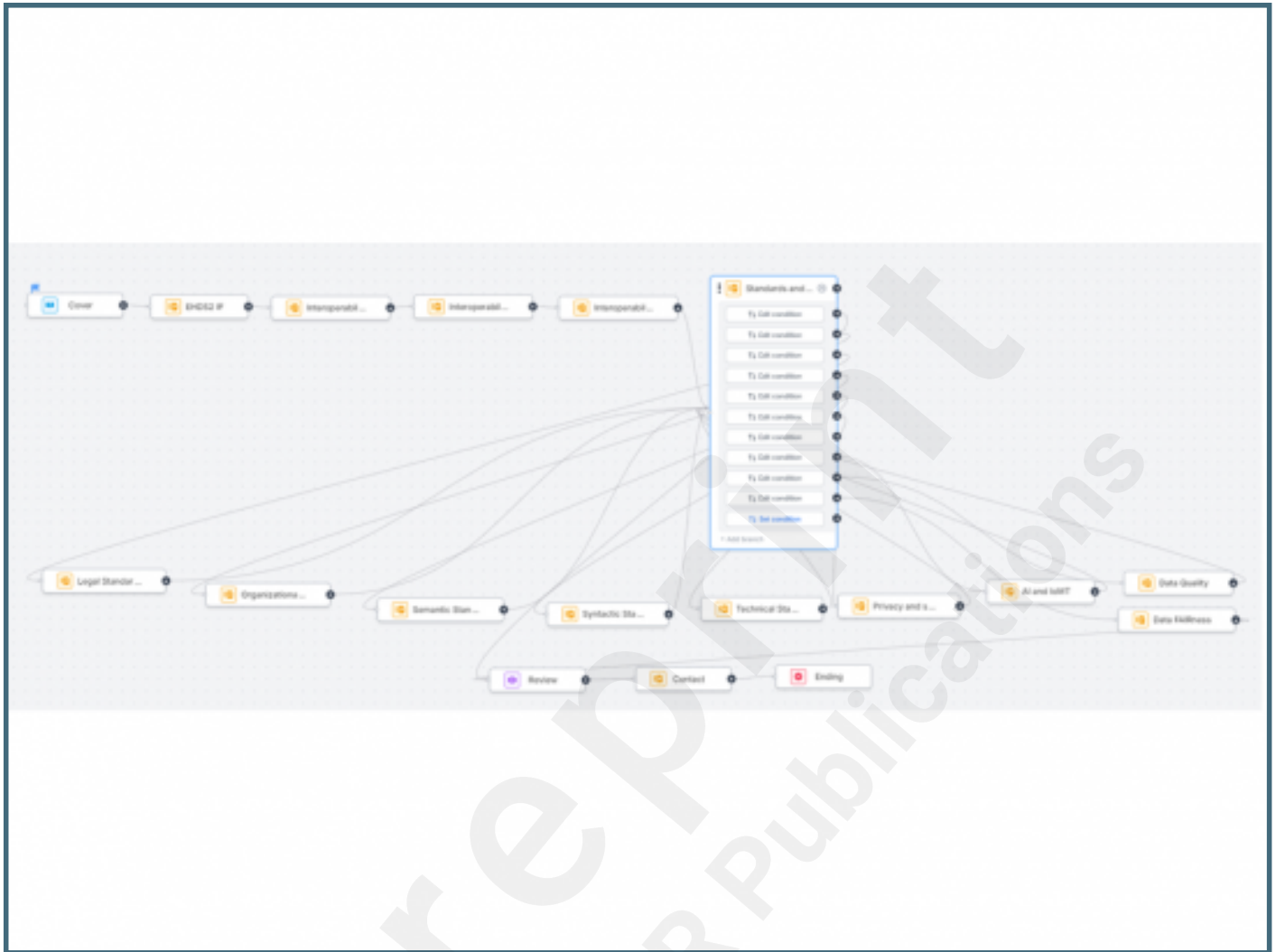
Please select the standards domain

 Legal interoperability ☐ Legal	 Organizational interoperability ☐ Organizational	 Semantic interoperability ☐ Semantic
 Syntactic ☐ Syntactic	 Technical interoperability ☐ Technical	 Privacy ☐ Privacy
 AI and IoMT ☐ AI and IoMT	 Quality ☐ Quality	 FAIRness ☐ FAIRness

Skip this part
☐

Next ->

The logic for navigating the interoperability toolkit.



Identifying the associated AI risk and obligations with referring to the guidance.

Requirements for health-related AI systems in the EU AI Act		
	Provider obligations	Deployer obligations
Unacceptable risk	☐	☐
High-risk	☐	☐
Low-risk	☐	☐
Minimal-risk	☐	☐
General purpose	☐	☐

Reference
van Kolf Schooten H, van Oirschot J. The EU Artificial Intelligence Act, (2024): Implications for healthcare. *Health Policy*. 2024 Sep 7;149:105152. doi: 10.1016/j.healthpol.2024.105152. Epub ahead of print. PMID: 39244818.

TOC/Feature image for homepages

The logos of the seven projects participated in the HSbooster health cluster.

