International Digital Health Regulatory Pathways

AI/ML how-to guide: Navigating global regulations & requirements

Optimizing strategic decision-making for AI/ML development in healthcare globally

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DIGITAL MEDICINE SOCIETY

Navigate the dynamic regulatory environment

Artificial intelligence/machine learning (AI/ML) in medical devices represents a cornerstone of modern healthcare innovation and is transforming digital diagnostics, therapeutics, and patient management with unprecedented precision for clinical applications.

In line with the rapid pace of AI/ML landscape evolution, policymakers at the local, national, and international levels are reshaping legislative and regulatory landscapes to address and mitigate new risks introduced by these technologies.

As such, digital health technology (DHT) developers can set out on their product development journey under one set of AI/ML regulations and, by a later phase of their product's lifecycle, be under a modified or different set of regulatory requirements.

In an ecosystem where regulations are not static, developers must know where to look for updates and how to navigate ongoing changes. This knowledge is particularly important since developers remain responsible for aligning with all relevant regulatory frameworks and requirements that govern the use of AI/ML throughout the product's entire lifecycle.

DHT developers are encouraged to use this guide to:

- ✔ Navigate the types and levels of legislative and regulatory frameworks related to the development, deployment, and use of AI/ML technologies.
- ✔ Build product development governance and processes that comply with relevant AI/ML regulatory requirements, standards, and best practices.
- ✔ Streamline product development and scale across national borders by identifying common regulatory requirements across jurisdictions.

Determine degree of AI/ML integration into medical devices

Key definitions from DiMe Glossary

Artificial intelligence is defined as “a technical and scientific field devoted to the engineered system that generates outputs such as content, forecasts, recommendations or decisions for a given set of human-defined objectives” [ISO/IEC 22989:2022].

Machine learning is a subset of AI and is defined as the “process of optimizing model parameters through computational techniques, such that the model's behavior reflects the data or experience” [ISO/IEC 22989:2022].

Machine Learning-enabled Medical Device (MLMD) is “a medical device that uses machine learning, in part or in whole, to achieve its intended medical purpose” [IMDRF/AIMD WG/N67].

Developers leverage AI/ML in DHT products to varying degrees, such as:

- in an auxiliary function as a wraparound, supportive, or secondary function of the medical device.
- in driving the core functionality of the product.

Regulatory implications can therefore vary greatly based on the type, functionality, and ability of AI/ML to adapt over time.

In some jurisdictions, the presence of any degree of AI/ML in a product automatically qualifies the product for a higher product risk class.

Other jurisdictions take a scaled approach where the product risk level and class increase based on the type of AI/ML used in the product (i.e., fixed vs. adaptive algorithms) and functionality (i.e., as an auxiliary function vs. as a core component).

Assess the regulatory framework landscape

Regulations that govern AI/ML in healthcare vary greatly and uniquely impact the use of AI/ML in clinical settings within each jurisdiction. While policymakers can adopt approaches that are shared across multiple jurisdictions, legislative and regulatory frameworks also account for the specific needs of the population and existing infrastructure.

> This situation results in a complex matrix of jurisdiction-specific requirements, yet also provides the opportunity for developers to identify commonalities across jurisdictions to create efficiencies in going to market.

AI/ML regulations and requirements—for both the general use of AI/ML across all sectors within a jurisdiction, in addition to healthcare-specific AI/ML regulatory requirements—are developed at the following levels:

 **International guidance and standards**	 **Regional requirements**	 **National and local requirements**
International organizations (i.e., the International Standards Organization (ISO), the Institute of Electrical and Electronics Engineers Standards Association (IEEE), the International Medical Device Regulators Forum (IMDRF), the World Health Organization (WHO)) develop formal standards and recommendations that form the foundation of many regional, national, and local requirements.	Regional bodies such as the European Union (EU) establish frameworks that can be adopted by member states related to the safety, interoperability, and security of medical devices.	National jurisdictions, in addition to local policymaking bodies where appropriate (i.e., state, provincial), represent the core of risk-proportionate approaches to AI/ML regulation.

Determine what is binding vs. non-binding

Regulations, policies, requirements, and standards for AI/ML have different degrees of bindingness.

Organizations such as the International Organization for Standardization (ISO), the International Electrotechnical Commission (IEC), and the Institute for Electrical and Electronics Engineers Standards Association (IEEE) develop standards for AI/ML algorithms and products. Yet, these standards are not binding for product developers until regional, national, or local policymakers implement a requirement that relevant products must align with the standard.

Similarly, organizations such as the International Medical Device Regulators Forum (IMDRF), the World Health Organization (WHO), and trade associations develop guidelines related to the development, implementation, and risk classifications of AI/ML algorithms and products. While none of these guidelines or recommendations are inherently binding, policymakers often adopt key elements into regulations that are binding.

Consider AI/ML's impact on product risk

A significant gap in the regulation of AI/ML is the lack of consistent, evidence-based benchmarks for assessing and standardizing product risk levels across jurisdictions. When product risks are perceived and stratified differently across regulatory bodies, it results in a fragmented regulatory landscape.

While some jurisdictions may categorize specific AI/ML applications—such as diagnostic algorithms or patient management tools—as high-risk and subject them to stringent scrutiny, other jurisdictions will not share the same risk stratification.

Developers need to be aware of this absence of agreed-upon risk benchmarks and be prepared to navigate the international landscape despite not having a standardized framework to work from.

Monitor evolving AI/ML regulations and guidance

AI/ML products are governed and influenced by numerous sets of relatively quickly evolving guidelines at the global, regional, and national levels. Therefore, developers should stay informed and compliant with regulatory updates whenever possible, utilizing various channels:

How to stay informed	Suggested actions
Register for agency and organization email listservs	Subscribe to receive the latest updates directly from regulatory agencies and relevant organizations.
Monitor federal and international regulatory dockets	Regularly check platforms like Regulations.gov in the U.S. and international counterparts to keep up with proposed changes.
Follow agency and regulatory body social media accounts	Engage with real-time updates and insights by following agencies on platforms like LinkedIn and official news feeds.
Provide formal comments on legislative and regulatory proposals	Actively participate by submitting comments during open consultation periods to influence policy development.
Engage with industry groups and regulatory consortia	Join associations and societies with AI/ML-focused work groups that work directly with regulatory bodies to stay informed on collective insights and guidance.
Attend relevant conferences and regulatory webinars	Gain deeper insights by attending events where regulatory updates and trends are discussed by industry and policy experts.
Engage with the academic and legal research community on evolving AI/ML policies	Keep up to date through research papers and journals that analyze regulatory changes and predict future trends.

Identify efficiencies in your regulatory approach

National agencies responsible for developing AI/ML regulations operate independently, each setting policies tailored to their jurisdiction. However, developers can identify common themes or core elements across these regulatory frameworks. This opportunity enables developers to streamline critical aspects of product development, launch, and sustained scaling both within and across different regions.

Examples of converging themes and elements across global approaches include:

- ✔ **Risk-based product stratification:** AI/ML-enabled products are often reviewed and authorized for market access along a risk continuum, typically ranging from self-attestation and product registration for low-risk products to full-scale regulatory compliance evaluations for higher-risk products.

- ✔ **Clinical evidence of effectiveness:** Products that incorporate AI/ML routinely demonstrate safety and effectiveness via systematic clinical investigations to verify a device's safety and performance. In situations where similar medical devices are already approved by the agency, clinical evidence evaluations (i.e., review of existing published data) may be acceptable.
- ✔ **Predetermined Change Control Plans:** Regulatory agencies are increasingly establishing newer programs for adaptive approaches to accommodate the non-deterministic nature of AI/ML products. These frameworks allow products to evolve within predefined limits throughout their life cycles, fostering safe and effective innovation.
- ✔ **Data governance and user protections:** Policymakers routinely implement protections to ensure that data generated and used by AI/ML products safeguard user privacy, maintain data security, and protect end users. These measures establish accountability for data handling practices, ensuring transparency and building trust in AI/ML technologies.

Even if certain regulations such as the European Union's (EU) General Data Protection Regulation (GDPR) are written by European policymakers, they are applicable to any company operating within the region, regardless of whether data processing takes place in Europe or not. As such, some elements or concepts of GDPR are being incorporated into other policy frameworks outside of Europe.

Comply with binding requirements

Regional requirements

In the EU, developers must navigate several key regulations, including the EU Artificial Intelligence (AI) Act and the European Health Data Space (EHDS).

The EU AI Act establishes a comprehensive, cross-sectoral framework to regulate AI within the EU. This legally binding framework imposes obligations on AI and machine learning (ML) product developers marketing their technologies in the EU and is part of a broader policy initiative to foster trustworthy AI. This initiative also includes the AI Innovation Package and the Coordinated Plan on AI. Adopting a risk-based approach, the EU AI Act focuses particularly on high-risk AI/ML systems, requiring developers to adhere to specific standards. Tools such as the EU AI Act Compliance Checker help developers meet these requirements.

EHDS, in comparison, facilitates and streamlines access to EU-wide real-world health data and aims to:

1. Empower individuals through increased digital access to and control of their electronic personal health data, at the national level and EU-wide.
2. Foster a single market for electronic health record systems, relevant medical devices, and high-risk AI/ML systems.
3. Provide a trustworthy and efficient setup for the use of health data for research, innovation, policy-making, and regulatory activities (secondary use of data).

National requirements

National jurisdictions, in addition to local policymaking bodies where appropriate (i.e., state, provincial), represent the core of risk-proportionate approaches to AI/ML regulation. National legislation and regulations can:

- Evolve and adapt to the changing technology landscape;
- Incorporate international and regional standards and frameworks;
- Take different approaches to AI/ML risk classifications;
- Account for adaptive AI/ML algorithms through predetermined change control plans; and
- Vary greatly from other jurisdiction approaches, even if internationally harmonized elements are incorporated into policies.

The Appendix provides examples of regional and national AI/ML-related policies and regulatory frameworks as of November 2024. These policies are subject to change and evolve, so developers are encouraged to regularly consult relevant agency websites for the latest information.

Develop holistic product strategies

The AI/ML legislative and regulatory landscape is complex and will significantly evolve over the coming months and years. DHT developers must comply with all pertinent requirements in each jurisdiction of operation, while also preparing for forthcoming changes.

Considerations to achieve this balance for the duration of a product's life cycle include:

- ✔ **Establishing a robust organizational process.** Developers are encouraged to implement rigorous software engineering and data quality practices aligned with international standards as soon in the process as possible.
    - Set up a resilient quality management system (QMS) and adopt stringent cybersecurity measures to safeguard sensitive healthcare data.
    - Refine data collection methodologies and align outcomes with ethical and legal standards.
    - Focus on strengthening data management strategies and ensure product development processes are synchronized with quality engineering practices.
- ✔ **Adhering to evidence-based clinical validation and regulatory submission best practices**. Employ high-quality data collection and evaluation frameworks to ensure that AI/ML models are regularly validated against stringent clinical parameters. IMDRF provides developers with 10 guiding principles for Good Machine Learning Practice (GMLP).
- ✔ **Adopting a multidisciplinary approach**. Embrace a collaborative development approach that includes statisticians, clinicians, engineers, end users, and other stakeholders.
- ✔ **Evaluating AI/ML products through their lifecycles**. Develop a clinical evaluation strategy that appropriately accounts for the interactive nature of AI/ML algorithms and products. Continuous evaluation, coupled with a summative evaluation, is essential to high-quality development and deployment that upholds transparency, scientific validity, and interpretability.
- ✔ **Setting out with the "end" in mind**. Integrate continuous learning strategies that align with risk-proportionate approaches and predetermined change control plans across the total product life cycle.

Be prepared to adapt

Developers are responsible for maintaining medical device integrity and effectiveness for the duration of each product's life cycle, while also being prepared to account for changes in regional, national, and local legislation and regulation. Planning ahead within and across countries can simplify regulatory submissions and accelerate product time-to-market, ultimately enhancing patient outcomes and fostering innovation.

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Appendix

For regional and national AI/ML-related policies and regulatory framework examples, visit the Library of Digital Health Regulations and filter resources by AI/ML, cybersecurity, or data privacy.

Relevant ISO & IEC standards include:

- ISO/IEC 42001: Information technology — Artificial intelligence — Management system
- ISO/IEC 22989: Artificial intelligence — Concepts and terminology
- ISO/IEC 23053: Framework for Artificial Intelligence (AI) Systems Using Machine Learning (ML)
- ISO/IEC 23894: Information technology — Artificial intelligence — Guidance on risk management
- ISO/IEC 27001: Information security, cybersecurity and privacy protection — Information security management systems — Requirements
- ISO/IEC 27040: Information technology — Security techniques — Storage security
- ISO/AWI 24051-2: Part 2: Digital pathology and artificial intelligence (AI)-based image analysis
- ISO/IEC 62304: Medical device software — Software life cycle processes
- ISO 13845: Medical devices — Quality management systems — Requirements for regulatory purposes