The FDA & EU New and Coming Standards for AI/ML in Medical Devices

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Development & Regulation

WE SIMPLIFY MARKET ACCESS FOR DIGITAL HEALTH AND MEDICAL DEVICES COMPANYS

Software Quality Assurance (SQA)

Our SQA methodology is a testament to our commitment to precision, covering strategic planning, meticulous testing, and rigorous documentation.

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Software Verification & Validation (V&V)

Our expertise ensures thorough V&V activities across a range of systems, guaranteeing compliance and reliability.

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Software Development

Our unique blend of Software Development with Regulation Process ensures excellence in functionality, maintainability, and compliance.

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Cyber Security

We provide a comprehensive cyber security framework for medical devices, assessing threats and vulnerabilities to ensure patient safety and device integrity.

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Risk Management

We recognize that risk management is a critical, mandatory aspect throughout the development, production, and maintenance phases of medical devices.

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Consulting & Training Services

Our Consulting & Training Services are designed to bridge knowledge gaps and empower teams in the medical device industry.

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Regulatory Compliance (MDR/FDA)

We are specializing in ensuring that your product aligns with the stringent regulations of the medical device industry and with the global standards.

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Implementation and management of compliance

with ISO standards

Our focus on ISO standards underscores our commitment to continuous improvement, regulatory compliance and patient safety.

Read More →

Our team of experts specializes in

- software development
- Regulatory
- quality processes
- Verification & Validation
- cyber security & risk management
- ISO certification

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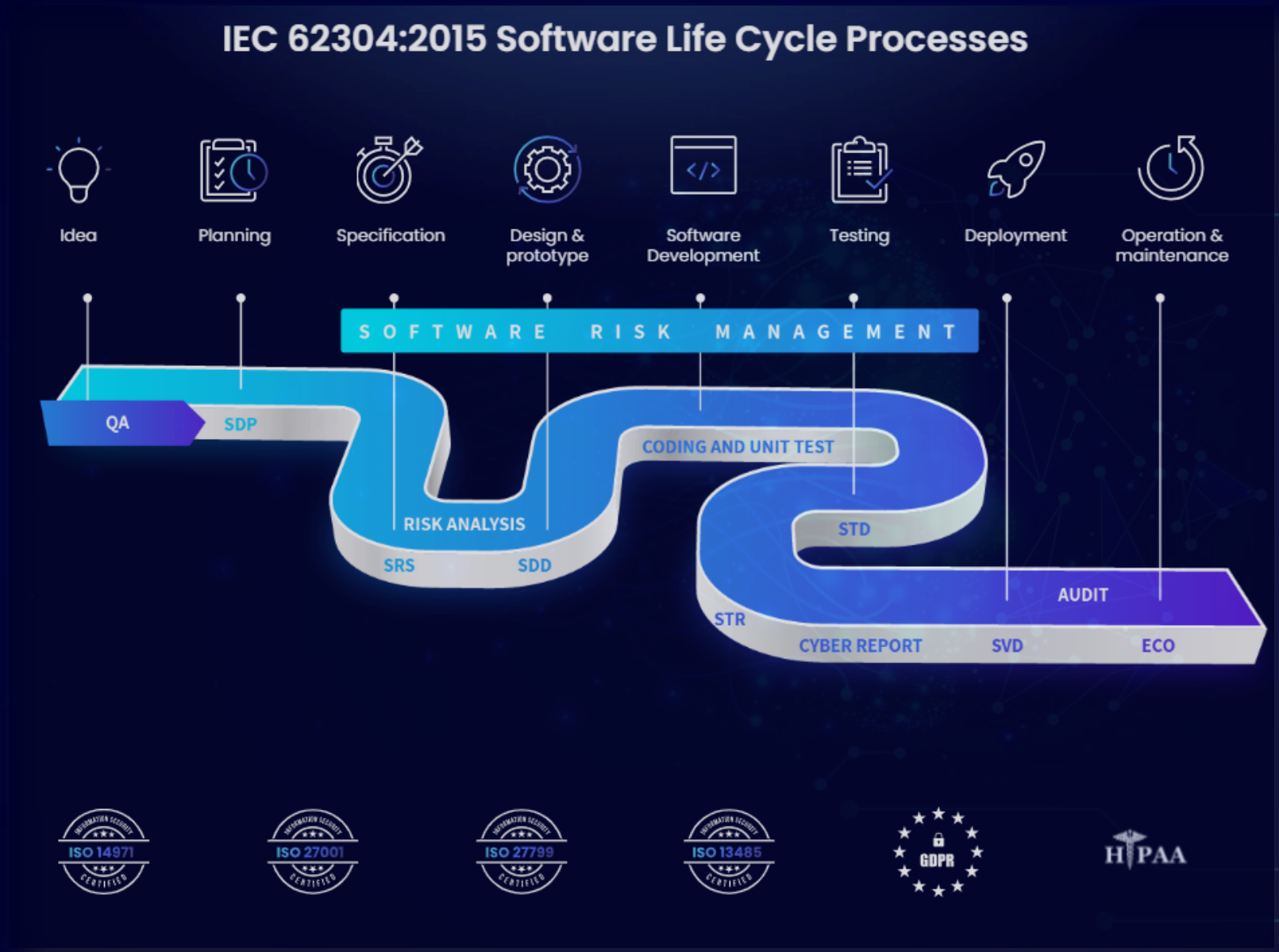

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Ensuring Patient Access to Safe & Effective AI/ML-Enabled Medical Devices

Updated in October 2023

~ 700 Authorizations of AI/ML-Enabled Medical Devices

1. A public resource on these devices and the FDA's work in this area
2. Show how Al/ML is being used across medical disciplines

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FDA's innovative pathways - Predetermined Change Control Plan (PCCP) Good Machine Learning Practice (GMLP)

FDA's Collaborative Patient-Centered Approach to AI-Enabled Devices

Published AI/ML-SaMD Discussion Paper

2019

First joined Collaborative Community related to AI/ML

WORKSHOP
Evolving Role of AI in Radiological Imaging

Public Workshop on AI/ML in Radiological Imaging

2020

PEAC Mtg on Patient Trust in AI/ML Devices

Published AI/ML Medical Device Software Action Plan

2021

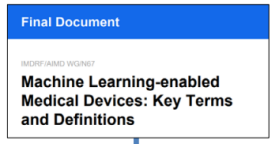
Posted List of Currently Marketed AI/ML Devices

WORKSHOP
Transparency of AI/ML-Enabled Medical Devices

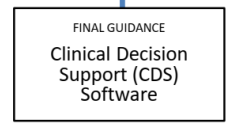
Public Workshop on Transparency of AI/ML Devices

Published GMLP Guiding Principles

2022



Contributed to IMDRF's Key Terms and Definitions



Published Final Guidance: Clinical Decision Support

2023

Published AI/ML PCCP Guidance

We're working collaboratively with stakeholders to build a proactive, patient-centered approach to AI-enabled devices that promotes health equity.

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EU's comprehensive AI Act for risk-based regulation of all AI systems

AI in Europe will create a unique ecosystem of trust.

Must ensure compliance with EU rules, including the rules protecting fundamental rights and consumers' rights, in particular for AI systems operated in the EU that pose a high risk.

Balanced and proportionate horizontal regulatory approach to AI - minimum necessary requirements to address the risks and problems linked to AI, without unduly constraining or hindering technological development or otherwise disproportionately increasing the cost of placing AI solutions on the market.

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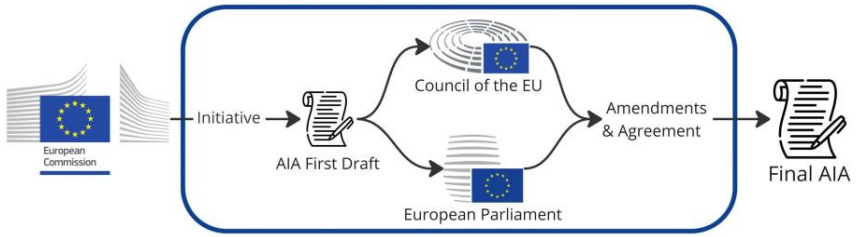
EU's comprehensive AI Act for risk-based regulation of all AI systems

On February 2, European Union Member States endorsed the world's first comprehensive legal framework regulating artificial intelligence in the EU.

The EU's Artificial Intelligence Act (AI Act) applies across industries—from medical device manufacturers to consumer app developers.

Once the European Parliament and European Commission formally adopt the AI Act, developers of medical devices with AI-based products and components will have an additional set of requirements to meet.

The requirements for AI systems will augment what's already required under the EU's Medical Device Regulation (MDR) and In-Vitro Diagnostic Regulation (IVDR).



Ordinary Legislative Procedure

"The EU lawmaking process, a well-orchestrated operation, involves a series of important bodies, including the European Parliament, the European Commission, and the Council of the European Union. Essentially, these three major institutions work in harmony to propose, debate, agree on and implement EU laws."

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What is different about ML vs. traditional quality/regulatory?

Machine learning - The data is what is defining the logic, not human experts.

But this leads to some problems…

- The data might be **incomplete** (e.g. missing important elements)
- The data might be **incorrect** (e.g. data from wearables might not be 100% accurate)
- Patterns may or may **not be relevant** (e.g. might be a coincidence in the data that is not clinically relevant)
- The data might not fully **represent** the target population
- Health & Healthcare **change over time** (e.g. more cases of flu during the winter – what if your data is from spring & summer?)

AI - Enabled Medical Devices: Opportunities & Challenges

OPPORTUNITIES

- **Significant positive impact on health care**

Earlier disease detection

More accurate diagnosis

New insights into human physiology

Personalized diagnostics and therapeutics

- **Applications across all medical fields**
- **Ability to learn, adapt, and improve performance**

CHALLENGES

- Fit-for-purpose data sets for development and testing, including diversity
- Identification and management of bias
- Opacity of some algorithms
- Ensuring transparency to users
- Providing oversight for an adaptive system

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Promoting Global Harmonization of Best Practice

Good Machine Learning Practice (GMLP)

- 10 guiding principles issued by FDA, UK, Canada
- Promote global harmonization of ML best practices
- Facilitate high-quality AI technology development

FDA U.S. FOOD & DRUG ADMINISTRATION

Health Canada Santé Canada

Medicines & Healthcare products Regulatory Agency

Good Machine Learning Practice for Medical Device Development: Guiding Principles	
Multi-Disciplinary Expertise are Leveraged Throughout the Total Product Life Cycle	Good Software Engineering and Security Practices are Implemented
Clinical Study Participants and Data Sets are Representative of the Intended Population	Training Data Sets are Independent of Test Sets
Selected Reference Datasets are Based Upon Best Available Methods	Model Design is Tailored to the Available Data and Reflects the Intended Use of the Device
Focus is Placed on the Performance of the Human-AI Team	Testing Demonstrates Device Performance during Clinically Relevant Conditions
Users are Provided Clear, Essential Information	Deployed Models are Monitored for Performance and Re-training Risks are Managed

Broader AI Standards Landscape

- **IEC, ISO, IEEE initiatives on AI governance, testing, risks**
- **Potential adoption into sector-specific FDA and EU rules**

- ISO/IEC JTC1, SC42, developing horizontal standards for all industries.
- IEEE also developing several AI standards.
- Existing medical device committees are looking at this technology, and ISO/IEC TC215 has created a Task Force to help medical device people develop new standards – create a “landscape” of other standards, collect use cases, etc.
- AAMI & BSI have collaborated to develop healthcare AI standards.

Health Equity - Guiding Principles for Algorithm Bias in Healthcare

Principles:

1. **Promote Health and Healthcare Equity:** Ensure equity is a core consideration throughout all phases of healthcare algorithm development, implementation, and evaluation.
2. **Transparency and Explainability:** Make healthcare algorithms and their operational mechanisms transparent and understandable to all stakeholders.
3. **Engagement with Patients and Communities:** Authentically involve patients and communities in the development and application of healthcare algorithms to build trust and ensure relevance.
4. **Fairness and Trade-offs:** Explicitly identify and address fairness issues and trade-offs, acknowledging the complexities and limitations of algorithms in healthcare.
5. **Accountability:** Establish clear accountability for the outcomes of healthcare algorithms, ensuring that they contribute to equity and fairness in healthcare delivery.

Goal:

By adhering to these principles, we aim to mitigate algorithmic biases and enhance the equity and effectiveness of healthcare services.

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Transparency is Fundamental to a Patient-Centered Approach

1. Allows patients, providers, and caregivers to make informed decisions
2. Supports proper use of a device
3. Promotes health equity
4. Facilitates evaluation and monitoring of device performance
5. Fosters trust and promotes adoption

Transparency supports the safe and effective use of AI-enabled medical devices.

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Transparency: Cornerstone of Trustworthy AI

Data Transparency

Key Elements:

- Social Determinants of Health
- Race, Ethnicity, & Language
- Gender Identity
- Sexual Orientation
- Date of Birth

Impact:
Empowers users with knowledge about the data driving the DSIs.

+

Performance Transparency

Key Elements:

- Clarity on intended use, training data, fairness, and maintenance.
- Creation of a model "nutrition label" for easy understanding.
- Accessible information through direct display, drill down, or link out functions.

Impact:
Enhances user understanding and trust in DSI performance.

+

Organizational Transparency

Key Elements:

- Thorough analysis and mitigation of risks.
- Governance covering socio-technical dimensions: Validity, Reliability, Robustness, Fairness, Intelligibility, Safety, Security, and Privacy.

Impact:
Ensures that organizations publicly disclose their governance and risk management practices, promoting accountability.

=

Trust worthy Predictive Models (FAVES)

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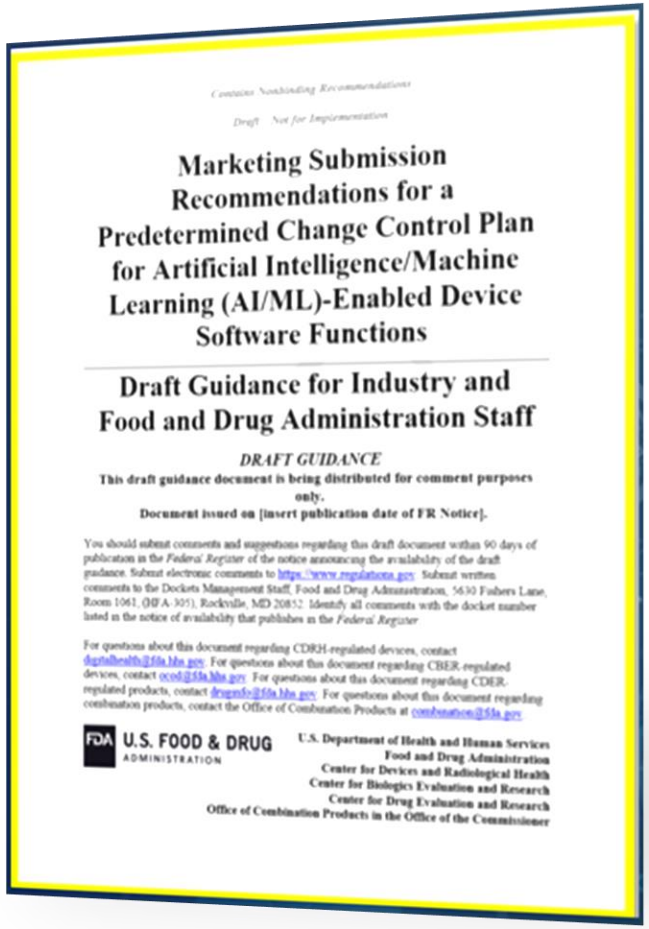
FDA's Predetermined Change Control Plan (PCCP)

- Science-based approach enabling continuous AI evolution and rapid iteration
- Facilitates more personalized medicine and faster medical device innovation
- Addresses performance across diverse populations throughout product lifecycle PCCP Benefits
- Allows rapid, continuous improvement of AI device performance
- Ensures considerations for race, ethnicity, disease severity, gender, age, geography



Contains Nonbinding Recommendations

Draft – Not for Implementation

Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software Functions

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

Document issued on [insert publication date of FR Notice].

You should submit comments and suggestions regarding this draft document within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions about this document regarding CDRH-regulated devices, contact digitalhealth@fda.hhs.gov. For questions about this document regarding CBER-regulated devices, contact ocod@fda.hhs.gov. For questions about this document regarding CDER-regulated products, contact druginfo@fda.hhs.gov. For questions about this document regarding combination products, contact the Office of Combination Products at combination@fda.gov.

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research
Center for Drug Evaluation and Research
Office of Combination Products in the Office of the Commissioner

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Proposed Components of PCCPs

Description of Modifications

"What" a manufacturer intends the algorithm to become as it learns

- Identifies specific, planned modifications to the device that the manufacturer intends to implement
- Draws a "range of FDA-authorized specifications" around initial device characteristics and performance

Modification Protocol

"How" the algorithm will learn/change while remaining safe and effective

- Describes methods that will be followed when developing, validating, and implementing the modifications to ensure the device remains safe and effective
- Methods described in Modification Protocol should be consistent with and support the modifications outlined in Description of Modifications

Impact Assessment

Describes modifications' benefits and risks, and how risks are mitigated

- Assesses benefits and risks of each individual modification, as well as collective impact of modifications, included in the Description of Modifications
- Discusses how activities proposed within Modification Protocol mitigate identified risks to continue to reasonably ensure the safety and effectiveness of the device

Predetermined Change Control Plan

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AI Requirements for Medical Devices: Bridging AI Act and MDR/IVDR

Lifecycle Approach
continuous, iterative process for the entire lifecycle of high-risk AI systems.

Data Governance
Ensure training, validation, and testing datasets are relevant, representative, complete, and error-free.

Technical Documentation
Draft documentation that proves compliance and allows authority assessment.

Event Recording
Design systems to automatically document critical events and modifications for risk identification and management.

Usage Instructions
Provide clear instructions to facilitate downstream compliance.

Human Oversight
Enable deployers to implement necessary human oversight mechanisms.

System Design
Ensure high levels of accuracy, robustness, and cybersecurity in system design.

Quality Management
Establish a comprehensive quality management system for ongoing compliance.

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34971 ML-related hazards (Application of ISO 14971)

Overthrust in ML

• Risks include overconfidence, underestimating real dangers, and varied levels of social trust, leading to uncritical acceptance of ML outputs.

• Influenced by user workload, company policies, and initial success stories, potentially leading to inappropriate reliance on ML, like in the case of emergency management.

Data Issues

• Security and privacy concerns with data storage, including risks of malicious access and failure in data anonymization, which could impact algorithm accuracy.

• Privacy concerns can introduce biases, particularly demographic-based, affecting the system's fairness and efficiency.

Other Critical Considerations

• Challenges such as failure to act on ML advice, data drift over time, and the gap between data abundance and genuine understanding, exemplified by misclassifications due to unconsidered factors like effective medical interventions.

Bias Management

The information used to create and test a product might not represent the target patient population, and therefore doesn't perform as well on different demographics.

Types of bias include:

Sample Bias

Data is not collected randomly

Coverage Bias

Data set does not match the target population

Proxy Variables

Sometimes you can't have the data element you want, so you find a "proxy" variable, which can result in bias

Implicit Bias

the development team might have their own assumptions about health care and they inadvertently make incorrect decisions based on their experience

Data Poisoning

Data poisoning is a technique designed to compromise the integrity of the training process of a machine learning model. This involves deliberately introducing misleading or incorrect information into the data set from which the model learns. This incorrect information can cause the model to make errors or exhibit biased behaviour after deployment.

The importance of robust data verification, security measures, and ethical considerations in developing and deploying AI in healthcare to mitigate the risks associated with data poisoning:

- **Patient Safety at Risk**
- **Diagnostic Accuracy Undermined**
- **Trust in Healthcare AI Compromised**
- **Regulatory and Legal Challenges**
- **Escalated Healthcare Costs**
- **Ethical and Equity Implications**
- **Remediation Difficulties**

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IEC 63450 Testing of AI/ML-enabled Medical Devices

Objective: Develop methods for medical device manufacturers to rigorously verify and validate AI/ML-enabled medical devices (AI/ML-MD). These are devices that leverage artificial intelligence, either partially or entirely, to fulfil their medical functions.

Scope of Activities:

- **Model Verification & Validation:** Ensure the AI/ML model's effectiveness and reliability in real-world medical scenarios.
- **Data Management:** Emphasize the selection, metrological characterization, and management of datasets to support AI/ML models' development and application.

Standards and Guidelines: Based on the comprehensive analysis of JTC1/SC7's ISO/TR 29119-11, which provides guidelines on software and systems engineering, specifically focusing on software testing for AI-based systems.

Timeline: Anticipate the release of a Committee Draft (CD) by 2024, setting a structured path for standardization in the testing and validation of AI-based medical devices.

Prioritized Guidance Documents that CDRH Intends to Publish in FY2024

Final Guidance Topics

- Remanufacturing of Medical Devices
- Medical Device Shortages - Implementation of Section 506J of the Federal Food, Drug, and Cosmetic Act
- Marketing Submission Recommendations for A Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software Functions

Draft Guidance Topics

- Artificial Intelligence/Machine Learning (AI/ML)-enabled Device Software Functions: Lifecycle Management Considerations and Premarket Submission Recommendations
- Select Updates for the 506J Guidance: Voluntary Notifications of Discontinuance or Interruption of Device Manufacture
- Select Updates for Premarket Cybersecurity Guidance: Cyber Devices
- Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices (revision)
- Pulse Oximeters – Assessing Clinical and Scientific Evidence (revision)
- Predetermined Change Control Plans for Medical Devices

MDR/IVDR and state of the art

MD/IVD AI components review

2023

The state of the art in AI has evolved, and continues to do so, with an increasing and more evident associated risk. Given this and the applicable MDR/IVDR requirements, a team of **AI experts will undertake a technical documentation assessment** specifically for the AI components of the device.

2027

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MDR/IVDR and state of the art

MD/IVD AI components review

GSPR - General Safety and Performances Requirements for MD in the EU

17.2. For devices that incorporate software or for software that are devices in themselves, the software shall be developed and manufactured in accordance with the state of the art taking into account the principles of development life cycle, risk management, including information security, verification and validation.

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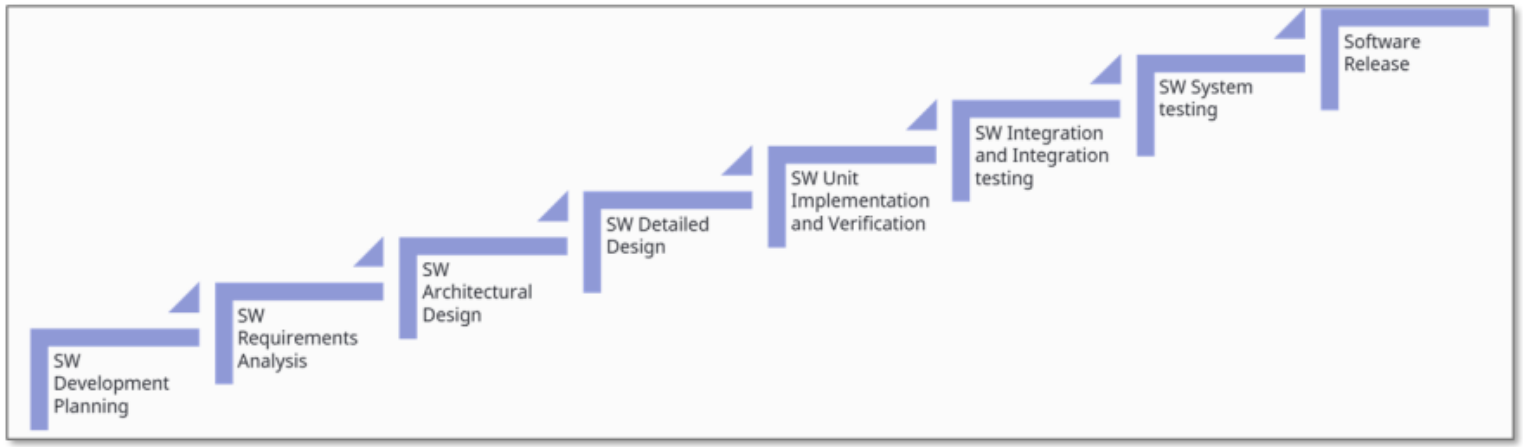

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2023

- Bias Mitigation
- Robustness
- Performance Evaluation
- Transparency

2027

ISO/IEC TS 4213:2022 (Performance) • ISO/IEC TS 24027:2021 (Bias) • ISO/IEC TS 24028:2020 (Trustworthiness) • ISO/IEC TS 24029-1:2021 (Robustness)

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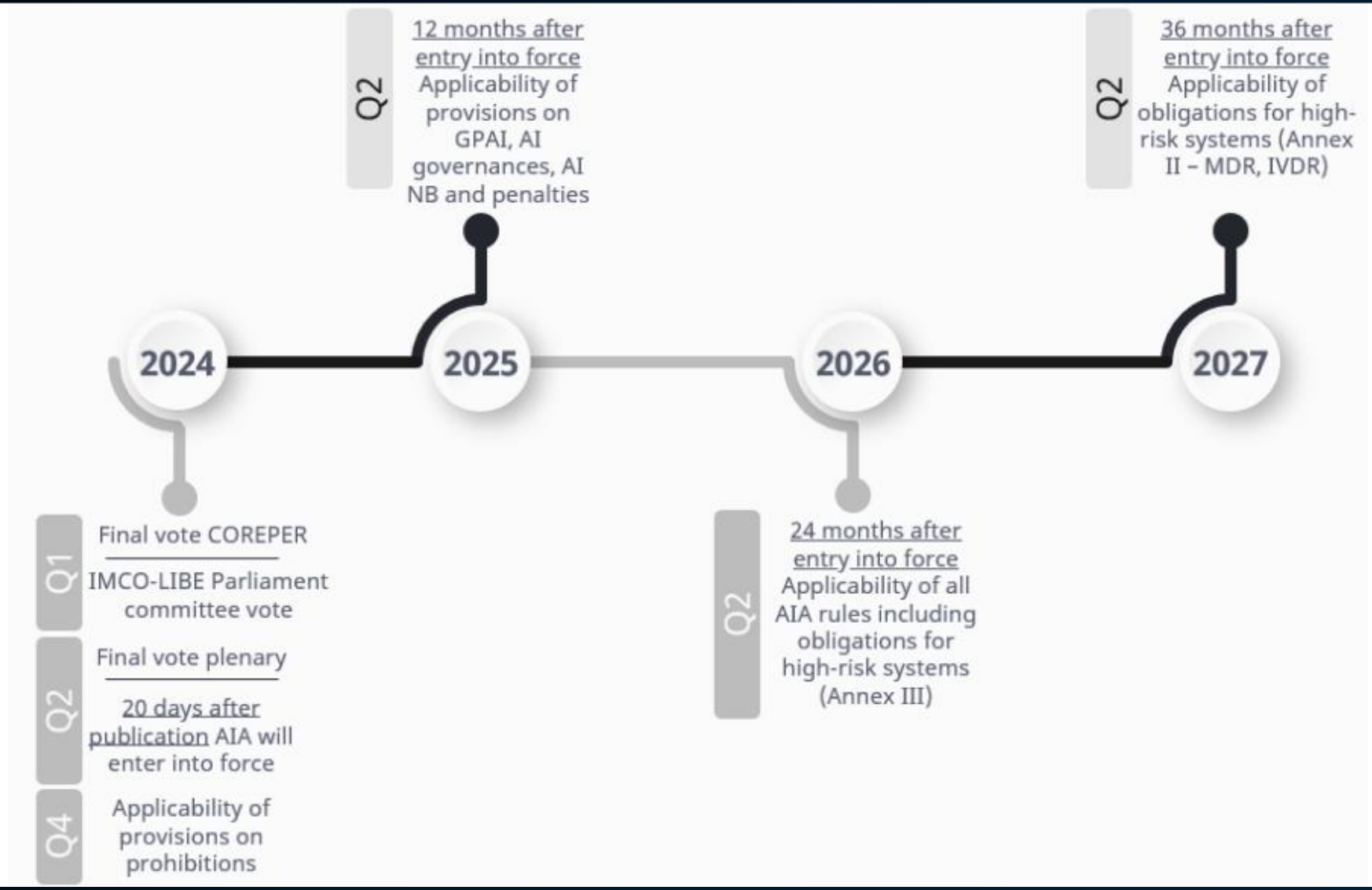
Timelines



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THANK YOU

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