

## Review

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# Regulating the future of laboratory medicine: European regulatory landscape of AI-driven medical device software in laboratory medicine

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**Abstract:** Artificial intelligence (AI) is rapidly transforming laboratory medicine, impacting medical devices and health-care practices. Despite these advancements, AI-based medical device software (MDSW) introduces a new layer of complexity in regulatory compliance. This paper outlines the regulatory landscape for MDSW and AI-driven MDSW, clarifying the responsibilities of laboratory professionals and manufacturers under the *In Vitro* Diagnostic Regulation (IVDR), ISO 15189:2022, and the Artificial Intelligence Act. An analysis of 89 MDSWs approved under the IVDR, derived from the European Database on Medical Devices (EUDAMED) reveals a diverse landscape of applications, ranging from digital pathology and molecular diagnostics to laboratory automation and clinical decision support. While Germany currently dominates the EU market for these devices, and the majority

of approved MDSW remain non-AI driven and classified as low-risk, the increasing presence of AI-powered Class C devices underscores the growing potential of software in complex diagnostic scenarios. However, realizing the full potential of AI in laboratory medicine requires careful navigation of the evolving regulatory landscape. Key challenges persist, including defining intended use, ensuring robust clinical evidence, mitigating data bias, and establishing rigorous post-market surveillance. Balancing regulatory oversight with innovation is critical to fostering the development of trustworthy AI systems without stifling progress. As regulatory frameworks continue to evolve, establishing clear validation methodologies and transparent compliance pathways will be essential to unlocking the full potential of AI in laboratory medicine while ensuring the highest standards of safety and clinical effectiveness.

**Keywords:** artificial intelligence; medical device software; regulation; laboratory medicine; diagnostics

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## Introduction

Artificial intelligence (AI) and its subset, machine learning (ML), are increasingly integrated into laboratory medicine, fundamentally transforming medical devices and healthcare practices [1]. One of the most impactful applications is in clinical decision support systems, which leverage extensive clinical datasets to develop diagnostic and prognostic models, reduce inconsistencies [2], and minimize subjectivity in test interpretation – ultimately enhancing patient care [1].

AI and automation are driving a paradigm shift in clinical laboratory operations by revolutionizing routine workflows [3]. AI-powered software and advanced robotic technologies enable laboratories to process higher volumes of tests with less reliance on manual intervention [4], thereby increasing efficiency and potentially reducing error rates. This convergence is reshaping traditional laboratory processes across all phases of the total testing cycle.

In the pre-analytical phase, AI/ML models are applied to streamline sample handling and quality assurance tasks. For instance, AI-driven systems can detect clots in blood samples [5], ensuring that only high-quality specimens proceed to the analytical phase, identify mislabelled samples and detect potential sample mix-ups [6], reducing errors that could compromise patient safety. In analytical phase, main use of the AI is digital morphological analysis of the blood cells to differentiate different types of cells [7, 8]. Moreover, AI-based quality control applications have been reported [9]. In the post-analytical phase, ML algorithms enhance diagnostic accuracy by providing predictive insights. These algorithms can analyse test results to predict diseases [10], identify the most probable variants causing rare diseases [11], differentiate between similar medical conditions [12], and biomarker level estimation [13]. Although these use cases from the literature are currently demonstrated as proof-of-concept examples, their clinical translation offers immense potential to improve the total testing process.

The integration of AI and ML models into medical devices marks a significant transformation in healthcare, offering the potential to enhance diagnostic accuracy, improve therapeutic outcomes, and streamline clinical workflows. However, as these technologies evolve, additional regulatory measures have been introduced to mitigate unique AI-related risks. Notably, the newly enacted Artificial Intelligence Act (AI Act) imposes requirements covering devices including AI-driven medical device software (MDSW), even if it is embedded in a broader test system [14].

This paper aims to delineate the regulatory landscape governing MDSW and AI-driven MDSW within laboratory medicine, with a particular focus on the synergistic

interactions between the *In Vitro* Diagnostic Regulation (IVDR), ISO 15189:2022, and the AI Act. Furthermore, we seek to elucidate the respective responsibilities of laboratory professionals and manufacturers concerning MDSW, as defined by the IVDR, AI Act, and ISO 15189:2022, acknowledging the increasing complexity of the regulatory environment. Finally, we address critical challenges such as data bias and regulatory overlap, advocating for a balanced approach to innovation that prioritizes both clinical effectiveness and patient safety.

## Importance of regulatory adherence

Adhering to regulatory standards for AI/ML-enabled medical devices is crucial for ensuring patient safety, device effectiveness, and overall trustworthiness. These standards provide a framework for the development, evaluation, and deployment of AI/ML-based medical devices, addressing the unique challenges posed by these technologies. Some of the key expected benefits of regulatory adherence are summarized below:

**Patient safety:** The most critical reason for adhering to regulatory standards is to ensure that medical devices are safe for use and do not cause harm to patients. This includes reducing the risk of algorithmic bias, poor generalization, and other issues that may affect the safety and effectiveness of the device [15].

**Device effectiveness:** Regulatory standards ensure that AI/ML-enabled medical devices perform as intended and provide accurate and reliable results. This is particularly important for diagnostic and treatment decisions, where the performance of an AI system directly impacts patient care [16].

**Trust and adoption:** Adherence to regulatory standards increases trust in AI/ML-enabled devices among healthcare professionals and patients, facilitating wider adoption of these technologies, which is essential for integrating AI into clinical practice [17].

**Market access:** Compliance with regulatory standards is a prerequisite for market access in many regions, including the European Union (EU) and the United States (US) Manufacturers must meet the requirements of these regulatory frameworks to legally sell their devices in these markets [18].

**Innovation and development:** While strict standards can be challenging, they can also foster innovation by encouraging the development of robust, well-validated, and trustworthy AI systems [19]. Clear regulatory pathways also provide a roadmap for innovators, helping them to navigate the complex regulatory landscape [20].

**Ethical considerations:** Regulatory compliance also ensures ethical standards are met, including transparency,

accountability, and a human-centric approach to AI development [21].

## Regulatory standards for AI-enabled medical device software

### Definitions

The appropriate terminology for AI-enabled medical devices varies depending on the specific regulatory context, including the EU's IVDR, and MDR.

**Medical device:** Under both the MDR and IVDR, a medical device is a broad category that includes instruments, apparatus, software, and other items intended for a medical purpose. This definition excludes products whose principal intended action is achieved by pharmacological, immunological or metabolic means.

AI/ML-enabled medical devices are considered under Software as a Medical Device (SaMD) or MDSW:

**SaMD:** SaMD is a general term used by International Medical Device Regulators Forum (IMDRF) for software that performs a medical function, but is not an essential component of a hardware medical device [22].

**MDSW:** MDSW is a term used by EU for a software designed to be used either independently or alongside other tools, for purposes outlined in the definitions of a “medical device” under the Medical Devices Regulation (MDR) or the *In Vitro* Diagnostic Medical Devices Regulation (IVDR) [23].

### Navigating the regulatory landscape for medical device software: MDR vs. IVDR

MDSW is considered under IVDR or MDR based on its intended purpose and its data source.

Under the MDR, MDSW encompasses any software intended for diagnosing, preventing, monitoring, treating, or alleviating diseases, investigating, replacing, or modifying anatomical or physiological processes, or providing therapeutic recommendations based on patient-specific data. Examples include AI software aiding in disease diagnosis through image analysis (e.g., radiology image analysis) and AI systems guiding therapy or surgery using real-time device data [23].

Under the *In Vitro* Diagnostic Medical Devices Regulation (IVDR), *In Vitro* Diagnostic (IVD) MDSW encompasses software intended to provide information about one or more of the following areas: physiological or pathological processes or states, congenital physical or mental impairments, predisposition to medical conditions or diseases, safety and

compatibility with potential recipients, treatment response or reaction predictions, or the definition and monitoring of therapeutic measures based on the *in vitro* examination of specimens derived from the human body. Examples include AI software analyzing laboratory data for disease prediction and algorithms used in genetic testing to provide actionable insights, such as cancer risk assessment [23].

A guiding flowchart for directing MDSW to its appropriate regulation is provided in Figure 1, adapted from Medical Device Coordination Group (MDCG) guidance [23]. Key differences between IVDR and MDR for medical device software is given in Supplementary Table 1.

### Medical device software according to ISO 15189:2022

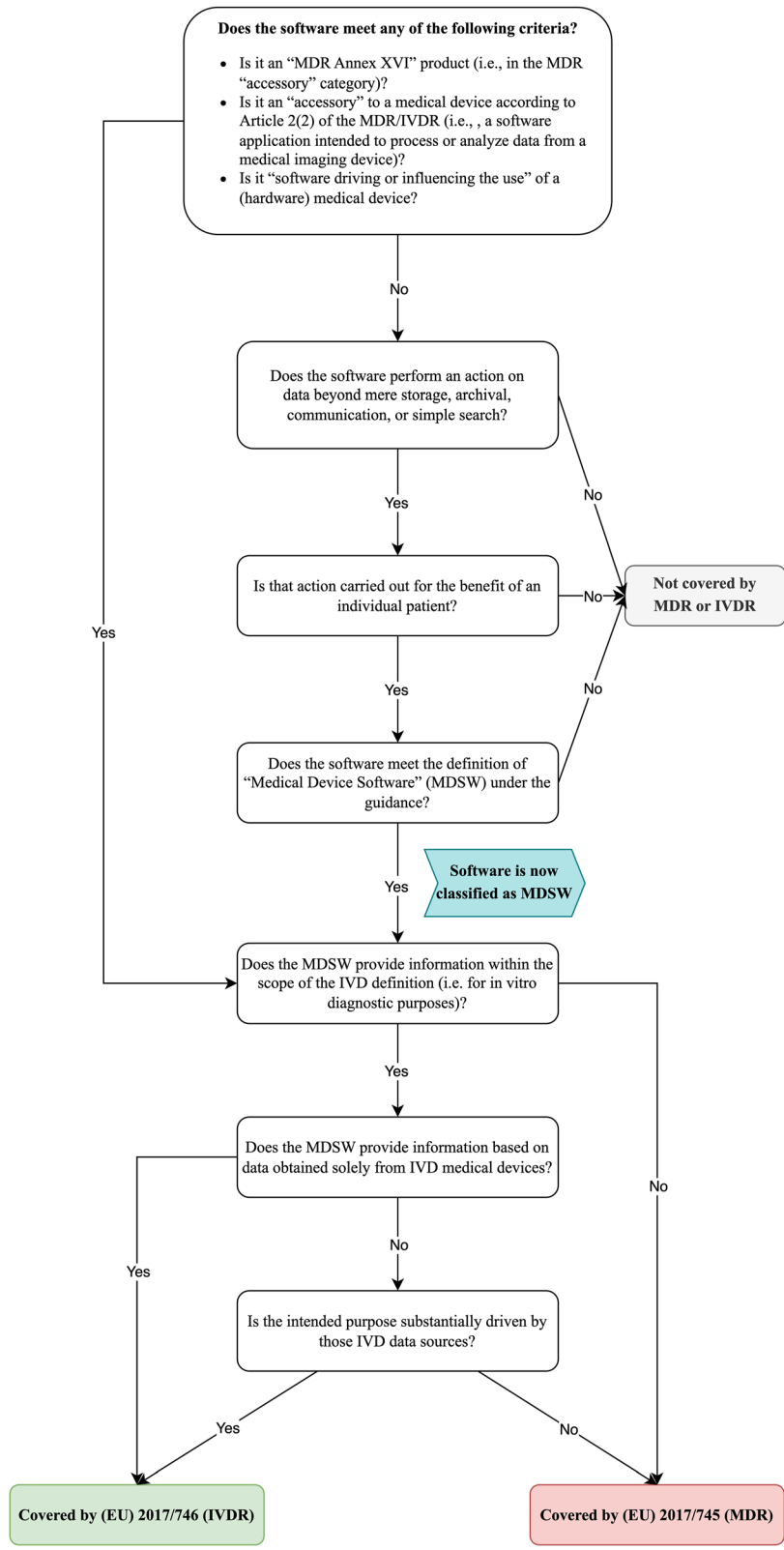
ISO 15189:2022 does not specifically discuss MDSW or software in detail, however, it does refer to the use of equipment which includes software. The standard acknowledges the importance of software in laboratory operations and its influence on the results of laboratory activities.

ISO 15189:2022 does have requirements regarding reported interpretations of laboratory results. This means that when MDSW contributes to interpretation, these requirements also apply to MDSW. Elements 7.2.2f and 7.2.4.2 require laboratories to document which aspects significantly impact the performance of the examination or interpretation. Element 7.3.7.3. a requires that the performance of interpretation be subject to external quality assessment (EQA), implying that MDSW shall be subject to EQA. The most subtle requirement is found in 7.3.4f, concerning the estimation of measurement uncertainty, which states, ‘*If the qualitative result of an examination relies on a test which produces quantitative output data and is specified as positive or negative, based on a threshold, measurement uncertainty (MU) in the output quantity shall be estimated using representative positive and negative samples.*’ This implies that any MDSW that uses input from quantitative laboratory results shall be subject to impact analysis of the MU of the input parameters on its reported outcome. The relevant aspects of software within the context of ISO 15189:2022 is given in Table 1 [24].

### Regulation of medical device software under IVDR

#### IVDR classification rules for medical device software

According to Annex VIII of the IVDR, the classification of IVD devices is determined by its intended purpose. Software that



**Figure 1:** A guiding flowchart to direct a medical device software to its appropriate regulation.

drives or influences the use of a device is classified in the same risk class as that device. Software that functions

independently is classified based on its own risk. If a device has multiple intended purposes resulting in different risk

**Table 1:** Key software-related requirements in ISO 15189:2022 and their implications [24].

| Section  | Details   | Implications for software   |
|--|---|---|
| 6.4 – Equipment                                  | Defines requirements for laboratory equipment, including software integration, selection, procurement, installation, and maintenance  | Software embedded in laboratory instruments must be properly tested and regularly maintained for compliance and functionality<br>The laboratory shall verify that the equipment conforms to specified acceptability criteria before being placed or returned into service<br>Malfunctions must be reported and addressed promptly   |
| 7.5 – Nonconforming work                         | Requires laboratories to have procedures for handling non-conforming work, including errors in examination results  | If software issues affect patient results, corrective actions must be taken<br>Laboratories should have mechanisms for reanalysis and issuing revised reports   |
| 7.6 – Control of data and information management | Establishes requirements for the validation, verification, and security of laboratory information systems (LIS), including data processing and storage. It requires that the system be validated by the supplier and verified for functionality by the laboratory before being put into use | Medical device software must be validated before use to ensure accuracy and reliability. This includes both supplier validation and laboratory verification of functionality<br>Changes to the software, including configurations, must be authorized, documented, and validated before implementation<br>System failures and corrective actions must be recorded<br>Cybersecurity measures must be implemented to protect the system from unauthorized access and safeguard data against tampering or loss |

classifications, the highest risk class applies. Similarly, if multiple classification rules apply, the rule resulting in the highest risk class shall be used.

Correct classification of IVDs, including MDSW, requires careful analysis. Rule 3, in particular, contains multiple clauses that can have significant implications and may be easily overlooked. Specifically, Rule 3(g) could apply to MDSW, as it pertains to tests used for disease staging, where an erroneous result could lead to a patient management decision resulting in a life-threatening situation. This means that MDSW used for the integrated interpretation of laboratory tests in the context of disease staging, where an erroneous result could lead to a life-threatening situation, will be classified as Class C rather than Class B. IVDR risk classification adapted for MDSW with hypothetical examples is given in Supplementary Table 2 [25].

**Medical device software approval under the IVDR**

Under the IVDR, obtaining market approval for MDSW necessitates a multi-faceted process. This process encompasses: precise qualification and classification based on the software’s intended use and associated risk; the compilation of comprehensive technical documentation; conformity assessment conducted by a notified body (with the exception of self-declaration for Class A devices); demonstration of performance in accordance with Annexes II and III of the IVDR; and the establishment of a robust post-market surveillance system. The technical documentation must meticulously detail the device’s design, manufacturing processes, and performance characteristics. Conformity assessment, a critical step, requires evaluation by EU-designated notified bodies (NBs) [26]. The European Commission publishes a list of list of these designated NBs on its official website [27], allowing manufacturers to select any legally designated NB. For IVDR class A devices, manufacturers can declare conformity themselves after drawing up technical documentation [25].

**IVDR-approved medical device software**

The European Database on Medical Devices (EUDAMED) is intended to provide public information on medical devices including IVDR-approved MDSW. The database is intended to enable the public to be informed about devices on the European Union market. The Unique Device Identification (UDI) system is used to identify devices through their distribution and use [25].

As of the EUDAMED access date of February 7, 2025, 356 MDSW were listed as conforming to the IVDR [28]. However, EUDAMED did not provide details regarding the intended use of these approved MDSW. Therefore, we investigated each listed software, documenting the manufacturer, risk class, and EU member state of approval from the EUDAMED website, and MDSW function from the manufacturers' websites. Our initial investigation of the 356 MDSW approved under IVDR revealed multiple listings for similar products from the same manufacturers, including different versions of the same MDSW. Consequently, we excluded these overlapping MDSW entries, resulting in a final count of 89 MDSW. EUDAMED reports MDSW type based on nomenclature; however, the types assigned in EUDAMED do not always align with the devices' intended uses. Therefore, we classified MDSWs based on their intended use, with definitions provided in Table 2. Based on this intended-use classification, Table 3 presents these 89 MDSW listed in EUDAMED that have emerged within the diagnostic laboratory landscape and better reflects the intended uses of these MDSW.

The distribution of intended use groups for software solutions in laboratory applications is illustrated in Figure 2A. The Digital Pathology, Imaging and Microscopy group dominates at 20.2 %, followed by the Nucleic Acid and Molecular Testing (16.9 %). Other notable groups include Laboratory Automation, Instrument Control and Workflow Management group at 13.5 % and Immunoassays, Allergy and Serology Testing (11.2 %), while Cytogenetics and Chromosome Analysis and Clinical Decision Support and Diagnostic Algorithms have the least representation.

Germany is the dominant EU market for placing devices, accounting for 38.2 %, as shown in Figure 2B. Ireland (10.1 %), Italy (9.0 %), and France (7.9 %) also contribute significantly. In contrast, Sweden and Czechia have minimal representation, each at 1.1 %.

The use of AI in medical devices is highlighted in Figure 3A, based on claims from manufacturer websites and instructions for use documents. The majority of MDSWs (87.6 %) are not AI-driven, with only a small proportion (12.4 %) incorporating AI, indicating limited adoption of AI in medical devices.

The risk classification of these devices is illustrated in Figure 3B, with the vast majority classified as low risk (Class A, 78.7 %). These devices include general laboratory software, such as laboratory information systems and tools for specimen handling, which pose minimal risk as they do not involve clinical data interpretation. Class C devices, representing 15.7 %, are MDSW critical for diagnostics, such as AI-driven tools for microbiology, antimicrobial susceptibility

**Table 2:** Definition of intended-use groups of medical device software.

| Group name  | Description  |
|---|--|
| Nucleic acid and molecular testing                                | Encompasses platforms that automate processes such as nucleic acid extraction, quantitative polymerase chain reaction, and next-generation sequencing data interpretation – including analyses of circulating tumour-derived DNA and circulating tumour DNA – pivotal for modern molecular diagnostics |
| Microbiology and antimicrobial susceptibility testing             | Focuses on automating bacterial culture plate analysis and antimicrobial susceptibility testing, streamlining workflows in microbial identification and resistance profiling   |
| Digital pathology, imaging and microscopy                         | Software solutions manage and analyse pathology images, ranging from breast immunohistochemistry to cervical cytology, thereby facilitating remote diagnostics and precise image interpretation  |
| Flow cytometry, hematology and blood banking                      | Includes tools that optimize flow cytometer workflows, cell enumeration, and integrated data management between instruments  |
| Laboratory automation, instrument control and workflow management | Covers middleware and control systems that integrate multiple laboratory instruments and streamline overall lab operations, ensuring seamless sample handling and data exchange  |
| Immunoassays, allergy and serology testing                        | Offers solutions for quantitative and semi-quantitative analyses of immunoglobulins and other serological markers, supporting allergy diagnostics and immunoassay interpretation   |
| Cytogenetics and chromosome analysis                              | Comprises advanced tools for automating karyotyping and fluorescence <i>in situ</i> hybridization (FISH) analysis to detect chromosomal abnormalities  |
| Point-of-care and at-home testing                                 | Provides accessible, user-friendly applications ranging from digital lateral flow test readers to diabetes management platforms for use outside traditional lab settings   |
| Instrument-specific analytical systems                            | Consists of software engineered for precise control and analysis on specific instruments, such as fluorescence analysers and mass spectrometry devices   |
| Laboratory information systems and data management                | Integrates data management across laboratory instruments, facilitating efficient workflow coordination and robust data exchange  |
| Clinical decision support and diagnostic algorithms               | Delivers decision-support tools that harness patient data and advanced algorithms to guide clinical diagnostics, such as liver fibrosis assessment   |

**Table 3:** Medical device software approved under IVDR.

| Device name                      | Risk class | Manufacturer            | Type   | Member state of the placing on the EU market of the device | AI-driven | Function   | Intended use groups   |
|----------------------------------|------------|-------------------------|--|--|-----------|--|---|
| bAPP                             | Class A    | Hyris Srl               | Nucleic acid testing instruments except microarrays – software accessories | Italy  | Yes       | AI-driven automatic data interpretation of nucleic acid testing  | Nucleic acid and molecular testing                                |
| Software Hi                      | Class A    | Edif instruments S.r.l. | Chemistry analysers – ivd medical device software                          | Italy  |           | Software to be used with analytical units to operate the device and streamlines lab workflows  | Laboratory automation, instrument control and workflow management |
| PhenoMATRIX                      | Class C    | Copan Wasp S.r.l.       | Various microbiology instruments – ivd medical device software             | Italy  | Yes       | AI-driven software suite that automates bacterial culture plate analysis by interpreting, segregating, tagging, and releasing plates based on colony features, lab rules, and LIS data                     | Microbiology and antimicrobial susceptibility testing             |
| Radian Expert System             | Class C    | Copan Wasp S.r.l.       | Antibiotic susceptibility analysers – medical device software              | Italy  | Yes       | AI-based disc diffusion antimicrobial susceptibility test interpretation   | Microbiology and antimicrobial susceptibility testing             |
| Software HALO Measure & Visual   | Class B    | Copan Wasp S.r.l.       | Antibiotic susceptibility analysers – medical device software              | Italy  |           | Software to facilitate the measurement of antimicrobial susceptibility testing halos   | Microbiology and antimicrobial susceptibility testing             |
| SureScreen Covid/Flu Test Reader | Class A    | TestCard Ltd            | Urine strip readers <sup>a</sup>   | Germany  |           | Digital reader application for lateral flow Covid/flu test reader  | Point-of-care and at-home testing                                 |
| Roche Combur-10 UX StripReader   | Class A    | TestCard Ltd            | Urine strip readers  | Netherlands  |           | Urine strip reader software  | Point-of-care and at-home testing                                 |
| IndiNet CRC                      | Class A    | 2cureX A/S              | Various sample processing instruments – ivd medical device software        | Denmark  | Yes       | AI-driven image analysis to determine tumor growth inhibition induced by specific anti-neoplastic drugs of patient derived 3D microtumors from fresh non-fixated samples of colorectal cancer (CRC) tissue | Digital pathology, imaging and microscopy                         |
| IndiTreat Image Uploader         | Class A    | 2cureX A/S              | Various general purpose ivd instruments – software accessories             | Denmark  |           | Software to facilitate the secure transfer of CRC screening image files from a local computer to a centralized server for downstream data processing and analysis  | Digital pathology, imaging and microscopy                         |

Table 3: (continued)

| Device name                                       | Risk class | Manufacturer                    | Type  | Member state of the placing on the EU market of the device | AI-driven | Function  | Intended use groups   |
|---|------------|---------------------------------|---|--|-----------|---|---|
| NGEx FFPE DNA Purification Software               | Class A    | Oncodia AB                      | Multiple clin. chem lab reagents – other                            | Sweden   |           | Software to facilitate automated extraction of nucleic acids from formalin-fixed, paraffin-embedded (FFPE) tissue sections  | Nucleic acid and molecular testing                                |
| AQUIOS STEM Software kit                          | Class A    | IMMUNOTECH SAS                  | Auxiliary and supplemental reagents for flow cytometry – other      | France   |           | Software to facilitate automated enumeration of CD34+ stem cells  | Flow cytometry, hematology and blood banking                      |
| REMISOL Advance                                   | Class A    | NORMAND-INFO S.A.S.U            | Various sample processing instruments – ivd medical device software | France   |           | Middleware/Software to facilitate sample workflow, autoverification, quality management   | Laboratory automation, instrument control and workflow management |
| Navios EX Instrument & Software                   | Class A    | Beckman Coulter Ireland Inc.    | Cytoflowmeters – software accessories                               | Ireland  |           | Software to facilitate flow cytometer workflow  | Flow cytometry, hematology and blood banking                      |
| MicroScan HighFlexX Software v2.9, Electronic     | Class B    | Beckman Coulter Inc.            | Antibiotic susceptibility analysers – medical device software       | Ireland  |           | Software to facilitate antimicrobial susceptibility testing   | Microbiology and antimicrobial susceptibility testing             |
| AQUIOS Designer Software                          | Class A    | Beckman Coulter Ireland Inc.    | Cytoflowmeters – software accessories                               | Ireland  |           | Software to automate the reagent combinations, sample preparation, tracking of QC results for flow cytometer analysis   | Flow cytometry, hematology and blood banking                      |
| Kaluza C Software                                 | Class A    | Beckman Coulter Inc.            | Cytoflowmeters – software accessories                               | Ireland  |           | Software to facilitate flow cytometer analysis  | Flow cytometry, hematology and blood banking                      |
| MicroScan LabPro Connect V5.0 System DVD Kit (MR) | Class B    | Beckman Coulter Inc.            | Antibiotic susceptibility analysers – medical device software       | Ireland  |           | Software to facilitate antimicrobial susceptibility testing   | Microbiology and antimicrobial susceptibility testing             |
| DxOne Workflow Manager                            | Class A    | Beckman Coulter Biomedical GmbH | Robotic sample processing systems – software accessories            | Germany  |           | Middleware/Software to facilitate sample workflow, autoverification, automation   | Laboratory automation, instrument control and workflow management |
| Fagron TrichoTest                                 | Class C    | Fagron Genomics                 | Micro-array instruments – ivd medical device software               | Spain  |           | Software to personalize alopecia treatment (androgenetic, areata, and telogen effluvium) by analyzing 16 SNPs related to treatment response and combining this genetic data with patient history to recommend the most effective personalized treatment | Nucleic acid and molecular testing                                |

Table 3: (continued)

| Device name                     | Risk class | Manufacturer              | Type  | Member state of the placing on the EU market of the device | AI-driven | Function  | Intended use groups                                   |
|---------------------------------|------------|---------------------------|---|--|-----------|---|---|
| ImmuLINK®                       | Class A    | Immucor, Inc.             | Blood grouping analysers – software accessories                                     | Germany  |           | Software solution for blood banks that facilitates data exchange and management between instruments, blood bank software, and LIS, enabling reporting, results comparison, automated reflex testing, remote validation/editing, and bidirectional communication | Flow cytometry, hematology and blood banking          |
| RAPTOR SERVER Analysis Software | Class C    | MacroArray Diagnostics    | Mixed panel multiparameter analysers – ivd medical device software                  | Austria  |           | Software to perform quantitative (sIgE) and semi-quantitative (tIgE, IgG) analysis, provides basic interpretation for allergy diagnosis support   | Immunoassays, allergy and serology testing            |
| MAGELLAN V7.X TRA               | Class A    | Tecan Austria GmbH        | Limited panel immunochemistry analysers – ivd medical device software               | Austria  |           | Software to control microplate readers and analyzes their results   | Immunoassays, allergy and serology testing            |
| RADIPREP                        | Class A    | KH Medical Co., Ltd.      | Reagents for dna and/or rna extraction and preparation: bacteria and/or virus       | Germany  |           | Software to automate DNA and/or RNA extraction and preparation  | Nucleic acid and molecular testing                    |
| LUCIA Cytogenetics              | Class C    | Laboratory imaging s.r.o. | Laboratory instruments for microscopic investigations – ivd medical device software | Czechia  |           | Software to assists lab professionals in analyzing chromosome images (karyotyping and FISH) to diagnose chromosomal disorders   | Cytogenetics and chromosome analysis                  |
| GOODGUT-Test                    | Class C    | GOODGUT, SLU              | Various general purpose ivd instruments – software accessories                      | Spain  |           | Software to analyze qPCR results of microorganisms in stool samples   | Microbiology and antimicrobial susceptibility testing |
| ZENIT HEP2 CLASSIFIER           | Class B    | Visia Lab S.r.l.          | Various general purpose ivd instruments – software accessories                      | Italy  |           | Software classifies positive/negative results for Zenit ANA HEp-2 (including intensity measurement and pattern/mitosis recognition), ANCA E/F (including pattern definition), and DNA crithidia slides  | Immunoassays, allergy and serology testing            |
| DNLAB IVD CORE                  | Class A    | Dedalus Italia SpA        | Various general purpose ivd instruments – ivd medical device software               | Italy  |           | Software managing the total testing process, for microbiology, and genetics labs  | Laboratory information systems and data management    |

Table 3: (continued)

| Device name   | Risk class | Manufacturer                                | Type  | Member state of the placing on the EU market of the device | AI-driven | Function  | Intended use groups   |
|---|------------|---|---|--|-----------|---|---|
| Oncobit PM Analyzer   | Class C    | Oncobit AG                                  | Tests for acquired genetic or chromosomal alterations – other                       | Germany  |           | Software to interpret specific cancer markers in circulating tumor-derived DNA (ctDNA) from the blood | Nucleic acid and molecular testing                                |
| ALTOSTAR CONNECT SW   | Class A    | Hamilton Bonaduz AG                         | Ivd general use consumables devices – other accessories                             | Germany  |           | Software controlling automation (analyzers, samples, controls)  | Laboratory automation, instrument control and workflow management |
| Field Verification Kit  | Class A    | Hamilton Bonaduz AG                         | Ivd general use consumables devices – other accessories                             | Germany  |           | Software used to ensure optimal pipetting performance   | Laboratory automation, instrument control and workflow management |
| cobas 8100 automated workflow series Language Pack – English version 4.8.en | Class A    | Hitachi High-Tech Corporation               | Various sample processing instruments – software accessories                        | Germany  |           | Software to facilitate automation (sample workflow etc.)  | Laboratory automation, instrument control and workflow management |
| cobas c 513 analyzer system Software Version 02-06                          | Class A    | Hitachi High-Tech Corporation               | Chemistry analysers – software accessories  | Germany  |           | Software for analyzer user interface  | Laboratory automation, instrument control and workflow management |
| ASI IVD System V 8.4  | Class A    | Applied Spectral Imaging Ltd                | Laboratory instruments for microscopic investigations – ivd medical device software | Germany  | Yes       | AI-based karyotyping and FISH analysis  | Cytogenetics and chromosome analysis                              |
| Pathological Diagnosis Image Processing Software                            | Class A    | Beijing Thorough Future Technology Co., Ltd | Devices for pathology tests – other   | Germany  |           | Analysis of pathology images  | Digital pathology, imaging and microscopy                         |
| IHC Pathology Image Processing Software                                     | Class A    | Hangzhou PathoAI Technology Co., Ltd.       | Various processing instruments for histology/cytology – ivd medical device software | Germany  |           | Analysis of pathology images  | Digital pathology, imaging and microscopy                         |
| Cervical Cytology Image Processing Software                                 | Class A    | Hangzhou PathoAI Technology Co., Ltd.       | Various processing instruments for histology/cytology – ivd medical device software | Germany  |           | Analysis of cervical cytology images  | Digital pathology, imaging and microscopy                         |
| Tencent AIMIS Digital Pathology Platform                                    | Class A    | Tencent Healthcare (Changsha) Co., Ltd.     | IVD instruments – other   | United Kingdom (Northern Ireland only)                     | Yes       | AI-based pathological image analysis  | Digital pathology, imaging and microscopy                         |
| Uni-medica Fluorescent Immunoanalyzer                                       | Class A    | Shenzhen Uni-medica Technology Co., Ltd.    | Immunochemistry readers   | Spain  |           | Software of a fluorescence immunoassay  | Immunoassays, allergy and serology testing                        |

Table 3: (continued)

| Device name   | Risk class | Manufacturer   | Type  | Member state of the placing on the EU market of the device | AI-driven | Function   | Intended use groups                                 |
|---|------------|--|---|--|-----------|--|---|
| Automatic Nucleic Acid System                         | Class A    | Shenzhen Uni-medica Technology Co., Ltd.                   | Various sample processing instruments – other                                       | Spain  |           | Software of automated nucleic acid extraction system                 | Instrument-specific analytical systems              |
| Uni-medica - Nucleic Acid Extractor                   | Class A    | Shenzhen Uni-medica Technology Co., Ltd.                   | Nucleic acid testing integrated extraction/amplification/detection systems          | Spain  |           | Software of nucleic acid extractor                                   | Instrument-specific analytical systems              |
| Portable Incubator                                    | Class A    | Shenzhen Superbio Technology Co., Ltd.                     | Various rapid test chemistry/immunochemistry instruments – other                    | Ireland  |           | Software of portable incubator                                       | Point-of-care and at-home testing                   |
| Breast Immunohistochemistry Image Processing Software | Class A    | Shanghai Sense-time Intelligent Technology Co., Ltd.       | Various general purpose ivd instruments – ivd medical device software               | Germany  |           | Software for breast immunohistochemistry image processing            | Digital pathology, imaging and microscopy           |
| Automatic Immunoblot Instrument                       | Class A    | Hangzhou Zheda Dixun Biological Gene Engineering Co., Ltd. | Immunochemistry instruments – other   | United Kingdom (Northern Ireland only)                     |           | Software of automatic immunoblot instrument                          | Immunoassays, allergy and serology testing          |
| Elisa Plate Reader                                    | Class A    | Biobase Bioindustry (Shandong) Co., Ltd.                   | Immunochemistry readers   | Germany  |           | Software of Elisa plate reader                                       | Immunoassays, allergy and serology testing          |
| Laboratory Data Management Software                   | Class A    | Shenzhen Mindray Bio-Medical Electronics Co., Ltd.         | IVD instruments – other   | Germany  |           | Software for laboratory data management                              | Laboratory information systems and data management  |
| Eonis EASI  | Class A    | Wallac Oy  | Nucleic acid testing instruments except microarrays – hardware accessories          | Finland  |           | Software to streamline molecular testing                             | Nucleic acid and molecular testing                  |
| mariPOC® Software                                     | Class A    | ArcDia International Oy Ltd                                | Limited panel immunochemistry analysers – ivd medical device software               | Finland  |           | Software of an automated point-of-care diagnostic platform           | Point-of-care and at-home testing                   |
| Case Manager DX                                       | Class A    | 3DHISTECH Kft.   | Laboratory instruments for microscopic investigations – ivd medical device software | Germany  |           | Digital pathology management system                                  | Digital pathology, imaging and microscopy           |
| Release 23SEP2013                                     | Class A    | RefLab Aps   | Limited panel immunochemistry analysers – software accessories                      | Denmark  |           | Software of immunochemistry analysers                                | Immunoassays, allergy and serology testing          |
| Agilent CytoDx Software                               | Class C    | Agilent Technologies, Inc.                                 | Various general purpose ivd instruments – ivd medical device software               | Denmark  |           | Software to analyze microarray images                                | Digital pathology, imaging and microscopy           |
| Alissa Interpret                                      | Class A    | Agilent Technologies Singapore (International) Pte Ltd     | Various general purpose ivd instruments – ivd medical device software               | Denmark  |           | Software for genomic data interpretation                             | Nucleic acid and molecular testing                  |
| LiverPRO  | Class B    | Evido ApS  | Chemistry analysers – ivd medical device software                                   | Denmark  |           | Software to diagnose liver fibrosis using age and blood test results | Clinical decision support and diagnostic algorithms |

Table 3: (continued)

| Device name   | Risk class | Manufacturer         | Type  | Member state of the placing on the EU market of the device | AI-driven | Function  | Intended use groups   |
|---|------------|----------------------|---|--|-----------|---|---|
| BLUESCAN1/BlueScan Scanner + DR DOT LIC4/ Dr Dot Software | Class A    | D-tek s.a.           | Automated immuno-chemistry analysers – low routine (throughput $\leq 100$ test/h) | Belgium  |           | Software for semi-quantitative interpretation of immunodot assays   | Immunoassays, allergy and serology testing                        |
| PMA.core  | Class C    | Pathomation BV       | Various general purpose ivd instruments – ivd medical device software             | Belgium  |           | Software for management of whole slide images in digital pathology  | Digital pathology, imaging and microscopy                         |
| Idylla™ Console Software Plus (CSW+)                      | Class A    | Biocartis NV         | Nucleic acid testing instruments except micro-arrays – software accessories       | Belgium  |           | Software for management of a molecular diagnostics system   | Laboratory information systems and data management                |
| EntericBio Workstation                                    | Class A    | Serosep Limited      | Robotic sample processing systems – other   | Ireland  |           | Software to streamline the detection of gastrointestinal pathogens in clinical samples  | Microbiology and antimicrobial susceptibility testing             |
| XF-1600 TBNK SW   | Class A    | SYSMEX Corporation   | Cytoflowmeters – ivd medical device software                                      | Germany  |           | Software to streamline cytoflowmeter workflow and to facilitate lymphocyte subset analysis  | Flow cytometry, hematology and blood banking                      |
| CyFlow WA   | Class A    | SYSMEX Corporation   | Cytoflowmeters – ivd medical device software                                      | Germany  |           | Software connecting haematology and clinical flow cytometry data to support comprehensive diagnostic workflows  | Flow cytometry, hematology and blood banking                      |
| Urinalysis Work Area Information Management System        | Class A    | SYSMEX Corporation   | Automated urine analysers – software accessories                                  | Germany  |           | Software integrates various urinalysis analyzers and streamlines workflow   | Laboratory automation, instrument control and workflow management |
| WeCheck for S onyx  | Class A    | ARKRAY Factory, Inc. | Various diabetes monitoring instruments – software accessories                    | Italy  |           | Software as a diabetes management tool that allows users to log blood glucose levels, meals (including photos and nutritional information), and other vital signs | Point-of-care and at-home testing                                 |
| IntelliPlex 1000 $\pi$ Code Processor (Software)          | Class A    | PlexBio Co., Ltd.    | Various general purpose ivd instruments – other                                   | Poland   |           | Software of automated workstation of multiplexing assays  | Instrument-specific analytical systems                            |
| PlexBio 100 Fluorescent Analyzer (Software)               | Class A    | PlexBio Co., Ltd.    | Chemistry instruments - other   | Poland   |           | Software of a fluorescence analyzer   | Instrument-specific analytical systems                            |
| 501RP+  | Class A    | Tosoh Corporation    | Various diabetes monitoring instruments – software accessories                    | Belgium  |           | Data management software to enhance laboratory workflow efficiency  | Laboratory automation, instrument control and workflow management |

Table 3: (continued)

| Device name   | Risk class | Manufacturer                            | Type  | Member state of the placing on the EU market of the device | AI-driven | Function  | Intended use groups   |
|---|------------|---|---|--|-----------|---|---|
| UV-VIS DETECTOR SPD-40 CL Software                      | Class A    | Shimadzu Corporation                    | Mass – spectrometry system  | Germany  |           | Software of Mass - spectrometry system/ high-performance liquid chromatography device | Instrument-specific analytical systems                            |
| LabSolutions Insight LCMS CL                            | Class A    | Shimadzu Corporation                    | Mass – spectrometry system  | Germany  |           | Software for management of multi-component mass spectrometry data                     | Instrument-specific analytical systems                            |
| PathoZoom® LiveView Macro, Scan & LiveView, Digital Lab | Class A    | Smart In Media AG                       | Laboratory instruments for microscopic investigations – ivd medical device software | Germany  |           | Software for the processing of pathology slide images                                 | Digital pathology, imaging and microscopy                         |
| P001 Medical device software                            | Class C    | Limbus Medical Technologies GmbH        | Various general purpose ivd instruments – ivd medical device software               | Germany  |           | Software for processing and interpretation of next-generation sequencing (NGS) data   | Nucleic acid and molecular testing                                |
| SIEMENS Protis Assessments                              | Class A    | Intellitec Healthcare IT Solutions GmbH | Limited panel immunochemistry analysers – software accessories                      | Germany  |           | Software for management of laboratory workflow  | Laboratory information systems and data management                |
| MH Guide  | Class C    | Molecular Health GmbH                   | Nucleic acid testing instruments except microarrays – ivd medical device software   | Germany  |           | Software to interpret genomic data from next-generation sequencing (NGS)              | Nucleic acid and molecular testing                                |
| Extended IPU  | Class A    | Sysmex Europe SE                        | Automated whole blood hematology analysers – ivd medical device software            | Germany  |           | Software to optimize laboratory workflows across multiple disciplines                 | Laboratory automation, instrument control and workflow management |
| Cube DataReader Software                                | Class A    | BIOSYNEX Technologies GmbH              | Medical device software – not included in other classes                             | Germany  |           | Software facilitates the transfer and management of measurement data                  | Laboratory automation, instrument control and workflow management |
| Labscope 4.3  | Class A    | Carl Zeiss Microscopy GmbH              | Laboratory instruments for microscopic investigations – software accessories        | Germany  |           | Software for acquisition of images and videos of microscopic samples                  | Digital pathology, imaging and microscopy                         |
| ZEN 3.9   | Class A    | Carl Zeiss Microscopy GmbH              | Laboratory instruments for microscopic investigations – software accessories        | Germany  | Yes       | Software to facilitate microscopic image acquisition, processing, and analysis        | Digital pathology, imaging and microscopy                         |
| RIDA®SEEK   | Class A    | R-Biopharm AG                           | Nucleic acid testing instruments except microarrays – software accessories          | Germany  |           | Software to interpret real-time PCR results   | Nucleic acid and molecular testing                                |
| RIDA qLine® Soft  | Class A    | R-Biopharm AG                           | Automated immunochemistry analysers – software accessories                          | Germany  |           | Software for the quantitative analysis of specific IgE antibodies                     | Immunoassays, allergy and serology testing                        |

Table 3: (continued)

| Device name  | Risk class | Manufacturer               | Type  | Member state of the placing on the EU market of the device | AI-driven | Function   | Intended use groups   |
|--|------------|----------------------------|---|--|-----------|--|---|
| RIDASOFT® FoodGuide  | Class A    | R-Biopharm AG              | Various general purpose ivd instruments – software accessories                      | Germany  |           | Software to interpret and analyze data from microarray enzyme immunoassay  | Immunoassays, allergy and serology testing                        |
| Hexalis Calcul, Dedalus LIS Calculation Engine             | Class A    | Dedalus Health-Care France | Various sample processing instruments – software accessories                        | France   |           | Software as a laboratory information system  | Laboratory information systems and data management                |
| My Uriki   | Class A    | Iki                        | Automated urine analyzers – software accessories                                    | France   |           | Software to enable at-home urine testing and obtain recommendations  | Point-of-care and at-home testing                                 |
| Endotest Diagnostic  | Class C    | Ziwig                      | Nucleic acid testing instruments except microarrays – ivd medical device software   | France   | Yes       | Software analysing salivary microRNA results for the early detection of endometriosis  | Nucleic acid and molecular testing                                |
| Visiocyt Bladder   | Class C    | VitaDX International       | Laboratory instruments for microscopic investigations – ivd medical device software | France   | Yes       | Software analyzes urine samples using advanced imaging to identify cancerous cells for early diagnosis of bladder cancer               | Digital pathology, imaging and microscopy                         |
| Yumizen P8000  | Class A    | HORIBA ABX SAS             | Automated whole blood hematology analysers – software accessories                   | France   |           | Software to enhance laboratory workflows and multi-instrument integration  | Laboratory automation, instrument control and workflow management |
| FullFocus  | Class A    | Paige.AI, Inc.             | Laboratory instruments for microscopic investigations – software accessories        | United Kingdom (Northern Ireland only)                     | Yes       | Software to assist pathological diagnostic processes   | Digital pathology, imaging and microscopy                         |
| Concentriq AP-Dx   | Class A    | Proscia, Inc.              | Various general purpose ivd instruments – ivd medical device software               | Netherlands  | Yes       | Software to view, interpret, and manage of pathology sample images for primary diagnosis   | Digital pathology, imaging and microscopy                         |
| Oncotype DX Breast Recurrence Score Computational Software | Class C    | Genomic Health Inc.        | Genetic tests – other   | Germany  |           | Software for generating a recurrence score using genomic assay designed to analyze the 21 specific genes within a breast cancer tissue | Nucleic acid and molecular testing                                |
| IDPEDx Software Module & Applications                      | Class A    | Illumina, Inc.             | Genetic tests – other   | Netherlands  |           | Software for facilitating targeted sequencing applications in clinical diagnostics   | Nucleic acid and molecular testing                                |
| Local Run Manager VeriSeq™ NIPT module                     | Class A    | Illumina, Inc.             | Genetic tests – other   | Netherlands  |           | Software for the management of sequencing for the non-Invasive prenatal testing  | Nucleic acid and molecular testing                                |

Table 3: (continued)

| Device name                       | Risk class | Manufacturer                   | Type   | Member state of the placing on the EU market of the device | AI-driven | Function  | Intended use groups                       |
|-----------------------------------|------------|--------------------------------|--|--|-----------|---|---|
| VeriSeq™ NIPT Workflow Manager v2 | Class A    | Illumina, Inc.                 | Genetic tests – other  | Netherlands  |           | Software provides a graphical interface that guides users through protocol selection and assay setup of non-Invasive prenatal testing | Nucleic acid and molecular testing        |
| Aperio GT 450 SAM DX Software     | Class A    | Leica Biosystems Imaging, Inc. | Digital laboratory microscopes   | Ireland  |           | Software for the management and monitoring of digital pathology slide scanner   | Digital pathology, imaging and microscopy |
| VeriSeq™ NIPT Workflow Manager v2 | Class A    | Leica Biosystems Imaging, Inc. | Laboratory instruments for microscopic investigations - software accessories | Ireland  |           | Digital slide viewing software to facilitate the qualitative review and interpretation of digital images of surgical pathology slides | Digital pathology, imaging and microscopy |

The information in the Table regarding whether the software is AI-driven is based on explicit statements found on the manufacturers' websites. <sup>a</sup>The claim in the EUDAMED database does not conform to the software's functionality.

testing, and genetic or cancer diagnostics, which directly impact patient care. Class B devices, accounting for 5.6 %, reflect moderate-risk applications. The absence of Class D devices in the plot aligns with their rarity, as they are reserved for the highest-risk applications like detecting transmissible agents or blood typing for transfusion. This distribution highlights the dominance of low-risk tools in clinical laboratories, while the representation of Class C underscores the growing role of software in challenging diagnostic cases.

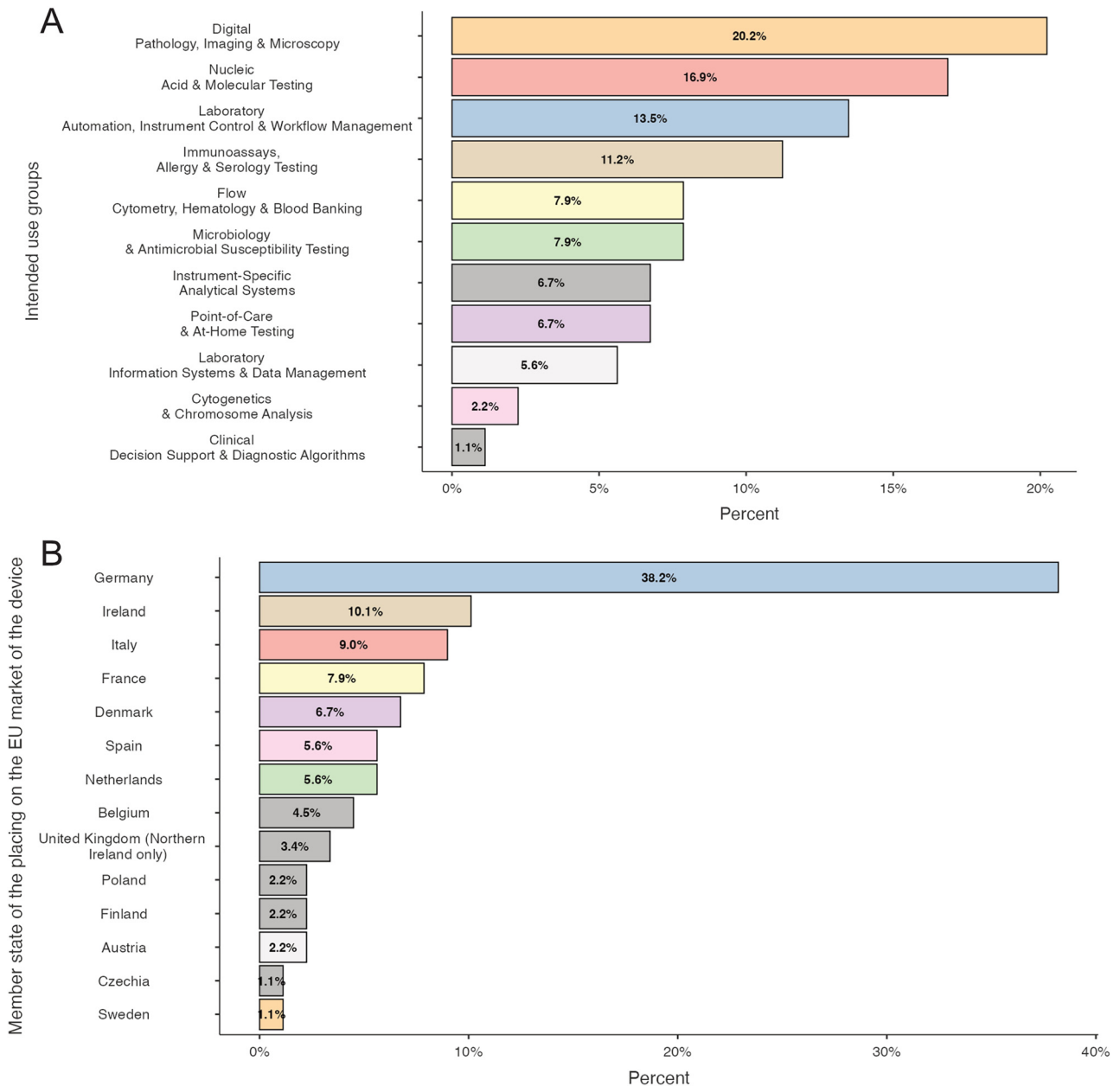
## The Artificial Intelligence Act – Regulation (EU) 2024/1689

The AI Act's goal is to create trustworthy, human-centric AI, ensuring protection of public health, safety, and fundamental rights within the EU [14]. The AI Act is intended to be complementary to existing IVDR and MDR. This means that AI-based MDSW used in laboratory medicine will need to comply with both the requirements of the IVDR and the AI Act, where applicable. The AI Act provides for a staggered timetable for implementation, so that the various sections come into force at different time (Figure 4).

The AI Act introduced the term “AI system,” a machine-based system designed to operate with varying levels of autonomy and that may exhibit adaptiveness after deployment. AI systems infer outputs, such as predictions, content, recommendations, or decisions, from input data, utilizing methods such as machine learning, logic-based, or knowledge-based approaches. Thus, the term “AI system” encompasses AI-based MDSW.

AI systems are classified as high-risk when they both function as a safety component or product under EU harmonisation legislation listed in Annex I such as IVDR and MDR, and when the product or AI system requires mandatory third-party conformity assessment under the legislations including MDR and IVDR prior to market placement or service. Consequently, AI-based MDSWs classified as class B, C, and D are considered high-risk AI systems under the AI Act. Among the eleven AI-based MDSW listed in Table 3, seven were class A and four were class C, meaning four class C MDSWs are required to comply with the high-risk AI system requirements of the AI Act.

The AI Act places ultimate responsibility on the manufacturer (or ‘provider’) to ensure that AI-driven MDSW complies with high-risk requirements where relevant. However, the ‘deployers’ of high-risk AI systems – which can include laboratory professionals – also have specific obligations.

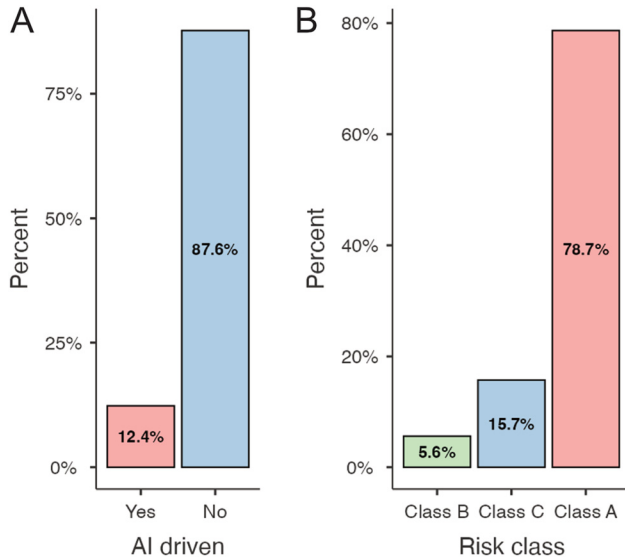


**Figure 2:** Intended use groups and EU market distribution of medical devices. (A) Distribution of medical devices by intended use group. (B) Distribution of medical devices across EU markets.

AI systems may evolve over time through self-learning and adaptation after deployment. Self-learning AI changes are not considered substantial modifications requiring a new assessment if they were pre-determined, assessed initially for conformity, and documented in the technical documentation as per Annex IV. Providers of high-risk AI systems must have a post-market monitoring system to address evolving risks from learning AI after deployment, acknowledging that their behaviour can change over time.

### Responsibilities of laboratory professionals and manufacturers regarding medical device software according to IVDR, AI Act, and ISO 15189:2022

The responsibilities of laboratory professionals and manufacturers with regard to MDSW are detailed in Tables 4 and 5, respectively. It is crucial to note that the AI Act pertains exclusively to AI-driven MDSW.



**Figure 3:** Proportion of AI-driven devices and device risk classifications. (A) Distribution of medical devices based on AI integration. (B) Classification of devices by risk level.

Key differences emerge in regulatory focus and the division of responsibilities between laboratory professionals and manufacturers regarding medical device software. Manufacturers face comprehensive obligations under both the IVDR and the AI Act for high-risk systems, including establishing robust quality management systems (QMS), lifecycle risk management, extensive technical documentation, conformity assessments, post-market surveillance, and product registration. In contrast, laboratory professionals' obligations are more focused on the correct use and monitoring of these devices, especially under the AI Act and IVDR, such as using devices per instructions, managing input data, monitoring performance, reporting incidents, and maintaining user logs for high-risk AI.

Regulatory differences are also notable. ISO 15189 uniquely mandates a comprehensive QMS and proactive risk management for the laboratory itself, irrespective of the devices used. The IVDR and AI Act primarily place QMS and primary risk management duties on the manufacturer, only requiring labs to have a QMS under IVDR if they create 'in-house' devices. The AI Act introduces specific requirements not explicitly mirrored in IVDR or ISO 15189, such as detailed data governance practices for AI training data incumbent on the provider, and explicit user obligations regarding human oversight and input data suitability for high-risk AI systems. Furthermore, while both IVDR and the AI Act require manufacturers to ensure performance and security, IVDR places a stronger emphasis on specific clinical performance evaluation for diagnostic purposes, whereas the AI Act focuses more broadly on accuracy, robustness, and cybersecurity metrics for AI systems.

## Challenges

As AI systems increasingly integrate into laboratory medicine and healthcare as MDSW, ensuring their safety, efficacy, and compliance with regulatory standards becomes critical yet challenging. The diverse and flexible nature of general-purpose AI models complicates determining their "intended use," directly influencing applicable regulations. Furthermore, issues such as data quality and bias, selection of appropriate performance metrics, and the accurate management of measurement uncertainty further complicate the landscape. Laboratories must navigate overlapping regulatory frameworks, including the AI Act, IVDR, and ISO 15189, while facing uncertainties regarding enforcement, liability, and resource-intensive compliance requirements. Balancing innovation with patient safety requires dynamic regulatory adaptation, robust post-market surveillance, and clear guidelines to ensure AI technologies enhance rather than compromise healthcare outcomes.

**Defining "intended use":** The "intended use" of an AI system can be difficult to determine, especially with general-purpose AI models like large language models that may have multiple applications. This is a challenge as the applicability of regulations based on intended use. For example, a general-purpose AI model, when incorporated into a medical device, becomes subject to medical device regulations based on the new intended use [29].

**Data quality and bias:** AI/ML models are heavily reliant on the quality of training data. If the data used for training is biased or not representative of the population in which the AI will be used, it can lead to inaccurate or unfair results. Thus, diverse data sets that represent different demographic groups to ensure the AI performs equitably are needed during the training phase [1]. Furthermore, the analytical bias and imprecision of input variables, such as those derived from laboratory tests, can also significantly affect the model's output. To mitigate this, the system's resilience to such variations should be evaluated through rigorous "stress tests".

**Selection of appropriate performance metrics:** Varying clinical scenarios may prioritize certain metrics over others (e.g., sensitivity vs. specificity) depending on the intended context of use. Notably, class imbalance in datasets can also skew results, necessitating careful consideration of which metrics to use, such as precision-recall curves [30].

According to ISO15189, laboratories are required to assess and manage the impact of measurement uncertainty (MU) associated with quantitative measurands [24]. Although ISO15189 does not explicitly mention Medical Device Software (MDSW), it does require laboratories to



**Figure 4:** Implementation timeline of the AI Act.

**Table 4:** Responsibilities of laboratory professionals regarding medical device software.

| Responsibility area                         | AI Act (Regulation (EU) 2024/1689)   | IVDR (Regulation (EU) 2017/746)  | ISO 15189:2022   | Comparison notes  |
|---|--|--|--|---|
| Use according to instructions               | Users of high-risk AI systems must use them in accordance with the instructions for use (Article 26(1))  | Implicit requirement derived from manufacturer's obligation to provide instructions for use (Annex I, 20.4.1) detailing the intended purpose. Labs making 'in-house' devices must define the intended purpose (Article 5(5)) | Laboratories shall have procedures for equipment handling and use (6.4.1) and shall follow established procedures (6.4.4)  | Overlap: all documents point towards using software as intended/instructed. AI Act specifically obligates 'users' regarding instructions for high-risk systems. ISO 15189 requires procedures for equipment use             |
| Data suitability and input control          | Users of high-risk AI systems must ensure, to the extent they control input data, that it is relevant and sufficiently representative (Article 26(4))  | Not explicitly detailed for standard users of CE-marked software. However, for 'in-house' devices, the lab is responsible for ensuring the device achieves its intended purpose (Article 5(5)), can imply data suitability   | Labs are responsible for pre-examination processes (7.2) and monitoring the validity of results (7.3.7). Information management requires ensuring data integrity (7.6)   | Overlap and distinction: all imply responsibility for data quality/suitability<br>The AI Act puts explicit obligations on users of high-risk AI regarding input data relevance  |
| Monitoring and reporting issues             | Users must monitor high-risk AI systems and suspend use if there is an incident or serious risk. Must inform provider/distributor and authorities about serious incidents/malfunctions (Article 26(5)) | Users report suspected serious incidents involving devices made available on the market to competent authorities (Article 82)  | Labs shall have procedures for managing nonconforming work and identifying/managing risks and opportunities for improvement (7.5). Adverse incident reporting for equipment required to the manufacturer and authorities (6.4.6) | Overlap: all require monitoring and reporting of problems/incidents   |
| Record keeping/logs generated by the system | Users of high-risk AI systems shall keep the logs automatically generated by that system, to the extent the logs are under their control for at least six months (Article 26(6))                       | Documentation for 'in-house' devices (Article 5(5))  | Labs shall maintain records for equipment including maintenance, calibration (6.4.7), examination results (8.4.3)  | Overlap and distinction: the AI Act specifically mandates users retain system-generated logs for high-risk AI. ISO 15189 has broad record-keeping requirements. IVDR emphasizes documentation for 'in-house' devices        |
| Validation/verification                     | User responsibility focuses on using the AI system within its validated scope as per instructions (Article 26(1)). (Validation itself is primarily a provider duty)                                    | For 'in-house' devices, the lab must validate the device (Article 5(5)), meeting general safety and performance requirements (Annex I)   | Labs shall verify equipment including software (6.5.2.c) and information systems before introduction (7.6.3.a)<br>Validation is required for changes to information systems (7.6.3.a)  | Overlap and distinction: ISO 15189 mandates verification and in case of changes validation. IVDR requires validation meeting Annex I for 'in-house' devices. AI Act user role is about correct use post-provider validation |
| Risk management                             | Users contribute to post-market monitoring (Article 72) by reporting issues (Article 26(5)). (Primary risk management is a provider duty)  | Primarily a manufacturer duty (Article 10(2), Annex I). Users contribute via vigilance reporting (Article 82). Labs making 'in-house' devices must establish processes (Article 5(5))  | Labs shall implement risk management activities throughout their processes, addressing potential harm (5.6, 8.5)   | Overlap and distinction: ISO 15189 mandates a proactive, lab-wide risk management process. AI Act and IVDR position the user more reactively (reporting issues), unless the lab makes 'in-house' devices under IVDR         |
| Quality management system (QMS)             | No explicit QMS requirement for users (providers' duty (Article 16.c)), but adherence to procedures ensuring compliance is necessary   | Required for manufacturers (Article 10(8)). Labs making 'in-house' devices also must establish QMS (Article 5(5)b)   | Labs shall establish, document, implement, and maintain a QMS compliant with ISO 15189 (Clause 8)  | Distinction: ISO 15189 mandates a comprehensive QMS for the lab. IVDR requires it for manufacturers and for labs only for 'in-house' devices. The AI Act does not explicitly require a user QMS but for providers           |

Table 4: (continued)

| Responsibility area                  | AI Act (Regulation (EU) 2024/1689)  | IVDR (Regulation (EU) 2017/746)  | ISO 15189:2022  | Comparison notes  |
|--------------------------------------|---|--|---|---|
| Staff competence and human oversight | User/Deployer of a high-risk AI system must ensure that any natural persons assigned human oversight possess the necessary competence, training, and authority, and are adequately supported (Article 26(2)). Implement human oversight measures based on IFU (Article 27(1)) | Not explicitly detailed as a distinct ‘human oversight’ requirement for standard users in IVDR, but competent use by healthcare professionals is assumed. Oversight is inherent in professional practice | Laboratory ensures personnel are competent, trained, and authorized for their tasks (6.2) | Overlap and distinction: competent personnel and oversight are implicit or explicit in all. The AI Act places specific requirements on the design for human oversight (provider duty) (Article 14(4)) and on the implementation of oversight by the user/deployer (Article 26(2)) |

evaluate how the MU of test results – used as inputs for further interpretations or algorithms – may affect the final interpretation or diagnosis. This requirement implies that laboratories using algorithms or software tools (including MDSW) to interpret laboratory data must consider how input MU influences the overall uncertainty and validity of the software’s outputs.

In practical terms, surely this means laboratories must first ensure that the MU of their quantitative inputs is within acceptable limits to avoid unreliable outcomes (following the principle of avoiding “garbage in, garbage out”). Since MU for the same analytes can vary between laboratories, evaluating and managing input MU cannot solely be the responsibility of the MDSW manufacturer. Instead, each laboratory implementing MDSW must verify that the MU of its laboratory tests meets any specified acceptable input MU provided by the manufacturer. Specifically, if the MDSW manufacturer provides predictions or performance metrics based on certain input MU assumptions, laboratories should ensure their own MU does not exceed these assumptions. If the manufacturer does not specify acceptable input MU, laboratories must independently verify that the overall performance metrics (sensitivity, specificity, and accuracy) of the MDSW remain valid and acceptable within their intended context of use.

However, even when a laboratory demonstrates excellent analytical performance, the output of Medical Decision Support Software (MDSW) tools may differ between laboratories if the input results come from measurands that are not harmonised. This lack of harmonisation can occur in several situations [31], such as a lack of a clear definition of the measurand, with examples including tumor markers and peptide hormones like parathyroid hormone [32] or growth hormone [33]. Another situation is inconsistent metrological traceability, as seen with ferritin [34]. Finally, differences in assay selectivity, where albumin [35] and creatinine [36] measurements can be affected by variations, can also lead to this issue.

When a MDSW interpretation tool rely on such non-harmonised input, the tool’s output cannot be consistently applied across different measurement methods. Therefore, transferring these tools between facilities requires careful clinical verification to ensure equivalent output when analyzing identical samples. If the equivalence of the output cannot be guaranteed by the equivalence of the input, the MDSW tool itself may need adjustments to achieve equivalent results. To assist laboratories in identifying potential risks of inequivalent input for MDSW, the LEAP checklist from the IFCC Working Group on Method Evaluation Protocols can be used by those initially documenting a new MDSW for evaluating and reporting analytical performance characteristics of clinical measurement procedures [37]. If the MDSW tool cannot be adjusted, laboratories must ensure that their input data is harmonised with the methods used to validate the MDSW before using it in their own laboratory. Furthermore, if a laboratory uses results from the same measurement procedure for a specific measurand in different applications or with different MDSW tools, they might need to apply different corrections to their results for each application. This is necessary to ensure the simultaneous equivalence of all MDSW tools using those results. In accordance with ISO 15189:2022, paragraph 6.5.2 on calibration, laboratories are also required to regularly verify the accuracy of their adjustments to the MDSW input and maintain detailed records of these corrections.

To enable laboratories to compare the equivalence of their MDSW tools as intended, EQA organizers need to establish schemes that ensure equivalent output when laboratories use the same MDSW with different analytical measurement procedures. Only then can doctors and patients confidently rely on equivalent clinical judgment based on identical samples, regardless of where or when the analysis is performed.

**Clinical evidence:** The lack of robust clinical evidence to support the safety and performance claims of medical AI devices is a concern. Many studies on AI models were

**Table 5:** Responsibilities of manufacturers/providers regarding medical device software.

| Responsibility area                    | AI Act (Regulation (EU) 2024/1689)  | IVDR (Regulation (EU) 2017/746)  | ISO 15189:2022   | Comparison notes  |
|--|---|--|--|---|
| Quality management system (QMS)        | Providers of high-risk AI systems must establish and implement a QMS (Article 16, 17)   | Manufacturers must establish, document, implement, maintain, keep up to date, and continually improve a QMS (Article 10(8)). Specific requirements detailed (e.g., strategy for regulatory compliance, processes for design, performance evaluation, etc.) | No direct obligations specified for manufacturers. However, labs need sufficient info from manufacturers for equipment management and verification/validation (implied by 6.4.4, 7.3.2), suggesting manufacturers should provide information to labs for QMS | Overlap: both AI Act (for high-risk AI) and IVDR mandate a QMS for the provider/manufacturer. IVDR Article 10(8) provides more explicit detail on the scope of the QMS for IVDs. ISO 15189 does not directly regulate manufacturers                     |
| Risk management                        | Providers must establish, implement, document, and maintain a risk management system throughout the AI system's lifecycle (Article 9)   | Manufacturers must establish, implement, document, and maintain a risk management system throughout the device lifecycle (Article 10(2); Annex I (Section 3))  | No direct obligations specified for manufacturers. Labs perform their own risk management (5.6, 8.5)   | Overlap: both AI Act and IVDR mandate a lifecycle risk management system for manufacturers. ISO assign risk management responsibilities to laboratories   |
| Technical documentation                | Providers of high-risk AI systems must draw up technical documentation before placing the system on the market and keep it updated (Article 11)   | Manufacturers must draw up and keep updated technical documentation demonstrating conformity (Article 10(4); detailed requirements in Annexes II and III)  | No direct obligations specified for manufacturers. Labs need manufacturer's instructions for proper equipment use (implied by 6.4.4)   | Overlap: both AI Act (for high-risk AI) and IVDR mandate comprehensive, up-to-date technical documentation before market placement  |
| Conformity assessment and CE marking   | Providers must ensure high-risk AI systems undergo the relevant conformity assessment procedure before market placement (Article 16, 43)  | Manufacturers must ensure devices undergo the relevant conformity assessment procedure before market placement (Article 10 (5), 17, 18)  | No direct obligations specified for manufacturers regarding CE marking   | Overlap: both AI Act and IVDR require conformity assessment and CE marking before placing the product (high-risk AI system/IVD device) on the EU market   |
| Instructions for use (IFU) and info    | Providers must ensure high-risk AI systems are accompanied by instructions for use (IFU) in an appropriate format, containing concise, complete, correct, and clear information for the user (Article 13)                                       | Manufacturers must provide information needed to identify the device and manufacturer, and safety/performance information, including IFU (Article 10(10); Annex I, Section 20). Specific requirements for software in Annex I (20.4.1(ah))                 | No direct obligations specified for manufacturers. Laboratories are required to adhere to manufacturer's instructions for proper equipment use (implied by 6.4.4)  | Overlap: both AI Act and IVDR require providers/manufacturers to supply clear and comprehensive IFU and relevant safety/performance information. IVDR Annex I has detailed content requirements for IVD labelling/IFU                                   |
| Post-market surveillance (PMS)         | Providers must establish and implement a post-market monitoring system (Article 72). Providers must report serious incidents (Article 73)   | Manufacturers must plan, establish, document, implement, maintain, and update a PMS system for each device (Article 10(9); Article 78). Must report serious incidents and field safety corrective actions (Article 82)                                     | No direct obligations specified for manufacturers. Labs report adverse incidents to manufacturers and authorities, (6.4.6)   | Overlap: both AI Act and IVDR mandate a proactive PMS system and reporting of serious incidents/corrective actions (vigilance)  |
| Data and data governance (AI specific) | Providers of high-risk AI systems must comply with specific requirements regarding training, validation, and testing data sets, including relevance, representativeness, error checking, and appropriate data governance practices (Article 10) | IVDR does not contain the same explicit 'data governance' requirements for training AI models as the AI Act. Focus is more on analytical/clinical performance data (Annex I, Annex XIII)   | No direct obligations specified for manufacturers related to AI specific data governance   | Distinction: the AI Act places specific, detailed requirements on providers regarding the governance, quality, and suitability of data used to train and test high-risk AI systems (Article 10), which are not mirrored in the same way in IVDR and ISO |
|  | Providers must ensure high-risk AI systems are designed and   | Manufacturers must ensure devices achieve the claimed  | No direct obligations specified for manufacturers. Labs need   | Overlap and distinction: the AI Act addresses all points using  |

Table 5: (continued)

| Responsibility area                 | AI Act (Regulation (EU) 2024/1689)   | IVDR (Regulation (EU) 2017/746)   | ISO 15189:2022   | Comparison notes  |
|-------------------------------------|--|---|--|---|
| Accuracy, robustness, cybersecurity | developed to achieve appropriate levels of accuracy, robustness, and cybersecurity throughout their lifecycle (Article 15)                   | performance (Annex I, Section 9) and address IT security risks, including protection against unauthorized access (Annex I, Section 16.4)  | secure information systems (7.6.3)                                 | the specific terms ‘accuracy, robustness, cybersecurity’ (Article 15). IVDR covers performance and IT security within general safety and performance requirements (Annex I)   |
| Clinical/Performance evaluation     | Primarily focused on technical documentation of performance, accuracy, robustness as per AI requirements (Annex IV)                          | Manufacturers must conduct a performance evaluation demonstrating conformity with general safety and performance requirements, including analytical and clinical performance (Article 56; Annex XIII) | No direct obligations specified for manufacturers                  | Distinction: IVDR places a strong emphasis on clinical evidence and performance evaluation (analytical and clinical performance) specific to the diagnostic purpose (Article 56, Annex XIII), which is more extensive than the AI Act’s focus on AI system accuracy/robustness in general terms |
| Registration                        | Providers of high-risk AI systems must register themselves and the system in an EU database before market placement (Article 49, Annex VIII) | Manufacturers must register themselves and their devices (using UDI) in the EUDAMED database (Article 26, Article 28)   | No direct obligations specified for manufacturers within ISO 15189 | Overlap: both AI Act and IVDR require registration of the provider/manufacturer and the product (high-risk AI system/IVD device) in relevant EU databases before market placement   |

retrospective or used single datasets for both training and validation, which could have led to overestimates of accuracy [38].

**Post-market surveillance:** Post-market surveillance is necessary to monitor the performance and identify any unintended outcomes or biases that may not have been detected during pre-market evaluations [39]. This requires robust systems for data collection and analysis, which can be challenging to establish and maintain [30].

**Overlapping regulatory frameworks:** Laboratory medicine already operates under stringent rules such as the IVDR, ISO 15189, and national healthcare laws. The AI Act introduces yet another layer of requirements, potentially leading to confusion or conflict in interpreting how and when AI-specific rules apply. Harmonising these overlapping frameworks without duplicating efforts or creating gaps in compliance is a significant challenge.

**Enforcement uncertainty:** While the AI Act sets forth broad obligations, detailed guidance and consistent enforcement practices across EU Member States are still needed. Laboratories struggle to make interpretive judgments about the AI Act’s requirements (e.g., criteria for human oversight or the scope of log retention). This uncertainty can force them to adopt conservative strategies, potentially delaying adoption of innovative AI technologies to avoid compliance risks.

**Resource-intensive compliance:** The AI Act’s emphasis on continuous monitoring, human oversight, and data governance places considerable demands on laboratory resources – budgets, personnel, and infrastructure. Smaller or resource-limited laboratories may struggle to meet the AI Act’s obligations, especially when these obligations come on top of existing ISO 15189 quality-management tasks (e.g., verification studies).

**Liability and accountability gaps:** Clarifying responsibilities for adverse events can be challenging when multiple stakeholders (providers, deployers, and even third-party data contributors) are involved. Although the AI Act and related medical device regulations distribute responsibilities, laboratories may still encounter uncertainties about liability if a misdiagnosis or patient harm arises from complex interactions between AI outputs, user inputs, and laboratory procedures.

**Integration with existing quality systems:** Many of the AI Act’s requirements – such as monitoring, and human oversight – are needed to be incorporated into a laboratory’s existing quality-management system. The processes like corrective and preventive actions and internal audits capture AI-specific risks (e.g., model underfitting) can be challenging, particularly when these processes were originally designed around traditional laboratory testing methods. Adding to this complexity is the need to develop

specific EQA tailored for evolving AI systems. These EQAs are crucial for ensuring the ongoing reliability and accuracy of AI systems that may change over time through self-learning, providing an independent evaluation of their performance.

**Balancing innovation and patient safety:** A key challenge for regulators is finding the right balance between fostering innovation in AI/ML and ensuring patient safety. Overly strict regulations can stifle innovation, while insufficient oversight can compromise patient safety [40]. As AI continues to evolve, regulatory frameworks must adapt to foster innovation while maintaining the highest standards of clinical effectiveness and patient care.

## Conclusions

The integration of AI/ML-enabled MDSW in laboratory medicine offers significant opportunities to enhance diagnostic accuracy, optimize workflows, and improve patient outcomes. However, the regulatory landscape governing these technologies remains complex, requiring stringent adherence to frameworks such as the IVDR, MDR and the AI Act. ISO 24051, which covers principles for the application of artificial intelligence in medical laboratories, is currently under development. This standard may help reduce uncertainties regarding the specific use of AI-based MDSWs in clinical laboratories and AI-specific responsibilities of laboratory professionals.

Ensuring regulatory compliance is essential for patient safety, device effectiveness, ethical standards, and facilitating market access. As AI-driven Medical Device Software (MDSW) evolves, regulatory frameworks must adapt dynamically to encourage innovation while upholding rigorous clinical performance and safety standards. Future efforts should focus on refining guidelines for specific domains like laboratory medicine to align technological advances with domain-specific regulatory requirements. Laboratory professionals must also understand their responsibilities in managing MDSW effectively and safely. EQA organizers should proactively develop and implement schemes that enable the assessment of inter-laboratory equivalence in MDSW output when analysing identical samples. Addressing these challenges proactively will enable AI-based MDSWs to fully transform laboratory medicine.

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## Use of Large Language Models, AI and Machine Learning

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