

February 2024
**The Impacts of the European Union In Vitro Diagnostic
Regulation Survey**

Results, Key Findings, and Recommendations

Association for Molecular Pathology



This report was produced by the Association for Molecular Pathology and supported in part by



DISCLAIMER

Although the criteria set forth in the In Vitro Diagnostics Regulation (IVDR) apply to each country in the European Union (EU), the compliance dates for IVDR implementation are staggered and differ according to requirements for each individual country.

Acronyms:

The European Union (EU)
European Free Trade Association (EFTA)
Conformite-Europeenne (CE)
Medical Device Regulation (MDR)
In Vitro Diagnostic Regulation (IVDR)
In Vitro Medical Devices Directive (IVDD)
Laboratory Developed Tests (LDTs)
Notified Bodies (NB)
National Competent Authorities (NCAs)
European Medicine Agency (EMA)
Research Use Only (RUO)

Definitions:

Definitions in the section below were adapted from the Biomedical Alliance in Europe: Main findings IVDR Questionnaire BioMed Alliance Report¹

*i. **Conformite-Europeenne In Vitro Diagnostic (CE-IVD):** used strictly according to the instructions for use (IFU) of the manufacturer for the application, the instrumentation/analyzer, the intended use, the sample matrix, the recommended calibration (frequency), internal quality control procedure, reference ranges and/or decision limits.*

a. CE marking: certifies that a product has met EU health, safety, and environmental requirements²

*ii. **Modified CE-IVDs:** as compared to the IFU; the modifications are considered to be minor if they do not change test effectiveness, test safety, and the downstream consequences for the patient. The modified tests are evaluated under the Quality Management System of the medical lab, e.g.:*

- 1. Making a dilution of the specimen in the recommended diluent, blank serum or saline solution;*
- 2. Required sample pretreatment due to e.g. extreme lipemia because of high, floating lipoproteins;*
- 3. Serum/plasma creatinine in an alternative body fluid after surgery;*
- 4. Performing a pretreatment with Polyethylene Glycol (PEG) for excluding macroamylasemia or macroprolactinemia; diversions from manufacturers' interference index values based on in-house validations;*
- 5. Use of formula and calculations by labs such as Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) for estimated Glomerular Filtration Rate (eGFR) reporting and anion gap calculation for electrolyte disturbances;*

¹ Biomedical Alliance Europe. (November 2021) *Main findings IVDR questionnaire BioMed Alliance.*
https://www.biomedeurope.org/images/news/2021/20211206_Findings_IVDR_Questionnaire_final.pdf

² International Trade Administration *Certifying Your Product with CE marking* [https://www.trade.gov/ce-marking#:~:text=The%20CE%20marking%20\(an%20acronym,requirements%2C%20which%20ensure%20consumer%20safety](https://www.trade.gov/ce-marking#:~:text=The%20CE%20marking%20(an%20acronym,requirements%2C%20which%20ensure%20consumer%20safety)

6. *Third party Internal Quality Control (IQC) in case the healthcare institution has clinical reasons for not running the IQC from the manufacturer;*

7. *Inclusion of a conversion factor (e.g. + 10%) to harmonize the results with those in other laboratories.*

iii. **Off-label CE-IVDs:** *means that the intended use of a CE-IVD differs or goes beyond the intended use as mentioned in the IFU of the manufacturer and affects clinical performance but for which clinical evidence has been gathered by a healthcare institution to justify its application for another intended use in a specific target group in a defined clinical care pathway and setting, e.g.:*

1. *Using a non-high sensitive troponin assay in a General Practitioner setting or in an ambulance for prehospital triage of acute coronary syndrome (ACS) patients, for the purpose of excluding patients suspected from ACS;*

2. *SARS-CoV-2 test on bronchoalveolar lavage fluid, where the test describes use of nasal swabs.*

iv. **Research Use Only (RUO) Kits:** *used according to the research insert of the manufacturer. Under the IVDR this test will become an LDT as the user of the test has to demonstrate the intended use and the clinical evidence requirements and other essential claims.*

v. **In-House In Vitro Device (IH-IVD)/Laboratory Developed Test (LDT):** *examples include:*

1. *Development of a (multiplex) liquid chromatography–mass spectrometry (LC-MS) method for immunosuppressive drug quantitation in kidney transplant patients, as a high quality replacement test for an inferior commercial immunoassay test in a tertiary care center.*

2. *Development of a flow cytometry antibody panel for an application for which no appropriate CE-IVD is available, such as measurable residual disease (MRD) measurements.*

3. *Development of up-to-date sequencing panels in hemato-oncology*

Definition of Legacy Devices below was taken directly from EU Unique Device Identification (UDI) Help Desk at the time of the survey release.

a. **Legacy Devices** *are defined as medical devices, active implantable medical devices and in vitro diagnostic medical devices - covered by a valid Directive certificate - that will continue to be placed on the market after the date of application of Regulation (EU) 2017/745 (MDR) or Regulation 2017/746 (IVDR).*

b. *Legacy devices shall be registered in EUDAMED in two cases:*

i. *a post-market surveillance and/or a vigilance report occurs;*

ii. *by the end of the transition period applicable for device registration, if no equivalent MDR or IVDR device is registered in EUDAMED.*

Updated Definition of Legacy Devices taken from the Medical Device Coordination Group established by Article 103 of Regulation (EU) 2017/745: Legacy Devices under the IVDR (hereafter 'legacy devices') should be understood as devices referred to in the 2nd or 3rd subparagraph of Article 110(3) IVDR, which are placed on the market or put into service after 26 May 2022 (i.e. the IVDR's date of application) and until the end of the respective transition period set out in the 2nd or 3rd subparagraph of Article 110(3), if the conditions laid down in the 1st subparagraph of Article 110(3)3 are fulfilled. Those devices can be: a) devices covered by a valid EC certificate issued by a notified body in accordance with Directive 98/79/EC on in vitro diagnostic medical devices (IVDD) prior to 26 May 2022; or b) devices for which a declaration of conformity was drawn up prior to 26 May 2022 in accordance with the IVDD and for which the conformity assessment procedure pursuant to the IVDR (contrary to the IVDD) requires the involvement of a notified body.³

Notified Bodies (NB): A notified body is an organization designated by an EU Member State (or by other countries under specific agreements) to assess the conformity of certain products before being placed on the market. These bodies are entitled to carry out tasks related to conformity assessment procedures set out in the applicable legislation when the intervention of a third party is required.⁴

European Commission: The European Commission represents the common interests of the EU and is the EU's main executive body. It uses its right of initiative to put forward proposals for new laws, which are scrutinized and adopted by the European Parliament and the Council of the European Union. It also manages EU policies (except for the Common Foreign and Security Policy (CFSP), which is conducted by the High Representative for CFSP, Vice-President of the European Commission), and the EU's budget and ensures that countries apply EU law correctly. Representation offices act as the Commission's voice across the EU. They monitor and analyze public opinion in their host country, provide information about EU policies and the way the EU works, and facilitate the Commission's cooperation with the host member country.

The work of these four main EU institutions, which covers the legislative and executive tasks of the EU, is complemented by the work of another three EU institutions: the Court of Justice of the European Union, the European Central Bank and the European Court of Auditors. These three institutions are responsible for managing the judicial, financial and external audit aspects of the European Union.⁵

National Competent Authorities (NCAs): A medicines regulatory authority in a European Union Member State.⁶

European Medicine Agency (EMA): The European Medicines Agency (EMA) protects and promotes human and animal health by evaluating and monitoring medicines within the European Union (EU) and the European Economic Area (EEA).⁷

³ Medical Device Coordination Group. (May 20 2022). MDCG 2022-8 - Regulation (EU) 2017/746 - Application of IVDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2022.

https://health.ec.europa.eu/system/files/2022-05/mdcg_2022-8_en.pdf

⁴ European Commission (2024) Public Health Bodies. https://health.ec.europa.eu/medical-devices-topics-interest/notified-bodies_en

⁵ European Union (2024) Types of institutions, bodies and agencies. https://european-union.europa.eu/institutions-law-budget/institutions-and-bodies/types-institutions-and-bodies_en

⁶ European Medicines Agency (2024) National Competent Authority. <https://www.ema.europa.eu/en/glossary/national-competent-authority>

⁷ European Union (2024) European Medicines Agency (EMA) Overview. https://european-union.europa.eu/institutions-law-budget/institutions-and-bodies/search-all-eu-institutions-and-bodies/european-medicines-agency-ema_en

Survey Background and Purpose:

Executive Summary: On May 5, 2017, the European Union (EU) published two regulations, the Medical Device Regulation (MDR) and the In Vitro Diagnostic Regulation (IVDR), which require medical device and in vitro diagnostic manufacturers that distribute products in the EU to adhere to new standards. To ensure quality assessment, the new IVDR replaced the In Vitro Medical Devices Directive (IVDD). Each member state will now be newly required to separately analyze Laboratory Developed Tests (LDTs) through their respective regulatory body. Many challenges have delayed the implementation of the IVDR.

The initial implementation of these regulations began on May 22, 2022, and though compliance dates are staggered, all laboratories in the EU and the European Free Trade Association (EFTA), which consists of member states Iceland, Switzerland, Norway, and Lichtenstein, were given the following compliance dates: May 26, 2025 for high-risk IVDs and May 26, 2027 for low-risk IVDs.⁸ However, the EU proposed amendments to the IVDR in January 2024 that would extend the compliance dates based on the risk class of the device, citing the need for patient access “to a wide range of medical devices while ensuring the transition to the new framework.” The new timeline would allow devices with a higher risk until December 2027 to comply and medium and lower risk devices would now be extended until December 2028.⁹

While the industry as a whole has expressed concerns that the new regulations will bring enormous challenges, clinical diagnostic laboratories and molecular diagnostics professionals in particular, seek to understand the full impact of the IVDR, which remains unclear.

Admittedly, the EU stated in 2023 “Despite considerable progress over the past years, the overall capacity of conformity assessment (‘notified’) bodies remains insufficient to carry out the tasks required of them. In addition, many manufacturers are not sufficiently prepared to meet the strengthened requirements of the MDR by the end of the transition period. This is threatening the availability of medical devices on the EU market.”¹⁰

⁸ European Commission (January 2023) *Proposal for a REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL amending Regulations (EU) 2017/745 and (EU) 2017/746 as regards the transitional provisions for certain medical devices and in vitro diagnostic medical devices* https://health.ec.europa.eu/system/files/2023-01/mdr_proposal.pdf

⁹ European Commission (January 2023) *Proposal for a REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL amending Regulations (EU) 2017/745 and (EU) 2017/746 as regards the transitional provisions for certain medical devices and in vitro diagnostic medical devices* https://health.ec.europa.eu/system/files/2023-01/mdr_proposal.pdf

¹⁰ European Commission (January 2023) *Proposal for a REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL amending Regulations (EU) 2017/745 and (EU) 2017/746 as regards the transitional provisions for certain medical devices and in vitro diagnostic medical devices* https://health.ec.europa.eu/system/files/2023-01/mdr_proposal.pdf

Survey Objective and Overview

Project Context	Project Objectives
<ul style="list-style-type: none">• AMP surveyed our international membership to understand the global scope and impact of the EU IVDR on clinical laboratories and patient access.• The survey was open from March 30th to April 28th, 2023 and available to all laboratory personnel (AMP members and non-members) that would potentially be impacted by the IVDR Implementation.• The survey assessed the following different aspects of the IVDR Implementation:<ul style="list-style-type: none">• Laboratory demographics.• Examples of perceived success or failures of the implementation process.• The impact on day-to-day laboratory operations and environment.• Laboratory perceived readiness for IVDR Implementation.• The CE Certification Process.• The Downstream impact(s) on patient access to molecular testing.• Impact on Finances and Workforce.	<p data-bbox="870 380 1359 470">Deploy and deploy survey to international AMP membership to collect quantitative results on impact of the IVDR Implementation</p> <p data-bbox="870 497 1359 567">Assess and analyze the quantitative results of the survey to better understand IVDR impact on laboratory testing and patient accessibility</p> <p data-bbox="870 594 1359 663">Present survey results at AMP Europe 2023 Congress</p> <p data-bbox="870 690 1359 760">Synthesize findings into a report that AMP may use to develop policy reform approaches and advocacy materials to share with key policy stakeholders</p>

Background: The Association for Molecular Pathology (AMP) is a medical professional society of just over 2,900 members that include pathologists, doctoral scientists, laboratory directors, basic and translational scientists, technologists, and trainees along with United States government officials and the in vitro diagnostics industry. During the 2021 AMP Annual Meeting and Expo, members discussed the potential implications of the IVDR. For example, key stakeholders were concerned about the potential impact the IVDR would have on in-house devices. Prior to the implementation of IVDR, manufacturers of in vitro diagnostic medical devices were responsible for obtaining CE-marked certification for their products destined for the European market. The IVDR does not change this requirement; however, according to the European Commission, the process will be more “stringent, especially in terms of risk classes and the oversight provided by notified bodies (NBs). There is also more emphasis on a life-cycle approach to safety, backed up by clinical data and post-market monitoring (‘vigilance’ and ‘post-market surveillance’)”¹¹. AMP membership sought to understand the global scope and impact the EU IVDR would have on clinical laboratories and patient access to care. Other stakeholders are concerned about its impact. For example, the European Hematology Association (EHA) stated, “Reaching IVDR compliance is a major burden for diagnostic laboratories.”¹²

In January of 2023, the European Commission released guidance on the health institution exemption, but many believe it does not provide adequate guidance or information for all laboratories required to comply with the IVDR.¹³

¹¹ European Commission (2024) *Public Health Manufacturer IVD* https://health.ec.europa.eu/medical-devices-new-regulations/getting-ready-new-regulations/manufacturer-ivd_en

¹² Lubbers BR, Dombink I, Kalina T, Hofmans M, Bruun MS, Stanworth SJ, Béné MC, Döhner K, Brüggemann M, Macintyre E, van Dongen JJM. *Experience With IVDR Implementation in Three Diagnostic Laboratories: Messages to EU Health Institutions, Diagnostic Healthcare Payers, and Authorities*. *Hemasphere*. 2023 Mar 7;7(4):e865. doi: 10.1097/HS9.0000000000000865. PMID: 36911048; PMCID: PMC9995097.

¹³ European Commission (2017) *Guidance on the health institution exemption under Article 5(5) of Regulation (EU) 2017/745 and Regulation (EU) 2017/746*. https://health.ec.europa.eu/system/files/2023-01/mdcg_2023-1_en.pdf.

Under Articles 106 and 48(6) of the Medical Device Regulation (EU) 2017/745 (MDR) and Regulation (EU) 2017/746 on In Vitro Medical Devices (IVDR) respectively, the European Commission is required to create an expert advisory panel for Medical Device Regulation, which supports the scientific assessment and advises the field of medical devices and in vitro diagnostic medical devices.¹⁴ The expert panels are tasked with the following:

- providing an opinion on the notified bodies' assessments of clinical evaluation of certain high-risk medical devices and the performance evaluation of certain in vitro diagnostic medical devices
- providing advice to the Medical Device Coordination Group (MDCG) and the European Commission concerning safety and performance of medical devices and in vitro diagnostic medical devices
- providing advice to manufacturers on their clinical development strategy and proposals for clinical investigations
- providing advice to EU countries, manufacturers and notified bodies on various scientific and technical matters
- contributing to the development and maintenance of relevant guidance documents, common specifications and international standards
- providing opinions in response to consultations from manufacturers, EU countries and notified bodies

The current website on the European Medicines Agency contains documents pertaining to medical device legislation that have not been updated since 2021.¹⁵ Though there have been press releases and the EMA began a pilot program consisting of expert panels that provide scientific advice to manufacturers of high-risk medical devices.

Scope: Molecular diagnostics professionals were surveyed to obtain their current level of knowledge and depth of understanding of the new regulatory and compliance requirements under the IVDR in the EU. The survey questions were also intended to evaluate the impact of IVDR implementation. Submissions were anonymous and the collected data was aggregated to inform advocacy and clinical practice programs on this issue.

Target Audience: For the purposes of this survey, priority was given to laboratories directly impacted by the new IVDR and located within the European Union and the United Kingdom, but the survey was made available globally.

Survey Design & Methodology:

AMP collected data from international members directly impacted by the IVDR and located in EU member states. AMP obtained information on laboratory compliance requirements and evaluated the potential impacts the new IVDR would have specifically for in-house testing. Participants in the survey included AMP members from the diagnostic manufacturing industry, individuals working in laboratories, and molecular professionals. This was helpful in identifying different challenges and levels of uncertainty

¹⁴ European Commission (2024). *Public Health Overview*. https://health.ec.europa.eu/medical-devices-expert-panels/overview_en

¹⁵ European Medicines Agency (2024) *Medical devices*. <https://www.ema.europa.eu/en/human-regulatory-overview/medical-devices#ema-inpage-item-13035>

in various laboratory settings. AMP sought input from a variety of stakeholders from the molecular diagnostic laboratory workforce to assess the broad implications stemming from the IVDR and to identify future trends in the field.

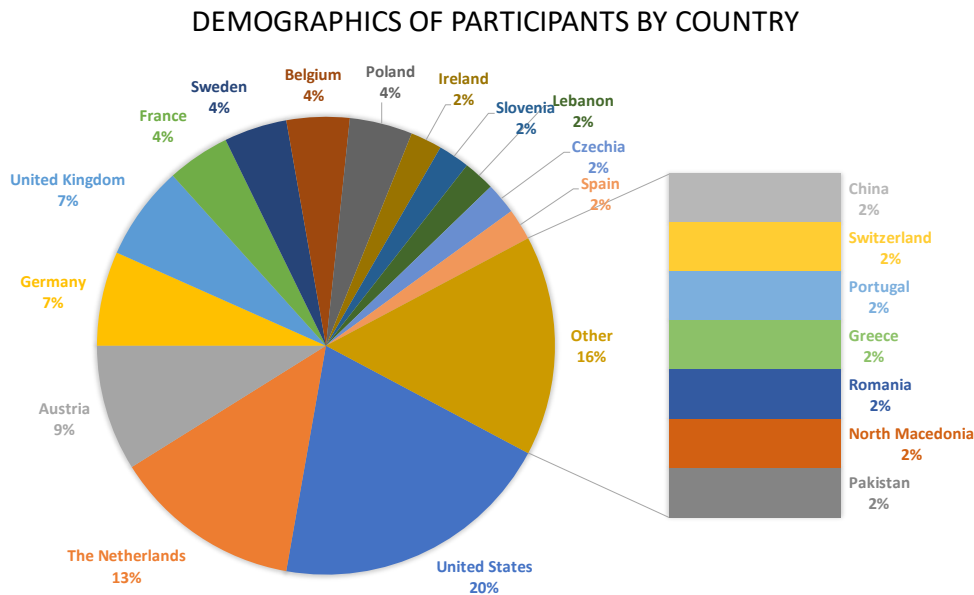
The 35-question survey employed multiple choice selections, including a “select all that apply” option, and free text question formats. Skip logic was employed to tailor follow-up questions based on responses. The survey assessed the following aspects of IVDR implementation:

- Laboratory demographics
- Examples of perceived success or failures of the implementation process
- The impact on day-to-day laboratory operations
- Perceived readiness for IVDR implementation
- The Conformité Européene (CE) Certification Process
- The downstream impacts on patient access to molecular testing; and
- Financial repercussions and impacts on the laboratory workforce.

The survey was made available to laboratory personnel (AMP members and non-members) potentially impacted by IVDR implementation from March 30 to April 28, 2023. The survey was distributed broadly via email and shared on social media. The results were summarized and compiled. Data was then exported into Microsoft Excel as needed to facilitate the comparison of more complex summary responses.

AMP Program Areas: Advocacy Team, led by Dr. Monika Franco. Dr. Franco would like to acknowledge all AMP staff for their assistance and support in conducting this survey, as well as our survey sponsor, Loxo@Lily.

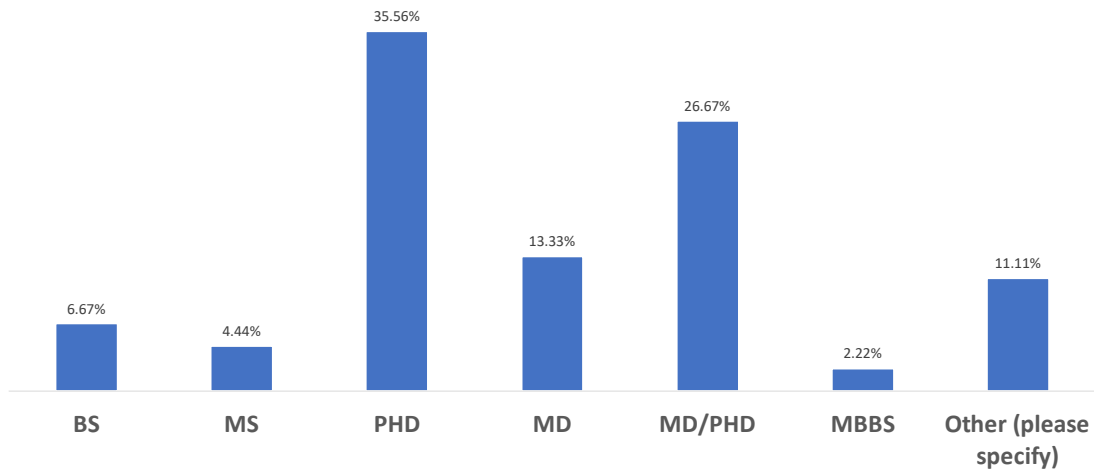
Demographics of Data Set and General Information:



We collected 45 responses with a 96% completion rate. The graph above displays the overall demographics by country. At least 20% of respondents were from the United States. There was a wide range of participants from around the world, including 8% from non-European countries: China, Lebanon, North Macedonia, Pakistan, and the United States of America. These countries have multi-national corporations and distribute IVDR products in the EU member states. The United Kingdom (UK), is no longer a part of the European Union and is not required to enact the IVDR. In response to the new regulations, the UK has enacted legislation that provides an extension to permit EU medical devices and in vitro diagnostic products that fall under the IVDR, to be introduced into the Great Britain market until June 30, 2030.¹⁶ For the purposes of this survey, AMP placed the UK under “EU” category. AMP did not design the survey to fully evaluate the impact on manufacturers distributing their products in the EU, however, their responses are included in the data below.

¹⁶ North American Science Associates, LLC. (June 22, 2023) *UK extends transition period for medical device and IVD products in new legislation.* <https://namsa.com/uk-extends-transition-period-for-medical-device-and-ivd-products-in-new-legislation/>

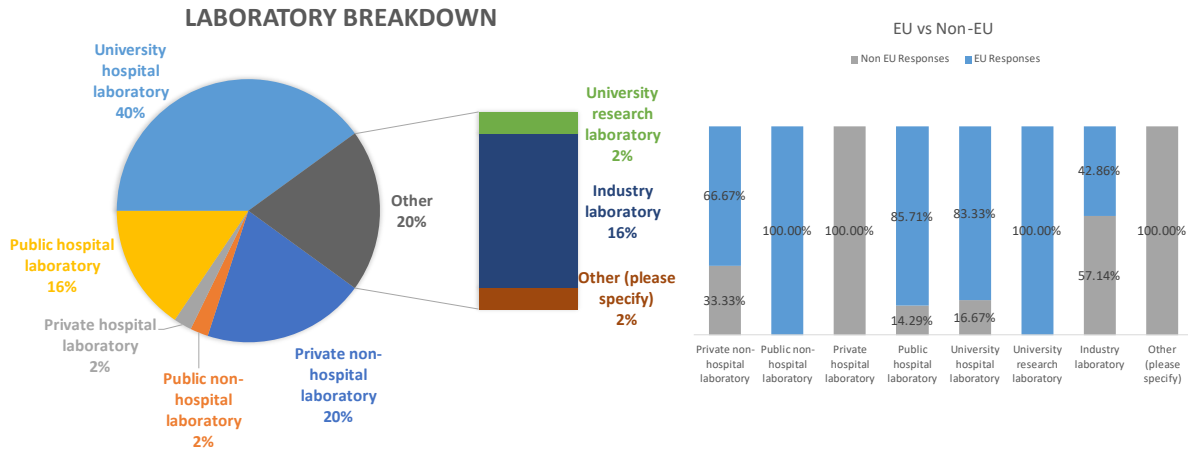
DEMOGRAPHICS BY HIGHEST DEGREE ACHIEVED



Survey participants held a variety of higher education degrees. The most prominent are listed below:

- PhD 35.5%
- MD/PHD 26.67%
- MD 13.33%

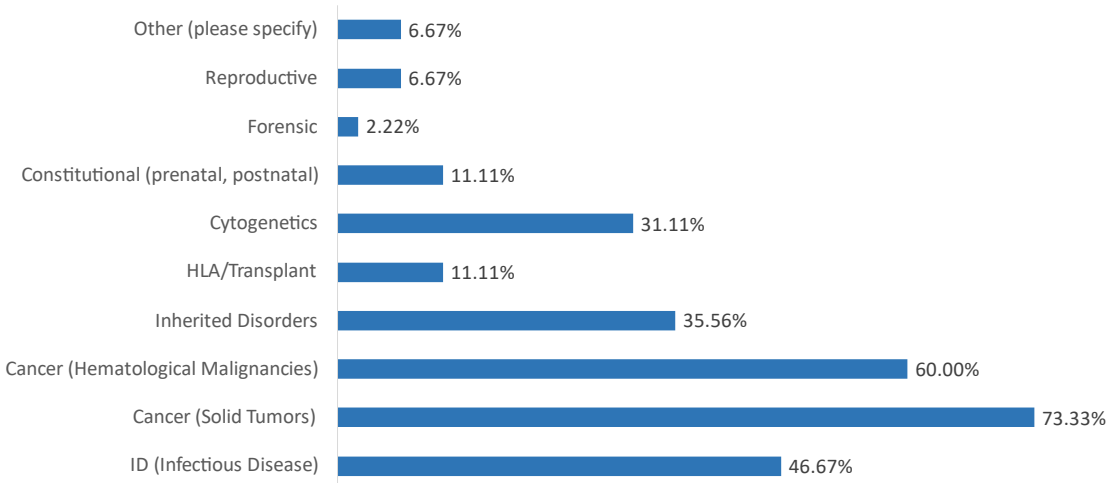
DEMOGRAPHICS OF PARTICIPANTS BY LABORATORY SETTING



The pie chart on the left shows the breakdown of respondents by laboratory setting. Approximately 40% of respondents categorized their laboratory as a university hospital laboratory, 20% as private non-hospital laboratory, 16% as a public hospital laboratory, and the rest from a variety of other settings such as university research laboratories or industry laboratories.

The bar graph on the right shows the breakdown of EU respondents vs Non-EU respondents per laboratory category.

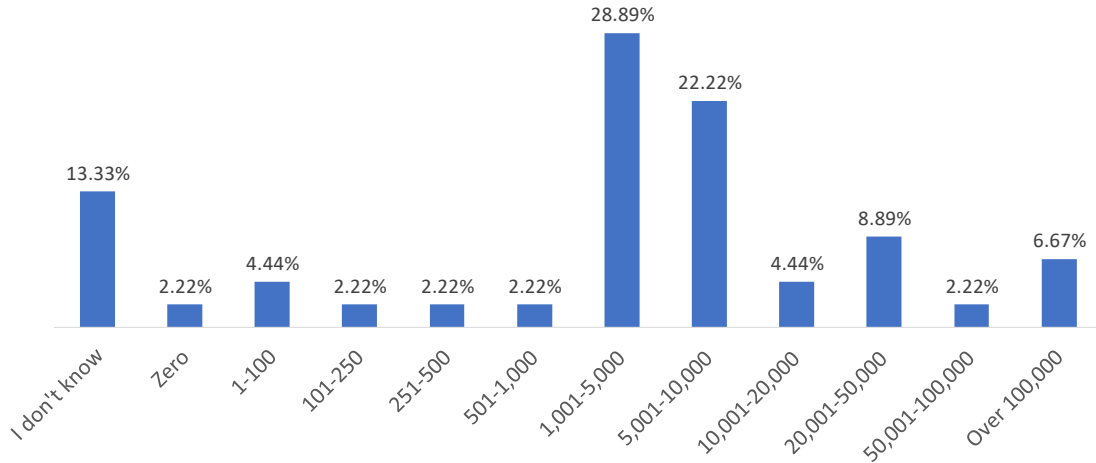
TESTING MENU BREAKDOWN



The above graph shows the types of molecular testing performed in the laboratories of the respondents. The participants had a wide variety of tests on their testing menus. The majority fell into five categories:

- Infectious disease (ID)
- Cancer (solid tumors)
- Cancer (hematological malignancies)
- Inherited disorders
- Cytogenetics

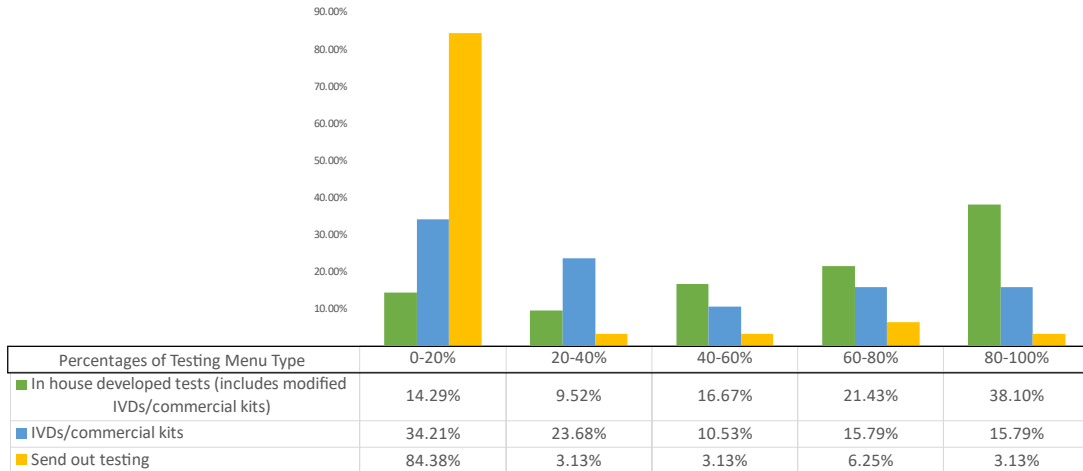
VOLUME OF MOLECULAR CLINICAL TESTS IN THE PAST 12 MONTHS



The respondents were asked about the volume of molecular clinical tests performed in their laboratories in the past 12 months.

- Over half of respondents' laboratories perform thousands of molecular tests in one year.
- Approximately 30% of respondents' laboratories performed 1,000-5,000 molecular clinical tests.
- 22% of respondents' laboratories performed 5,001-10,000 tests.
- The other participants reported varied testing volume, either below or above.

TESTING MENU BREAKDOWN: PERCENTAGES OF TESTING MENU BY TYPE: IN HOUSE-IVD, IVDs, SEND OUT TESTING

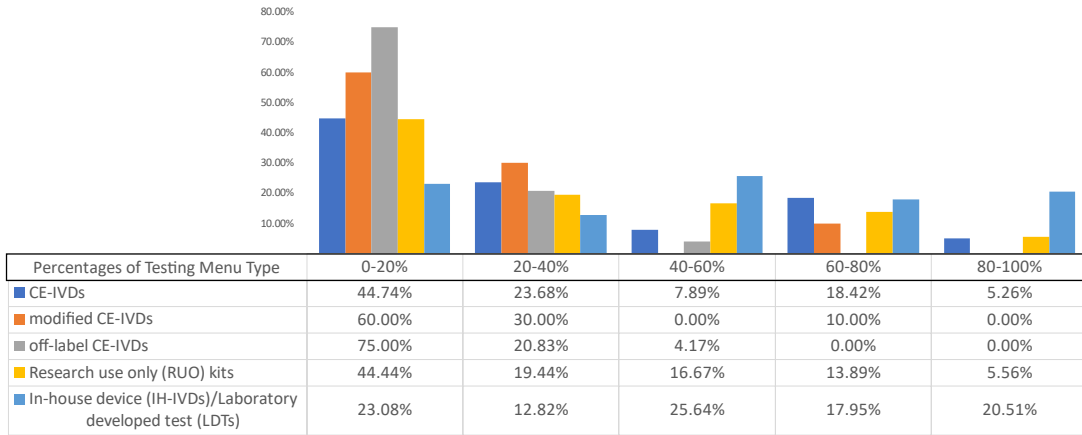


AMP asked about the proportion of tests on participants' laboratory test menus in each of the following categories:

- In-house developed tests, which includes modified IVDs/commercial kits,
- Unmodified IVDs/commercial kits, and
- Tests that are sent out to be performed at an external laboratory.

The results are depicted in the graph above. The majority of survey respondents' test menus consist of in-house developed tests.

WHAT PERCENTAGE OF IN-HOUSE IVDS ARE THE FOLLOWING: CE-IVDS, MODIFIED CE-IVDS, OFF-LABEL CE-IVDS, RUO KITS AND IH-IVDS/LDTS

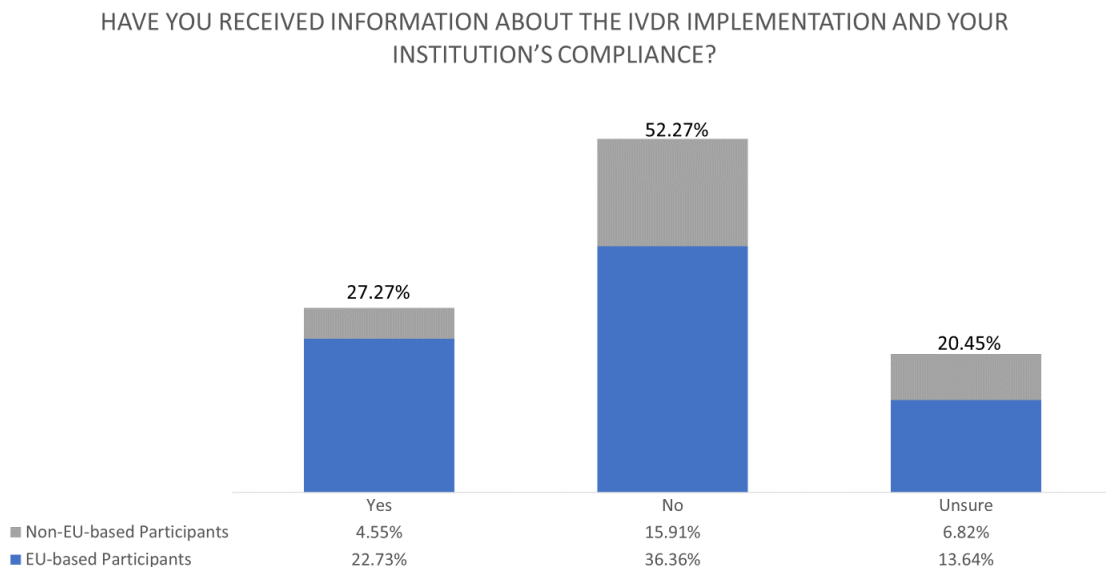


AMP followed up by asking what percentage of their in-house IVDs consisted of CE-IVDs, modified CE-IVDs, off-label CE-IVDs, RUO kits, and IH-IVDs/LDTS.

Reported Impacts of the In Vitro Diagnostic Regulation:

In this section of the survey, participants were asked the degree to which the IVDR impacts their ability to perform day-to-day duties, workflow, testing menus, and patient access. The bar graphs below have three different percentages per question/response. The percentages on top of each bar represent the percentage of the total number of responses. Each bar is also separated into percentages that represent responses from individuals located in EU member states (depicted in blue) and those outside of the EU, or non-EU respondents (shown in gray).

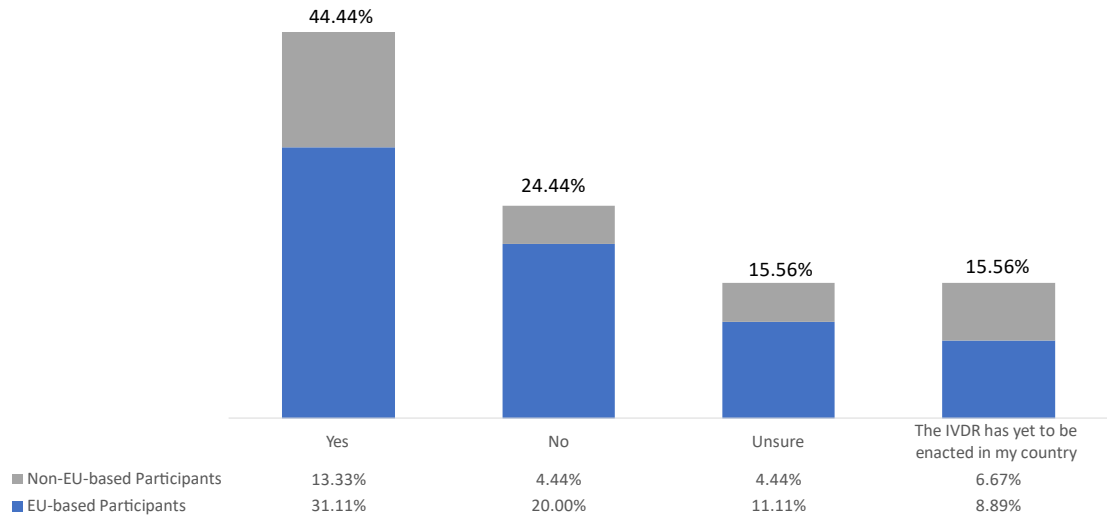
As a reminder, the criteria set forth in IVDR apply to EU and EFTA member states. The compliance dates for IVDR implementation are staggered and differ according to each individual member state's requirements. Therefore, this data is not a comprehensive analysis of the IVDR.



Many respondents lack information about compliance requirements.

Seventy-three percent of participants either received no information or were unsure if they had received information about their institution's compliance. AMP also asked participants to elaborate on their experiences with obtaining IVDR information. Of those participants who provided information, eight participants commented that the overall information received was inadequate. For example, three participants did not receive proper instructions on compliance requirements. One participant noted they received information, but not as it related to compliance. Another respondent was "made aware of the process but [was provided with] little to no guidance on what is required". Five other participants relayed they had to use sources outside of their institutions to obtain information, i.e., "second-hand from clients", a webinar series, or "questionnaires" to determine if they are in compliance. These results indicate that information about the IVDR and how an institution is complying with the new regulations is not being readily disseminated to laboratory professionals.

HAS THE IVDR IMPACTED YOUR DAY-TO-DAY LABORATORY ACTIVITIES?



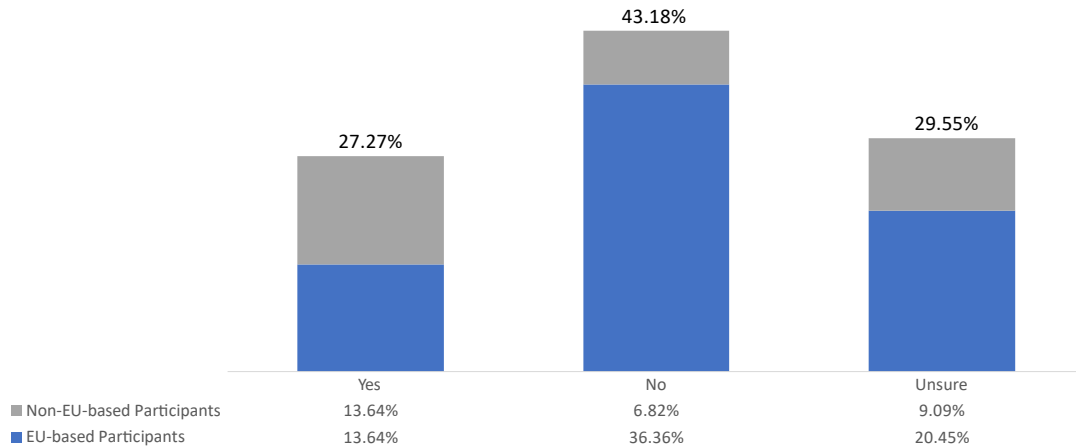
IVDR is impacting day-to-day activities of laboratories.

Over 40% of participants, including non-EU participants, indicated that the IVDR implementation has impacted their daily laboratory activities. Almost 30% of participants were either unsure or have yet to start the compliance process.

AMP requested more information from participants who responded “yes” to having a change in laboratory activities. Eight participants expressed concerns about compliance requirements including increased administrative and financial burdens noting the “increased documentation requirements”, and the need to “increase laboratory personnel”. Additionally, four respondents cited the IVDR would limit ability to “disseminate research” or entirely lose the ability to “share LDT’s with other labs.” Another cited “several in-house tests have already been replaced.” Another responded shared that the “sheer volume of testing required to show the effectiveness and safety of devices that have been on the market for over 20 to 30 years has been almost insurmountable.” Three non-EU participants reported they would no longer be able to offer tests to European clients, including one that “had to withdraw 75% of our patient care devices from the EU....and had to halt most of our research in the EU.”.

Two participants highlighted positive changes since the IVDR Implementation such as bolstering innovation through “new research development” and “overall standardization of laboratory practices” including pre-analytical and analytical phases, reagents storage, lab data logs, results reporting, reporting of errors, and identifying potential workflow hazards.

HAVE THERE BEEN ANY MAJOR CHANGES THAT NEEDED TO BE MADE TO YOUR LABORATORY/TESTING PRACTICES SINCE IMPLEMENTATION OF THE IVDR?

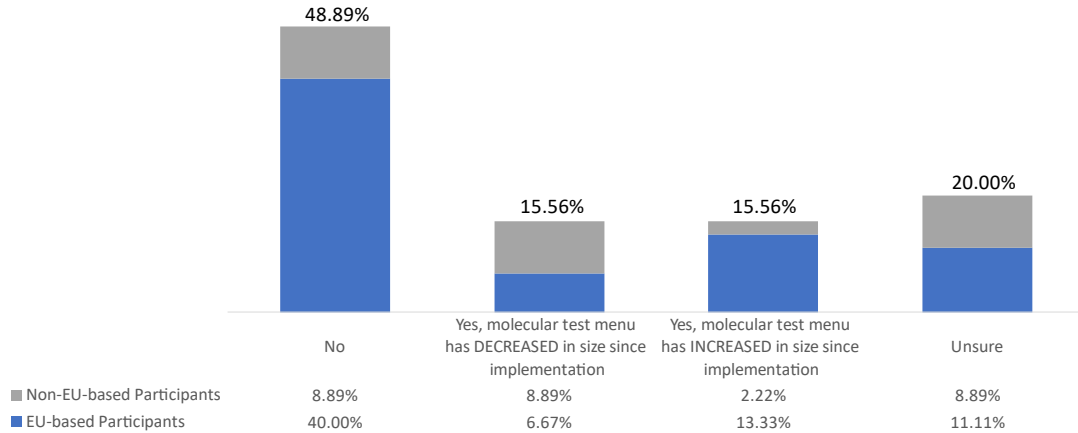


There have been significant changes to laboratory/testing practices as of March 2023.

Approximately 30% of respondents reported that the IVDR implementation resulted in changes being made to their laboratory/testing practices. However, likely due to the early stage of implementation of IVDR, the majority of respondents have not made major changes to their practices.

AMP asked participants who responded “yes” to provide additional details regarding major changes to their laboratory and testing practices. Overall, respondents expressed apprehensions about the IVDR, citing a “lack of guidance” and “ambiguous instructions” for proper implementation. One respondent noted that the IVDR has led to the complete redevelopment of their “precision testing model” and that they have had little to no guidance from their NB. This person continued by explaining that there has been an increase in overhead costs for their implementation of new practices and testing models. Additionally, one laboratory that previously distributed in-house developed reagents to other laboratories “has stopped doing so, since this is not allowed under IVDR.” Three participants noted the new IVDR regulations have also caused laboratories to change their testing menus. One participant reported their laboratory has switched from “developing in-house tests to using sequence figure virtual methods” and another has “chosen to work in-situ within the laboratory instead of off-site”. Other survey participants located outside of the EU highlighted that the new IVDR regulations have “already increased costs” and that they are “no longer able to offer testing to European patients.”

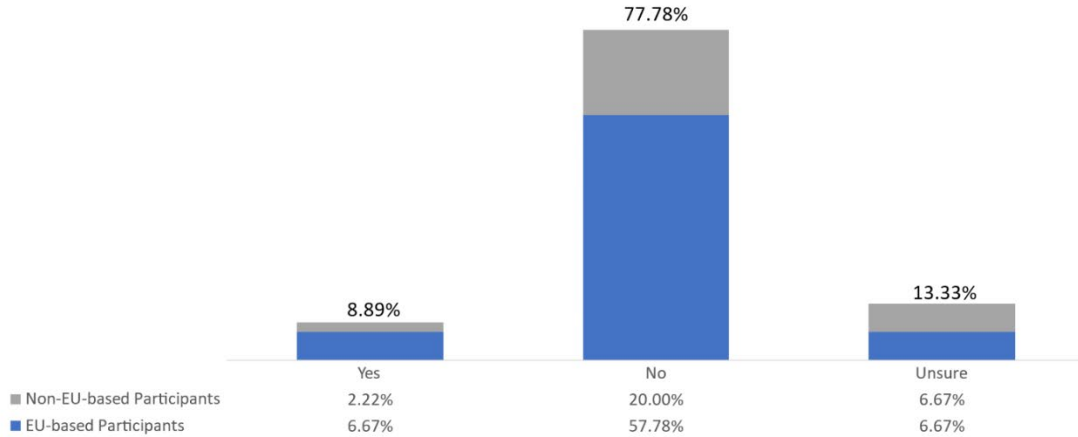
HAVE THERE BEEN ANY CHANGES TO YOUR TESTING MENU SINCE THE IMPLEMENTATION OF THE IVDR?



Early stages of implementation across EU and EFTA member states as of March 2023 show few testing menu changes.

A large concern for the laboratory community was the anticipated consolidation of testing menus as a result of the IVDR. Thus, AMP asked survey participants about changes to their testing menus since the initial IVDR implementation. However, as of March 2023, approximately 50% of survey respondents reported that there had been no change to their testing menu. Interestingly, around 15% saw an increase in size since the implementation.

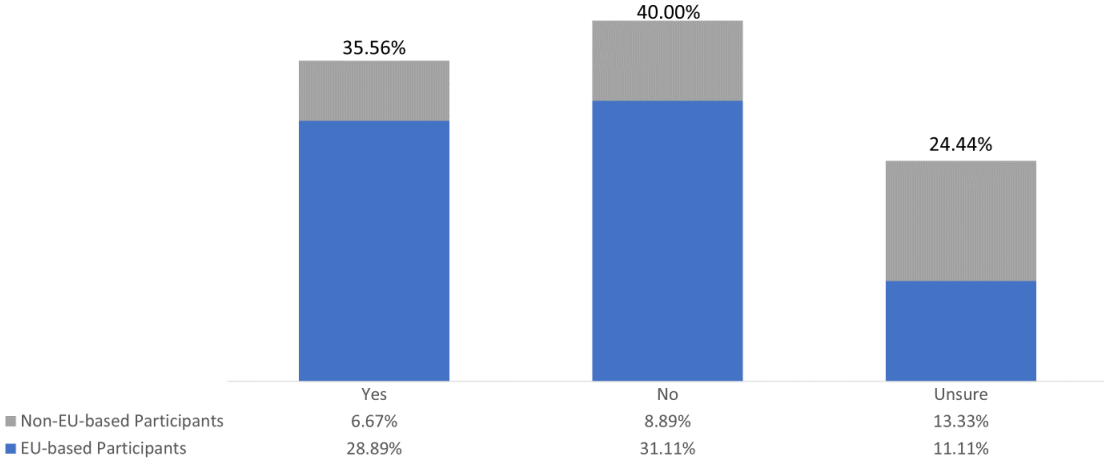
DID YOU STOP OFFERING ANY LDTs, CE-IVD MODIFIED, OR RUO TESTING AFTER THE IMPLEMENTATION OF IVDR?



Most laboratories had not reduced their testing menu as of March 2023.

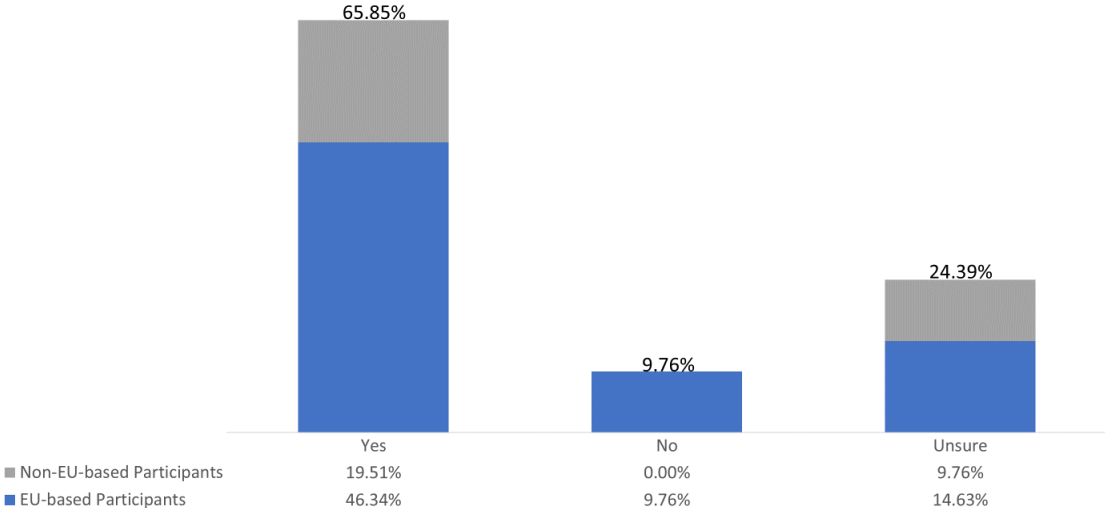
The majority of participants reported they have not stopped offering LDTs or in-house testing as of March 2023, further supporting the finding that many testing menus have not changed as a result of IVDR at this time.

ARE YOU PLANNING TO MAKE ANY CHANGES TO YOUR TESTING MENU TO COMPLY WITH IVDR REQUIREMENTS?

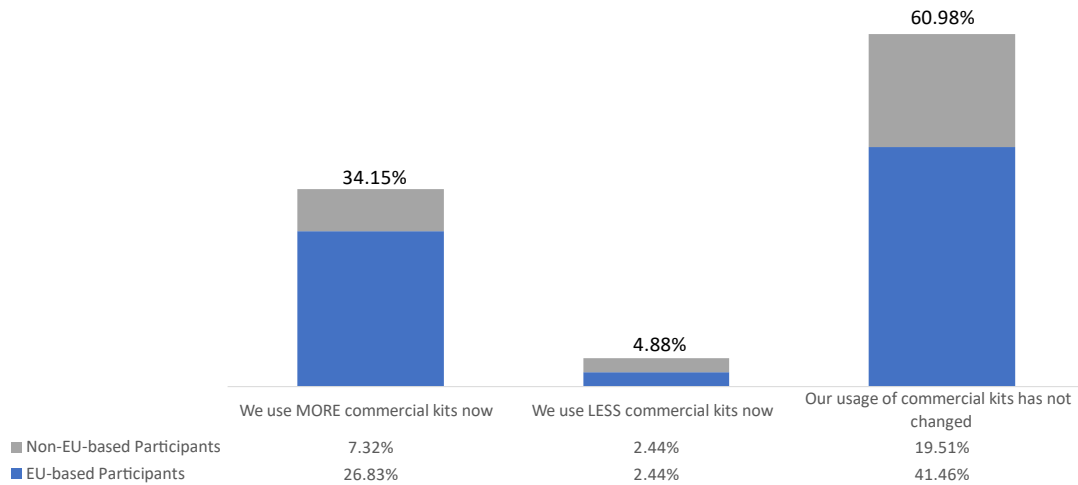


As previously stated, many respondents reported that they have yet to make changes to their testing menu. However, with additional inquiry, some respondents reported that their laboratories are planning changes in the future. Approximately 35% of respondents anticipated there being a need to make changes to their menu. Approximately 25% of respondents were unsure of whether changes would be made. Of note, 40% of respondents reported that they are not planning to change their menu.

DOES YOUR LABORATORY PLAN TO DEVELOP NEW IN-HOUSE TESTS?



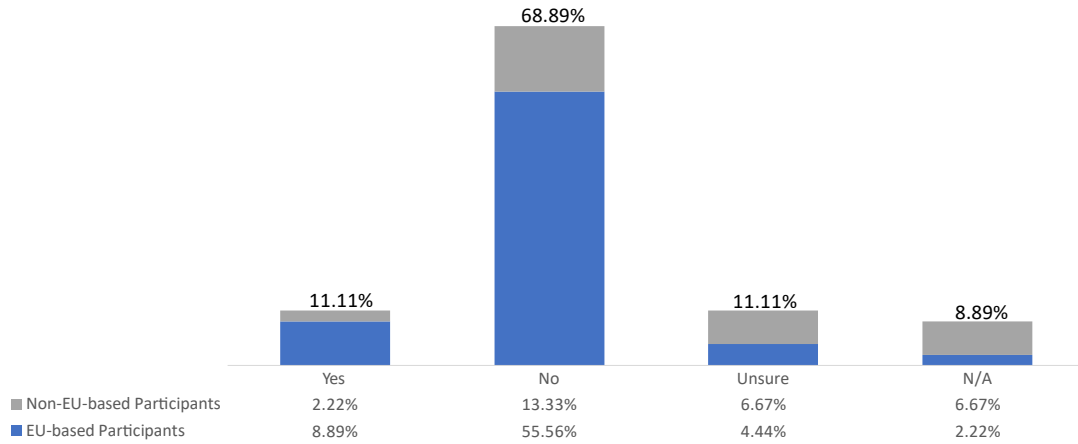
HOW HAS YOUR USAGE OF COMMERCIAL PRODUCTS/KITS CHANGED?



Laboratories plan to continue developing in-house tests.

One of the largest concerns with the implementation of the IVDR is whether laboratories would be forced to stop developing new in-house tests and therefore rely on commercially developed kits. As of March 2023, more than half of the respondents stated their use of commercial kits had not changed at the time. However, 35% reported that they had increased their use of commercial kits. Still, less than 10% of participants reported that their laboratory intended to stop developing new tests. Over 60% of respondents reported that they intend to develop new in-house tests.

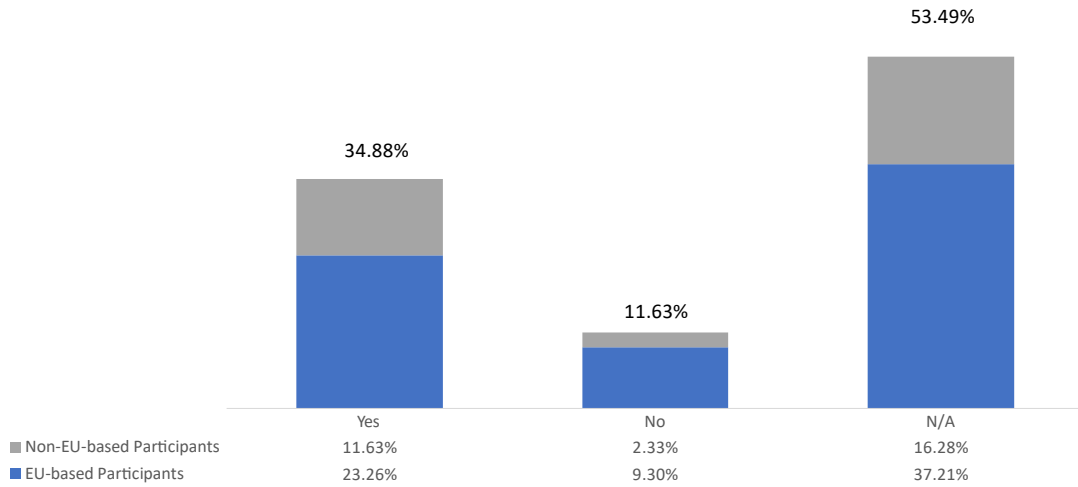
HAS YOUR LAB UNDERGONE THE PROCESS TO GET YOUR IN -HOUSE PIPELINE
(CONFORMITÉ EUROPÉENE) CE MARKED UNDER IVDR?



Most have not yet pursued obtaining a Conformance Europeenne (CE) mark certification for their in-house tests.

Almost 70% of respondents had yet to pursue obtaining a CE mark certification for their in-house tests as of March 2023.

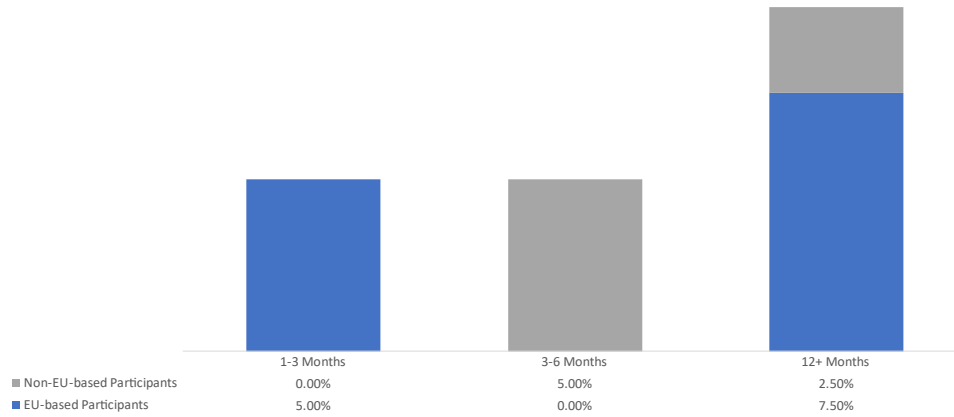
DID YOU OR ARE YOU EXPERIENCING HURDLES IN COMPLETING CE CERTIFICATION PROCESS?



Significant challenges with CE Certification applications continue.

Of those respondents who have initiated the CE Certification process, nearly 35% reported that they have experienced hurdles. Several participants reported challenges with the process, including delays in administrative validations of certifications, financial concerns (fee changes), lack of proper communications from accrediting bodies, and a significant time that is required for the CE Certification process.

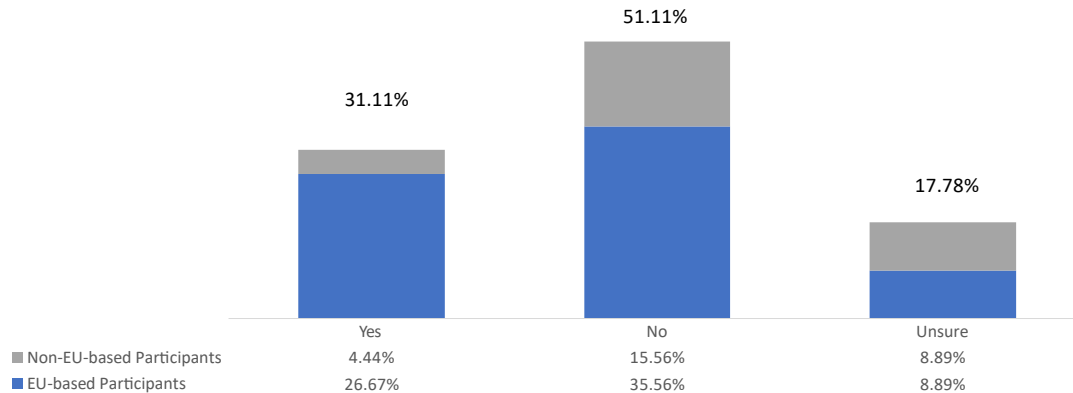
If you completed the CE Certification process, what was the time frame for this process?



Unpredictable time frames for CE Certification process increase burden on labs.

Our data show very different time frames of completion for the CE certification process. AMP questioned participants for additional information to understand the reasons for the variability. Three laboratories pointed to administrative burdens, including one that has not received a response from the government in over a year and another that has been in this process for 24 months.

HAVE YOU HAD ANY DISCUSSIONS WITH PAYERS OF YOUR LABORATORY TESTING SERVICES, IN ORDER TO PREPARE FOR THE NEED TO MEET THESE NEW STANDARDS THAT ARE OUTLINED IN THE MDCG IVDR HEALTH INSTITUTION EXEMPTION GUIDANCE?

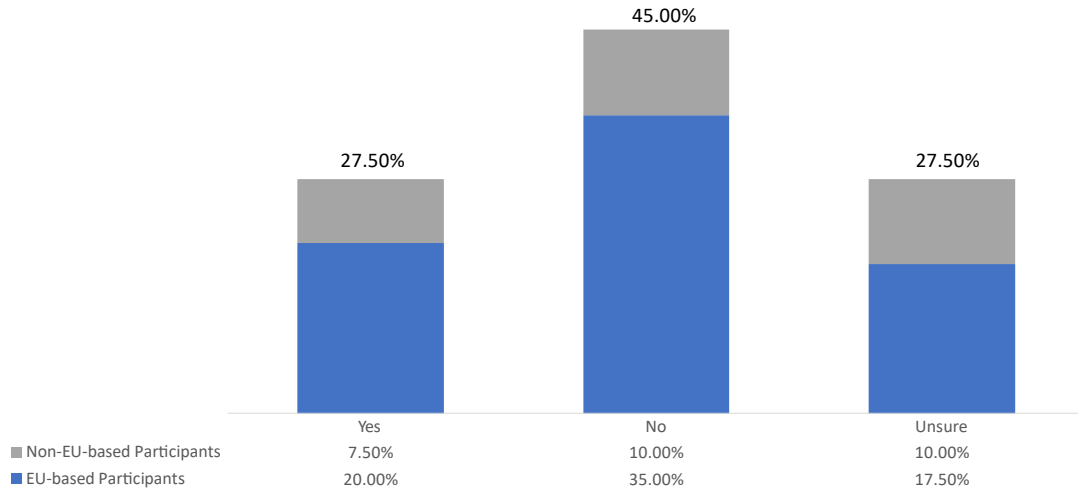


Under one-third of those surveyed have met with payers to prepare for the impacts of IVDR.

Given that several participants expressed concern about increased financial burden, it is troubling to see that less than one-third of participants have met with payers to discuss how the IVDR would impact their reimbursement. AMP is concerned that if the costs for laboratories increase due to the IVDR, the revenue they currently receive from payers will not be sufficient to offset the costs. These concerns are supported by an assessment performed by the European Hematology Association (EHA) that describes the challenges faced by three large university hospitals in the EU and their struggle to meet the requirements for IVDR compliance.¹⁷ In this assessment, the financial burden was one of the main issues, and in response, the EHA recommended the following: “Healthcare system authorities, insurance companies, and other payers should allocate an increased budget for reimbursement of diagnostic testing (estimated 10%–15%), as this will be critical for increasing quality under the IVDR while preserving rare disease diagnostics.”

¹⁷ Lubbers BR, Dombrink I, Kalina T, Hofmans M, Bruun MS, Stanworth SJ, Béné MC, Döhner K, Brüggemann M, Macintyre E, van Dongen JJM. *Experience With IVDR Implementation in Three Diagnostic Laboratories: Messages to EU Health Institutions, Diagnostic Healthcare Payers, and Authorities*. *Hemasphere*. 2023 Mar 7;7(4):e865. doi: 10.1097/HS9.0000000000000865. PMID: 36911048; PMCID: PMC9995097.

DO YOU BELIEVE THE IVDR STREAMLINED THE IVD DEVELOPMENT PROCESS?



Labs report the development process for IVDs needs to be streamlined.

Forty-five percent of participants believe that the IVDR has not streamlined the IVD development process. Many respondents feel concerned about the process moving forward, with some participants describing the new regulation as a major hindrance, particularly in the financial department. Twenty-four respondents commented about the financial burden that they have experienced or expect to experience due to the IVDR. Burdens included “expanded overhead”, “[increased] price in reagents”, “time commitment” and the need to “hire a consultant firm.”

Other trends in the survey data set:

- Respondents pointed to three prominent quality control standards that their laboratories are using to prepare to meet the health institution exemption: ISO 15189, ISO 13485, ISO 14871
- Participants had both constructive and cumbersome experiences with panels that are composed of both modified IVDs and in-house tests.
- Over 20 participants believed that the IVDR will significantly impact clinical trial enrollment and/or patient access to care.

Key Findings:

- As of March 2023, many laboratories have not modified their test menu due to the IVDR.
- The IVDR has impacted:
 - Reporting requirements
 - Interlaboratory knowledge-sharing
 - Finances
 - Workload/documentation burden

The above impacts are exacerbated by:

- Lack of communication by institutions
- Lack of uniform implementation and increased confusion within the laboratory diagnostics community
- Lack of resources and support to implement changes

The survey results showed that many laboratories are unprepared to conform to regulations set by the IVDR and that there is a general sense of frustration and concern about the process currently and moving forward.

Conclusion

The implementation of the IVDR for many laboratory professionals has been difficult. Our results showed that many laboratory professionals have had to dedicate additional time and resources to understand the complexities of the IVDR. With the new obligation to provide increased documentation under the IVDR, an additional burden has been placed on laboratory staff and many may need to hire additional staff. Given the current laboratory workforce shortage, compounded by the COVID-19 pandemic, laboratories will find it even more challenging to recruit and retain professionals in this specialized area of medicine. Notably, **one participant commented that they removed 75% of their offered devices.**

To ensure compliance under the IVDR, the laboratory community must receive proper instruction and education from the European Commission and their respective NBs. Potential changes in payer compensation with an increased financial burden will prove very challenging.

The new IDVR regulations and associated compliance requirements are unclear to many laboratories located in the EU, EFTA, and several non-EU countries. As a result, it may be challenging for laboratory

professionals to adapt and fully implement these requirements by May 2025. This survey is only a snapshot of participants' experience with IVDR implementation as of March 2023. At this early point in implementation, many participants did not see a significant change to testing practices or their respective testing menus. However, this may reflect the timing of the survey as many expressed concerns for the future as the process continues.

AMP plans to conduct a follow-up survey in 2025 and again in 2028 after the IVDR has been fully implemented for three years to track laboratory progression throughout the IVDR process.

Recommendations

AMP recommends molecular diagnostic professionals partner with laboratories and the National Competent Authorities (NCAs) to reduce administrative and other resource burdens while substantially increasing a more thorough understanding of the new IVDR requirements.¹⁸

This could be achieved through collaborations between laboratories and medical professional associations to assist with compliance regulations and guidelines, and potentially increase engagement with other stakeholders, policymakers, and regulators.

AMP also supports the recommendation of the European Hematology Association (EHA) to have healthcare system authorities, insurance companies, national health systems, and other payers allocate additional funding dedicated to properly reimburse diagnostic testing developed to comply with the IVDR.¹⁹ AMP agrees with the EHA's assessment that under the IVDR, this will be critical for preserving rare disease diagnostics.²⁰

AMP Recommendations for the European Union:

AMP recommends the European Commission, European Medicine Agency, and National Competent Authorities facilitate meetings between the clinical laboratory community and regulatory experts to better ensure that laboratories can meet the standards of the IVDR.

AMP also recommends bolstering existing online resources. The European Commission, European Medicine Agency, and National Competent Authorities should also provide additional educational materials and communications, including regularly updated vital documents pertaining to medical device legislation and regulations, on their webpage to assist with streamlining the regulatory process.

¹⁸ European Medicines Agency (2024) *National Competent Authorities (human)* <https://www.ema.europa.eu/en/partners-networks/eu-partners/eu-member-states/national-competent-authorities-human>

¹⁹ Lubbers BR, Dombrink I, Kalina T, Hofmans M, Bruun MS, Stanworth SJ, Béné MC, Döhner K, Brüggemann M, Macintyre E, van Dongen JJM. *Experience With IVDR Implementation in Three Diagnostic Laboratories: Messages to EU Health Institutions, Diagnostic Healthcare Payers, and Authorities*. *Hemasphere*. 2023 Mar 7;7(4):e865. doi: 10.1097/HS9.0000000000000865. PMID: 36911048; PMCID: PMC9995097.

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