**BioMed Alliance – Questionnaire IVDR for diagnostic laboratories**

*On 26 May 2022 the new EU Regulation on in vitro diagnostic medical devices (the IVDR) will come into full effect, replacing the old legislation (the IVDD). This will have* ***substantial consequences for diagnostic laboratories****:*

* *Under the IVDR, they will be responsible for generating sufficient clinical evidence and technical documentation for their in-house devices (IH-IVDs or lab developed tests/LDTs)*
* *If equivalent CE marked IVDs (CE-IVDs) are available from manufacturers, these will have to be used instead; use of IH-IVDs is not permitted anymore in this situation*
* *CE-IVD tests sold after 26 May 2022 have to be CE marked under the IVDR, with the exception of 1) IVDD-certified CE-IVDs placed on the market before the date of application (e.g. at a distributor) can still be sold until 2025 and 2) CE-IVDs with a valid IVDD certificate issued by a notified body (this only concerns certain high-risk tests) can be sold until 2024*
* *Laboratories that use IH-IVDs need to work under an appropriate Quality Management System (ISO 15189 or applicable national provisions)*
* *A more detailed description of the consequences of the IVDR for diagnostic laboratories can be found in the attached* [*publication*](https://journals.lww.com/hemasphere/Fulltext/2021/05000/The_New_EU_Regulation_on_In_Vitro_Diagnostic.2.aspx)

*This means that the transition to the IVDR needs to be prepared carefully by diagnostic laboratories, including making an assay inventory. The BioMed Alliance aims to support this preparation in order to ensure continuity in laboratory diagnostics beyond May 2022. With this questionnaire, we aim to gain insight into the current situation for medical laboratories, in particular the degree of (un)preparedness of medical laboratories for the IVDR implementation, and the impact that the IVDR will have on their test menu. Your input will enable us to supply you with relevant information and to better represent you in the process of EU implementation of the IVDR.*

*Note that your contribution will be treated as strictly confidential; laboratory-specific information will never be shared with third parties or made public.*

*In case you have any questions, please contact Dr. Bart Lubbers:* [*b.r.lubbers@lumc.nl*](mailto:b.r.lubbers@lumc.nl) *or Dr. Isabel Dombrink:* [*isabel.dombrink@uksh.de*](mailto:isabel.dombrink@uksh.de)

*Thank you in advance for your contribution!*

# In which country is your laboratory located?

Click or tap here to enter text.

# With which Medical Society/BioMed Alliance member (or their national counterpart) is your laboratory associated?

EAACI (European Academy of Allergy and Clinical Immunology)

EASD (European Association for the Study of Diabetes)

EASL (European Association for the Study of the Liver)

EFIS (European Federation of Immunological Societies)

EFLM (European Federation of Clinical Chemistry and Laboratory Medicine)

EHA (European Hematology Association)

ERA-EDTA (European Renal Association – European Dialysis and Transplant Association)

ESC (European Society of Cardiology)

ESCMID (European Society of Clinical Microbiology and Infectious Diseases)

ESE (European Society of Endocrinology)

ESHG (European Society of Human Genetics)

ESHRE (European Society of Human Reproduction and Embryology)

ESMO (European Society for Medical Oncology)

ESP (European Society of Pathology)

FEBS (Federation of European Biochemical Societies)

UEG (United European Gastroenterology)

Other: Click or tap here to enter text.

None

# What type of laboratory are you running?

Private non-hospital laboratory

Public non-hospital laboratory

Private hospital laboratory

Public hospital laboratory

University hospital laboratory

University and research laboratory

Industry laboratory

Other: Click or tap here to enter text.

# In which diagnostic fields is your laboratory active?

Allergology

Blood transfusion/Transfusion medicine

Cardiology

Clinical chemistry

Diabetes

Endocrinology

Gastroenterology

Genetics (Human genetics/germline defects)

Genetics (Oncogenetics/acquired defects)

Hematology

Hepatology

Infectious diseases

Immunology/Medical Immunology

Microbiology/Medical microbiology/Bacteriology

Nephrology

Oncology

Parasitology

Pathology (Anatomic pathology)

Pathology (Clinical pathology)

Pharmacology/Toxicology

Urology

Virology

Other: Click or tap here to enter text.

# How many CE-IVDs, modified CE-IVDs, off-label CE-IVDs, RUO kits and IH-IVDs/LDTs are currently implemented in your laboratory?

*Please provide an estimate of the number of assays that you are running for each category per diagnostic field,* ***following the definitions as mentioned below****. Please also describe a few examples per category in the second table.*

*Additional information can be provided in the comments field below.*

*With this information, we will be able to give the national authorities and European Commission a realistic view of the use of the different categories of assays, and how the IVDR is expected to impact on their use.*

1. ***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.*
2. ***CE-IVD used with minor modifications*** *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.:*
   * *Making a dilution of the specimen in the recommended diluent, blank serum or saline solution;*
   * *Required sample pretreatment due to e.g. extreme lipemia because of high, floating lipoproteins;*

* *Serum/plasma creatinine in an alternative body fluid after surgery;*
* *Performing a pretreatment with PEG for excluding macroamylasemia or macroprolactinemia; diversions from manufacturers’ interference index values based on in-house validations;*
* *Use of formula and calculations by labs such as CKD-EPI for eGFR reporting and anion gap calculation for electrolyte disturbances;*
* *Third party IQC in case the healthcare institution has clinical reasons for not running the IQC from the manufacturer;*
* *Inclusion of a conversion factor (e.g. + 10%) to harmonize the results with those in other laboratories.*

1. ***Off-label CE-IVD test*** *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.:*
   * *Using a non-high sensitive troponin assay in a General Practitioner setting or in an ambulance for prehospital triage of ACS patients, for the purpose of excluding patients suspected from ACS;*
   * *COVID-19 test on bronchoalveolar lavage fluid, where the test describes use of nasal swabs.*
2. ***Research use only (RUO) kit*** *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.*
3. ***In-house device (IH-IVD)/Laboratory developed test (LDT)****, e.g.:*

* *Development of a (multiplex) 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.*
* *Development of a flow cytometry antibody panel for an application for which no appropriate CE-IVD is available, such as MRD measurements.*
* *Development of up-to-date sequencing panels in hemato-oncology.*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Diagnostic field | Number of implemented assays: | | | | |
|  | CE-IVDa | CE-IVD with minor modificationsb | Off-label CE-IVDc | RUOd | IH-IVD/LDTe |
| Allergology | # | # | # | # | # |
| Blood transfusion/  Transfusion medicine | # | # | # | # | # |
| Cardiology | # | # | # | # | # |
| Clinical chemistry | # | # | # | # | # |
| Diabetes | # | # | # | # | # |
| Endocrinology | # | # | # | # | # |
| Gastroenterology | # | # | # | # | # |
| Genetics (Human genetics/ germline defects) | # | # | # | # | # |
| Genetics (Oncogenetics/  acquired defects) | # | # | # | # | # |
| Hematology | # | # | # | # | # |
| Hepatology | # | # | # | # | # |
| Infectious diseases | # | # | # | # | # |
| Immunology/Medical Immunology | # | # | # | # | # |
| Microbiology/Medical microbiology/Bacteriology | # | # | # | # | # |
| Nephrology | # | # | # | # | # |
| Oncology | # | # | # | # | # |
| Parasitology | # | # | # | # | # |
| Pathology (Anatomic pathology) | # | # | # | # | # |
| Pathology (Clinical pathology) | # | # | # | # | # |
| Pharmacology/Toxicology | # | # | # | # | # |
| Urology | # | # | # | # | # |
| Virology | # | # | # | # | # |
| Other: Click or tap here to enter text. | # | # | # | # | # |
| Other: Click or tap here to enter text. | # | # | # | # | # |
| Other: Click or tap here to enter text. | # | # | # | # | # |

*a-e) explanation is given above the table*

|  |  |
| --- | --- |
| Assay category | Examples |
| CE-IVDa | Click or tap here to enter text. |
| CE-IVD with minor modificationsb | Click or tap here to enter text. |
| Off-label CE-IVDc | Click or tap here to enter text. |
| RUOd | Click or tap here to enter text. |
| IH-IVD/LDTe | Click or tap here to enter text. |

# Comments:

*For example, was the difference between the first three categories clear, did you check the manufacturers’ instructions for use or is this an estimate?*

Click or tap here to enter text.

# CE-IVDs/CE-IVDs with minor modifications: Have you contacted the manufacturers and/or distributors of the CE-IVDs that you use about whether or not they will CE mark their assays under the IVDR?

*After May 2022, manufacturers are (with few exceptions) only allowed to market diagnostic tests that are CE-marked under the IVDR.*

For all assays

For some assays; estimation of percentage: Click or tap here to enter text.

I did not yet contact any manufacturers/distributors because: Click or tap here to enter text.

# What was their response?

Most assays will be CE marked under the IVDR and timeline are clear

Most assays will be CE marked under the IVDR but timelines are **not** clear

Most assays will **not** be CE marked under the IVDR

Other: Click or tap here to enter text.

# Other categories (Off-label CE-IVDs, RUOs, IH-IVDs/LDTs): Did you check whether equivalent CE-IVDs are available (IVDD or IVDR) that could replace your current assays?

*Under the IVDR, IH-IVDs can only be used when the target patient group's specific needs cannot be met, or cannot be met at the appropriate level of performance, by an equivalent CE-IVD available on the market; IVDD = in vitro diagnostics Directive, the “old” EU legislation this will be replaced by the IVDR.*

For all assays

For some assays; estimation of percentage: Click or tap here to enter text.

I did not yet check for equivalent CE-IVDs because: Click or tap here to enter text.

# What were your findings?

*For example, for which percentage of these assays is an equivalent CE-IVD available?*

Click or tap here to enter text.

# Under which Quality Management System (QMS) is your laboratory currently working?

ISO 15189 (accredited)

ISO 15189 (not accredited)

National requirements: Click or tap here to enter text.

Other: Click or tap here to enter text.

We do not work under a QMS

# Under which Quality Management System (QMS) is your laboratory planning to work under the IVDR?

ISO 15189 (accredited)

ISO 15189 (not accredited)

National requirements: Click or tap here to enter text.

Other: Click or tap here to enter text.

None

# If you currently do not work under a QMS, but are planning to implement a QMS: When did you start/are you planning to start with the implementation?

Click or tap here to enter text.

# Do you think your laboratory will be prepared for the IVDR on 26 May 2022?

*The IVDR will fully apply on 26 May 2022, meaning that in less than one year, all diagnostic laboratories will need to be fully compliant with IVDR Art. 5.5 and Annex I for all off-label CE-IVDs, RUOs and IH-IVDs/LDTs, as defined above.*

Most likely

Maybe

No

I don’t know because: Click or tap here to enter text.

# What are the issues that you are/expect to be facing during your preparations for the IVDR?

*Your input on this question is vital for the BioMed Alliance to support appropriate IVDR implementation while representing all diagnostic disciplines.*

Click or tap here to enter text.

# Which solutions are needed to support diagnostic laboratories with timely and appropriate preparations for the IVDR? Can you explain how these solutions contribute to this?

*Your input on this question is vital for the BioMed Alliance to support appropriate IVDR implementation while representing all diagnostic disciplines.*

Click or tap here to enter text.

# Do you have any comments, questions or concerns regarding the IVDR that are not mentioned above?

Click or tap here to enter text.

*Thank you very much for completing the questionnaire!*

*Please return the completed questionnaire to Anne-Claire Cazottes:*

[*anne-claire.cazottes@biomedeurope.org*](mailto:anne-claire.cazottes@biomedeurope.org)