Position of European consortia in the IVDR era: Support for in-house devices (IH-IVDs) and CE marked IVDs (CE-IVDs)

Bart R. Lubbers and Jacques J.M. van Dongen

Dept. of Immunology, Leiden University Medical Center, Leiden, The Netherlands.

Introduction

After a transition phase of 5 years, the new Regulation (EU) 2017/746 on *in vitro* diagnostic medical devices[1] (the IVDR) will fully apply on May 26th, 2022. The IVDR sets out the rules for the European Union (EU) market for *in vitro* diagnostic medical devices (IVDs) for all actors involved. An important consequence for manufacturers of IVDs is that the requirements concerning proof of performance before launching a product and evaluation of clinical experience afterwards (i.e. clinical evidence and post-market surveillance; see section "CE marking of IVDs") are stricter than in the preceding EU legislation on IVDs (Directive 98/79/EC on *in vitro* diagnostic medical devices[2]; IVDD). As a result, manufacturers will have to rely more often on new clinical data, and therefore on collaborations with diagnostic laboratories to acquire such data.

For health institutions and their diagnostic laboratories, the IVDR also has several important consequences.[3] Their current assay portfolio may need to be adapted, as the availability of commercial, CE marked IVDs (CE-IVDs) might change and new rules are introduced for the use of in-house devices (IH-IVDs). Since use of IH-IVDs will only be allowed for applications for which CE-IVDs are not available or do not have an appropriate level of performance, laboratories that develop new diagnostic methods need to take the IVDR into account when making decisions about innovation and IP management. Furthermore, the increased need for clinical data supporting CE-IVDs provides laboratories with opportunities to set up valuable collaborative research, e.g., performing state-of-the-art research and contributing to (knowledge about) the safety and quality of CE-IVDs, aiding the diagnostic community.

This report summarizes the relevant IVDR requirements for manufacturers, including clinical evidence and post-market surveillance. Subsequently, this report explores different scenarios related to innovation, IP and collaboration with manufacturers that might occur under the IVDR, on the basis of different categories of IVDs (i.e. low to very high complexity CE-IVDs and IH-IVDs). To continue to perform optimal research and diagnostics under the IVDR, diagnostic laboratories should be aware of the changes brought about by the IVDR. Importantly, European research consortia consisting of diagnostic laboratories can play a supportive and coordinating role in the described scenarios.

IVDR requirements for manufacturers

CE marking of IVDs

When a manufacturer wishes to place an IVD on the market, documentation needs to be generated that demonstrates that the requirements dictated by the IVDR have been fulfilled (i.e. regulatory compliance has been reached). This "technical documentation" includes design and manufacturing information (including intended purpose), a risk management plan, data on safety and performance, instructions for use, a declaration of conformity and a post-market surveillance plan. The exact requirements, and hence the depth of this documentation, are determined by the class of the IVD (see also Table 3 on page 14 in the introduction chapter). The manufacturer needs to submit the documentation to a notified body (see below), which evaluates whether all applicable requirements have been fulfilled (a process called "conformity assessment"). If this is deemed not to be the case, the notified body will request the manufacturers to adapt/supplement the documentation, e.g. to collect additional clinical evidence and add this to the documentation. When a certificate is issued based on successful conformity assessment, the manufacturer is allowed to label the IVD with the "Conformité Européenne" (CE) mark and sell the "CE-IVD" on the EU market. Non-sterile Class A devices are an exception to this; they do not have to be assessed and certified by a notified body. Instead, they can be self-certified by the manufacturer after reaching compliance with the IVDR, after which they can issue a declaration of conformity and CE mark the product.

Conformity assessment by notified bodies

Notified bodies are organizations that perform third-party conformity assessment activities including calibration, testing, certification and inspection under a range of EU legislations, including the IVDD and IVDR. To become designated to certify IVDs, notified bodies need to apply for accreditation (based on requirements dictated by the applicable legislation) in the EU member state that they are located in. So far, 14 notified bodies have applied to be designated for the IVDR, but only 4 of them have received this designation to date: BSI (the Netherlands), DEKRA, TÜV SÜD and TÜV Rheinland (Germany).[4] Manufacturers are free to contract any notified body in any member state for certification of their IVDs, as long as the IVDs fall within the scope of the notified body's designation (i.e. proven competence during accreditation).

Clinical evidence: requirements and data sources

The clinical evidence requirement is meant to ensure a high level of safety and performance of each IVD that is placed on the market. Demonstration of clinical evidence ('performance evaluation') should be based on ***scientific validity, analytical performance and clinical performance data*** (see IVDR chapter 56 and Annex XIII).[1] It is critical that this data fully supports the ***intended purpose*** that is claimed by the manufacturer. Therefore, defining the intended purpose (which specifies e.g. the analyte, the condition(s) that are to be detected, the specimen type(s) required and the intended user) is one of the first steps that a manufacturer should take when working on regulatory compliance of a product.

Scientific validity (the association of an analyte with a clinical condition or a physiological state[1]) is typically based on existing scientific peer-reviewed literature; other sources mentioned in the IVDR are relevant information on the scientific validity of other IVDs measuring the same analyte, consensus expert opinions/positions from relevant professional associations, proof of concept studies or clinical performance studies.

Analytical performance is the ability of a device to correctly detect or measure a particular analyte, e.g. analytical sensitivity, analytical specificity, trueness, precision (repeatability and reproducibility), limit of detection (LOD) and limit of quantitation (LOQ) (see also Table 4 on page 15 in the introduction chapter).[1] Analytical performance is principally demonstrated by analytical performance studies, performed in part by the manufacturer and in part by external laboratories (e.g. when testing reproducibility).

Clinical performance is the ability of a device to yield results that are correlated with a particular clinical condition or a physiological or pathological process or state in accordance with the target population and intended user, i.e. proof of performance based on clinical data.[1] Main parameters include diagnostic sensitivity and diagnostic specificity. All analytical and clinical performance parameters should be demonstrated unless it is justified that certain parameters are not applicable. Detailed information about performance parameters can be found in more specialized documents.[5, 6]

Performance studies should be performed in circumstances similar to the normal conditions of use, e.g. use by the intended user, on the target population. According to Annex XIII, demonstration of clinical performance can be based on scientific peer-reviewed literature, published experience gained by routine diagnostic testing and/or clinical performance studies.[1] Scientific literature can include articles, guidelines and textbooks, as long as the data is peer-reviewed.[7] MedTech Europe has proposed that e.g. external quality assurance data and customer testing results are valid sources of data from routine diagnostic testing, as long as sufficient information is available to assess the significance of the data.[7] In practice, a manufacturer will evaluate which data is already available (e.g. by systematically reviewing the literature according to a specified search protocol), and only perform new clinical performance studies when this is necessary to supplement the clinical evidence so that it fully covers the intended purpose. Alternatively, the intended purpose can be adjusted so that it corresponds with the available clinical evidence (with the possibility to extend the intended purpose at a later moment). Evidently, the need for additional clinical performance studies is much higher for new products than for existing products.

Requirements for performance studies are written in IVDR Article 57 and Annex XIII Section 2. These concern e.g., appropriate registration of the study, appropriate documentation (including details about the device and its intended purpose and the study design), data management, compliance with applicable ethical guidelines and informed consent. Additional requirements in Article 58-77 and Annex XIV apply in case of studies involving invasive procedures or companion diagnostics, or interventional performance studies (as opposed to studies with left-over samples).[1] Additional details on clinical performance studies can be found in the ISO 20916 standard "*In vitro* diagnostic medical

devices — Clinical performance studies using specimens from human subjects — Good study practice".

As an example, for a particular clinical performance study, a manufacturer might recruit 5 clinical sites that each analyze 20-50 samples (covering all relevant indications, age groups and specimens, and being representative of as broad a range of results as possible). However, the sample size will always depend on IVD specifics, the required confidence level and the availability of suitable samples.

Overall, it can be concluded that manufacturers can benefit from existing data in case the device was already on the market as a research use only (RUO) product and/or as a CE-IVD under the IVDD. In particular for new products, or in case changes are made to a product that might affect the performance characteristics, new data should be collected. Logically, diagnostic laboratories are straightforward partners for manufacturers for such data collection.

Post-market surveillance: requirements and data sources

The IVDR requires manufacturers to proactively collect and evaluate data from the use of a CE-IVD and to update all documentation accordingly (see IVDR Article 78 and Annex XIII Part B). In contrast to the IVDD, which requires the manufacturer to perform post-market surveillance at least once every 3 years, the IVDR requires this ***at least once per year*** for Class C and D devices. This should assure the safety and performance throughout the lifecycle of the device, e.g. by timely detection and correction of malfunctions and by improvement of effectiveness.

The part of post-market surveillance that addresses continuous performance evaluation (update of clinical evidence) is called post-market performance follow-up. Appropriate methods for data sourcing include gathering of clinical experience gained (e.g. patient registers, post-market clinical performance studies), collecting feedback from users, screening of scientific literature and of other sources of performance or scientific data (e.g. quality assurance activities).[1, 7] In particular in case of 'triggers' such as the identification of new risks, limits to performance or contra-indications (e.g. due to emergence of new mutations), generation of new performance data might be necessary. Comparable to initial collection of clinical evidence, diagnostic laboratories can also play a key role in collecting data in the context of post-market surveillance.

Consequences of the IVDR for innovation, IP management and collaboration with manufacturers

IVDs can be categorized according to their level of complexity (Figure 1). High complexity IVDs are e.g. multi-step, multi-technology and labor-intensive assays, and/or assays requiring complex analysis. Complexity generally correlates with costs, but there is also an association with the type of IVD (i.e. CE-IVD or IH-IVD), as IH-IVDs tend to be more complex than CE-IVDs.[8] This can be explained at least in part by the higher commercial viability of simpler tests. For example, it is more elaborate and requires more expertise to

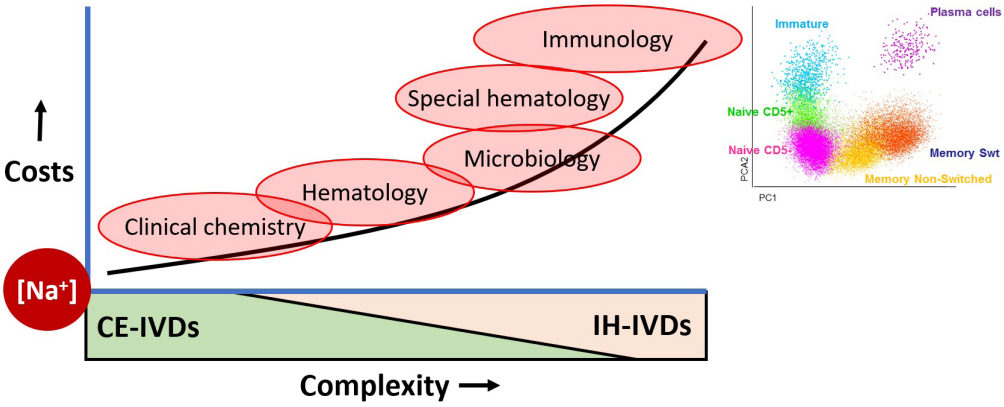

Figure 1. Relation between IVD complexity, costs, CE-IVD/IH-IVD ratio and diagnostic specialty. Examples of low complexity IVDs (blood sodium level test) and high complexity IVDs (detection of leukocyte subsets by multi-color flow cytometry) are given.

develop, validate and reach regulatory compliance for more complex tests. Furthermore, more specific applications, such as diagnosis and monitoring of rare diseases, often require more specialized (complex) tests but at the same time are associated with a smaller market. Finally, average IVD complexity (and consequently the ratio between CE-IVDs and IH-IVDs) in a particular laboratory logically depends on its diagnostic field as well as its level of specialization (Figure 1).[8, 9]

Focusing on innovation, IP and collaboration with manufacturers under the IVDR, relevant scenarios will be explored below, organized by IVD category and complexity.

Scenario 1: Low-medium complexity CE-IVDs

Low-medium complexity CE-IVDs, such as simple blood tests, are expected to stay on the market, i.e. to be CE marked under the IVDR on time (Figure 2). They are associated with a high frequency of use (i.e. they are well-sold) and sufficient data will often be available.

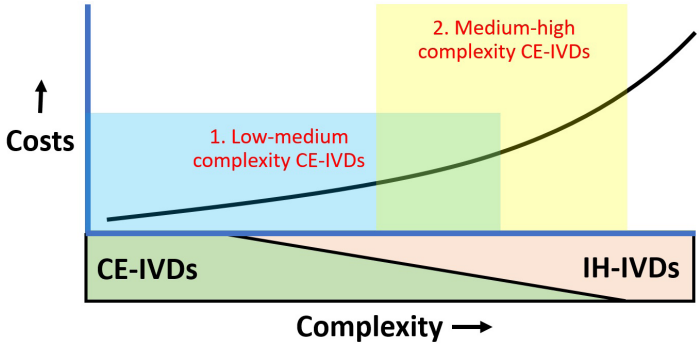

Figure 2. Representation of low to medium complexity and medium to high complexity CE-IVDs.

Scenario 2: Medium-high complexity CE-IVDs

Antibody panels for multi-color flow cytometry and multiplex PCR assays are examples of medium to high complexity CE-IVDs (Figure 2). Possible hurdles for CE marking are limited resources of the manufacturer (as a result of the increased efforts and costs required for regulatory compliance), limited capacity of notified bodies (see section "CE marking of IVDs" and Figure 3) and/or unavailability of appropriate performance data. Because of this, manufacturers are expected to prioritize/focus their regulatory efforts. This means that some CE-IVDs, in particular less frequently used (sold) IVDs, might be (temporarily) discontinued. If this happens, laboratories will need to decide whether or not to develop/implement an IH-IVD for the same application, to stop offering the test or to outsource it/send samples to another laboratory.

Contribution to quality and safety of CE-IVDs

The IVDR requires manufacturers to collect more extensive clinical evidence than the IVDD. In particular, manufacturers might depend on diagnostic laboratories for new clinical performance and post-market surveillance data from their assays. As laboratories continuously receive clinical samples, they have a unique position to validate new assays with the appropriate clinical samples.

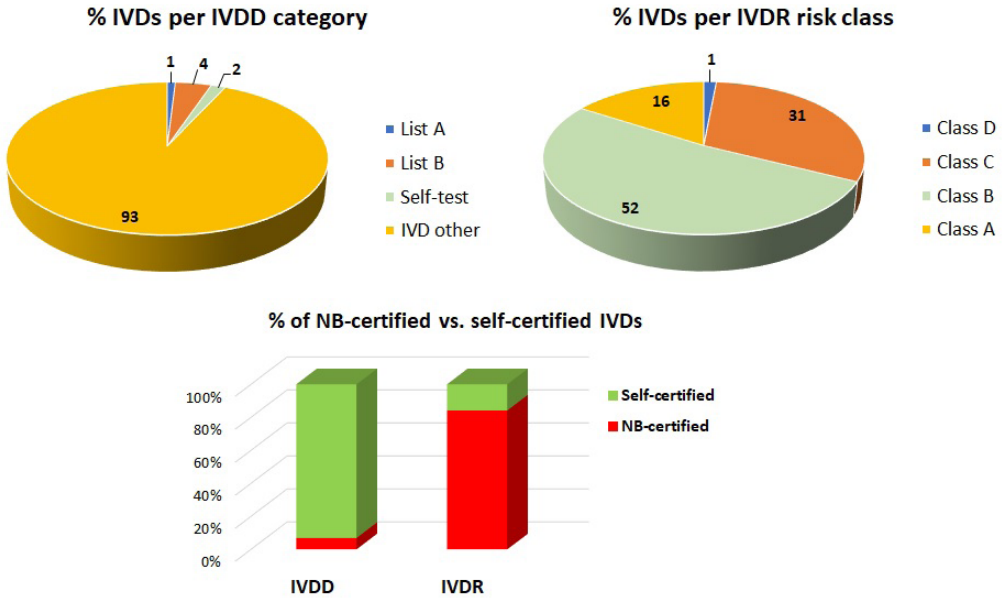

Figure 3. Changes in IVD classification/risk class in a representative selection of IVDs in the Netherlands (n=946).[10] a) Under the IVDD, only List A, List B and Self-test IVDs are certified by a notified body (7%); other IVDs are self-certified. b) Under the IVDR, only non-sterile Class A IVDs are self-certified (i.e. >84% are certified by a notified body). c) Illustration of the increase in dependency on notified bodies associated with the replacement of the IVDD by the IVDR. Graphs made based on data from the Dutch National Institute for Public Health and the Environment (RIVM), 2018.[10]

For diagnostic laboratories, data collection for industry (on a collaborative basis) can be interesting as it can result in new insights, publications and other benefits – depending on the amount of effort e.g. early access to new products, free kits or a compensation fee. If the IVD has been on the market already as an RUO or CE-IVD, a manufacturer might be able to rely on other (existing) data sources instead (see section "CE marking of IVDs").

Scenario 3: Medium complexity IH-IVDs

Many diagnostic assays and assay principles have their origin in (academic) diagnostic laboratories. Often, the reason to develop and use IH-IVDs is the lack of availability of CE-IVDs for a specific application.[8] It is currently not uncommon that, once a suitable CE-IVD becomes available – which is a realistic scenario, in particular for less complex IH-IVDs (Figure 4) – laboratories continue the use of their IH-IVD.[8]

Under the IVDR, it is not an option anymore to use an IH-IVD when an equivalent CE-IVD with an appropriate level of performance is available.[3] In this situation, the IVDR requires laboratories to switch to the CE-IVD (in case more than one suitable CE-IVD is available, the laboratory is free to choose one of these). For laboratories that invested in innovation, this means that they run the risk that they have to switch to another assay with the same level of performance, or even to buy their own assay from a manufacturer – unless they protected their assay by patent filing and/or decided to commercialize their IH-IVD. For these and other reasons, it will be crucial to consider appropriate strategies for innovation in diagnostics, IP strategy and interaction & collaboration with industry under the IVDR.

Protection and commercialization of novel IP

Novel tests and technologies developed by (academic) laboratories are generally made public by publication in scientific journals. By protecting new intellectual property (IP) before publication via filing of a patent, the inventors obtain power over commercial exploitation of their invention. This is especially important in case of IP with commercial potential. On the basis of a license agreement, the resulting patent can be licensed to a manufacturer. Of course, such IP strategy is not new, but it will become more relevant under the IVDR.

Importantly, IP protection via patent filing does not exclude publications about all technical details of the invention and its applications. Instead, it makes diagnostic innovations even more relevant and more viable for actual usage in diagnostic patient care.

Co-development of an IVD by one or more laboratories and a manufacturer, preferably already initiated during the assay design phase, can also be an attractive option. Possible advantages are sharing of knowledge, sharing of investment costs, optimization of assay development, and a more efficient CE marking process. When co-developing an IVD, it is still preferred to patent the invention.

An advantage of collaboration with industry on IVD development and commercialization is that the IVD will usually become available for the diagnostic community (i.e. for a lot of patients). By choosing to commercialize their IH-IVD, the laboratories of the inventors might avoid having to purchase another CE-IVD when it becomes available on the market.

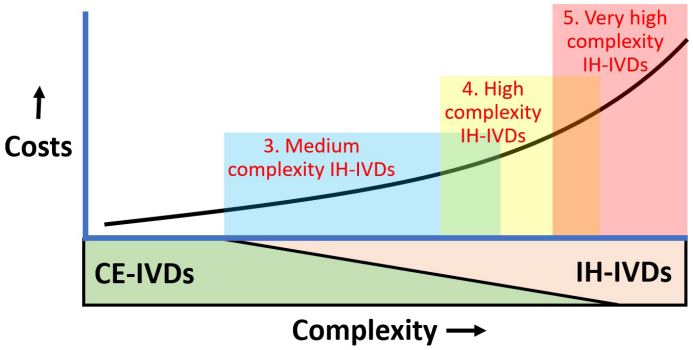

Figure 4. Representation of medium complexity, high complexity and very high complexity IH-IVDs.

Moreover, in return for licensing their IP, inventors might negotiate a discount for purchasing the IVD from the manufacturer, and/or royalties. Such income can subsequently be used to continue innovative research, for example in the form of sustainable research networks. Finally, manufacturers might be further interested to extend a collaboration in order to obtain (additional) clinical performance data.

Scenario 4: High complexity IH-IVDs

For high complexity IH-IVDs, no equivalent CE-IVDs might be available, or at least not with an appropriate level of performance (Figure 4). For example, when the IH-IVD performs better than available CE-IVDs, the use of the IH-IVD will be preferred.

When IH-IVDs are used under the IVDR (i.e. after the date of full application, May 26th, 2022), laboratories should generate the required clinical evidence and documentation accordingly.[3] In line with the quality objectives of the IVDR, IH-IVDs are preferably composed of reliable, high-quality reagents with limited lot-to-lot variability.[5] Such products should be manufactured under stringent quality control. Manufacture under *good manufacturing practice* (GMP) is a good way to assure products of consistent grade, purity and activity.[5]

Even though often no suitable CE-IVDs might be available to replace high complexity IH-IVDs, it can happen that such CE-IVDs become available in the future. This means that there is a continuous "risk" that the IVDR demands a switch to a commercial alternative. Consequently, different scenarios should continuously be considered for each IH-IVD, including commercialization. Finally, IP protection is highly advised when use of IH-IVDs is continued, especially for IH-IVDs with commercial potential. Such IP protection places the scientists-inventors in the appropriate position for guiding their diagnostic product to the market, in a balanced collaboration with the selected manufacturer, which best fits with the developed novel diagnostic product, both technically and with respect to market position.

Scenario 5: Very high complexity IH-IVDs

Typically, no equivalent CE-IVDs are available for the highest complexity class of IVDs (Figure 4). This means that laboratories will continue to depend on their IH-IVDs. However, the complexity of the assay might be reduced, e.g. by improving accuracy/decreasing

troubleshooting, developing guidelines or using advanced software/automated analysis. In such case, it might be possible to increase its potential for commercialization. Even though such an innovative process can be a significant (group) effort, this has the advantage that the assay can become available for use in routine diagnostics by the (global) community. Two examples from the ESLHO networks follow below.

EuroClonality: Molecular assays for diagnosis of leukemias and lymphomas

The EuroClonality Consortium was initiated in 1995-1996 and formally started off in 1998 as BIOMED-2 Concerted Action BMH4-CT98-3936 with the aim to design novel diagnostics for detection of clonal lymphoid cells, in order to discriminate between reactive lymphocytes (e.g. cells responding to bacteria of viruses) and clonal cell expansions of lymphocytes (i.e. malignancies). For different immunoglobulin (IG) and T-cell receptor (TR) genes, primer sets were designed flanking the variable (V), diversity (D) and joining (J) regions of these genes (Figure 5).[11-13] In case of a reactive lymph node, IG/TR gene amplification followed by analysis by GeneScan technology leads to a multi-peak pattern that indicates the presence of PCR products of different lengths. However, in case of leukemia or lymphoma, many cells are derived from the same cell, i.e. one malignantly transformed lymphocyte, resulting in one single peak. Since IG/TR genes consist of a large number of gene segments, many primers needed to be designed, tested and combined in order to end up with an assay that can detect normal/reactive versus clonal lymphoid cell populations with a high accuracy.

Extensive design and evaluation processes together with immunologists, molecular biologists, hematologists, and pathologists from 47 European institutes finally resulted in the approval of a total of 6 IG/TR primers sets: *IGH, IGK, IGL, TRB, TRG* and *TRD*. The strength of

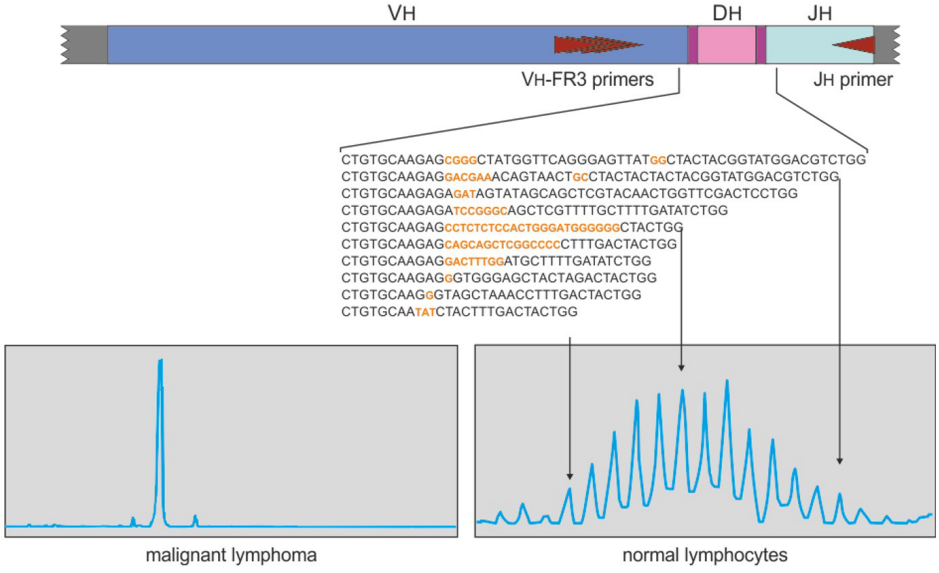

Figure 5. Innovative design of a multiplex PCR assay for detection of lymphoma based on analysis of IGH gene rearrangements.[11]

the (super) multiplex primer design brought the advantages of both efficient primer sets per IG/TR locus as well as the demonstration of the complementarity of the primer sets, such as combined usage of both *TRG* and *TRB* primer sets and combined usage of *IGH* and *IGK* primers sets.[12, 14-16] This highly complex technical design process took the EuroClonality Consortium more than 3 years. Subsequently, extensive clinical studies were performed over a series of 4 years, finally including over 650 cases with malignant or reactive lymphoproliferations, and demonstrating the power of the designed primer sets.[12-16] Collection of a large number of clinical samples from patients with rare diseases (369 B cell malignancy and 188 T cell malignancy samples) was only possible because of the many laboratories that aligned their efforts during these **clinical performance studies.** The innovative IG/TR target-specific multiplex primer tubes were commercialized together with Invivoscribe (San Diego, CA), and as a result are now used for diagnostic patient care in virtually all countries around the world.

EuroFlow: PIDOT antibody panel for diagnosis of primary immunodeficiencies

The EuroFlow Consortium was initiated in 2004-2005 and formally started in 2006 as Specific Targeted Research project (STREP), supported by the European Commission (LSHB-CT-2006-018708), with the aim to develop new flow cytometry-based diagnostic methods and tools. Flow cytometry can be used to discriminate between cells with different characteristics, based on staining them with fluorochrome-conjugated, marker-specific antibodies. Initially the EuroFlow Consortium fully focused on the diagnosis, classification and monitoring of leukemias and lymphomas (L&L), resulting in multiple screening tubes, classification tubes, and minimal residual disease (MRD) tubes. Most of these antibody tubes were designed according to differentiation and maturation pathways in order to be able to understand the deviation from normal in case of L&L patients. The extensive experience with leukocyte differentiation and maturation pathways and the consequent detection of many different leukocyte populations appeared to be perfectly applicable in other fields in Hematology and Immunology, such as for the diagnosis and classification of patients with a primary immunodeficiency as well as for immune monitoring in several disease conditions from infectious diseases and auto-immune diseases as well as in immunotherapies.

Today's possibilities of multi-color flow cytometry are far-reaching, but this also makes the technique very complex. However, by combining panel design/product development with data analysis using advanced software, complex flow cytometry assays can be adapted for routine diagnostics. For example, by going through a complex iterative process of design-testing-evaluation-redesign over a 6-year period, EuroFlow managed to create an easy-to-use 8-color 12-antibody panel for diagnostic screening of primary immunodeficiencies (the PID Orientation Tube; PIDOT).[17, 18] To be able to compare patient samples to samples from healthy subjects, age-related reference values were acquired. Based on the PIDOT tube and corresponding reference values, absence of disease-specific leukocyte populations can be clearly visualized for e.g. STAT3, IL2RG SCID, RAG2 SCID (Figure 6).[19] The clinical performance studies described in this publication were performed by 10 EuroFlow institutes and included samples from 321 healthy subjects and 233 PID patients; these studies provided valuable data on **scientific validity** (the association between a 'fingerprint' of leukocyte populations and primary immunodeficiencies), **analytical performance** (e.g. reproducibility) and **clinical performance** of the assay.

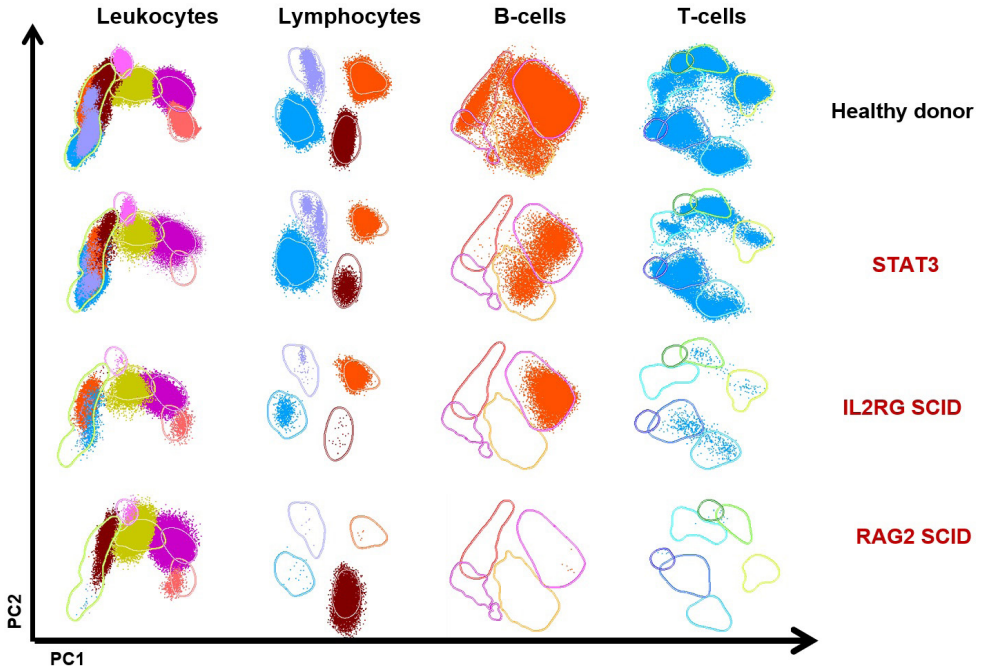

Figure 6. Detection of deficits in specific leukocyte subsets based on the EuroFlow PIDOT tube.[17]

These and other innovative flow cytometry antibody panels have been patented by EuroFlow and are available as CE-IVD products from Cytognos (Salamanca, Spain) and BD Biosciences (San Jose, CA).

Discussion

The IVDR has different fates in store for different IVDs. Organized by IVD type (CE-IVD vs. IH-IVD) and complexity, a number of realistic scenarios were explored with attention to the implications for innovation, IP management and collaborations. Even though complexity is surely not the only factor determining the fate of an IVD (e.g. IVD class, frequency of use and adequate preparation and planning by a manufacturer also play a role), this provided a useful framework for this exercise. Hence, scenarios were related to the type of IVD for which they are most likely, but not exclusively, to occur. It should also be kept in mind that the details of the scenarios will ultimately depend on implementation and interpretation of the IVDR by the European Commission and national competent authorities (e.g. guidance, jurisprudence) and support of implementation and translation into practice by manufacturers, notified bodies and diagnostic laboratories (see Figure 7).

Many of the currently available CE-IVDs will stay on the market under the IVDR, often supported by additional clinical evidence. In order to obtain sufficient performance data, companies might look for collaboration with (networks of) diagnostic laboratories. Some CE-IVDs will be discontinued due to a compromised profitability or a limited capacity to CE mark IVDs.

If IH-IVDs are used for applications for which suitable CE-IVDs are available, laboratories will have to use a CE-IVD rather than their own IH-IVD. If no such suitable CE-IVD assay is available, IH-IVDs can continue to be used if the applicable requirements of the IVDR are fulfilled. Ideally, GMP grade reagents are sourced to facilitate consistent performance of IH-IVDs. When a laboratory, or network of laboratories, has developed their own IH-IVDs, and these assays meet the safety and performance of available CE-IVDs, commercialization might be considered. It is advised to protect the IP whenever possible, and to make use of the strong collective position.

The fact that CE-IVDs will be "dominant" over IH-IVDs under the IVDR will affect incentives and opportunities for IVD commercialization. In addition, manufacturers will require data from new clinical studies more frequently. This means that collaboration between industry and diagnostic laboratories will become more common in the coming period. Ideally, this is done under transparent and fair agreements and in a synergistic way so that both sides (and ultimately the patient) benefit.

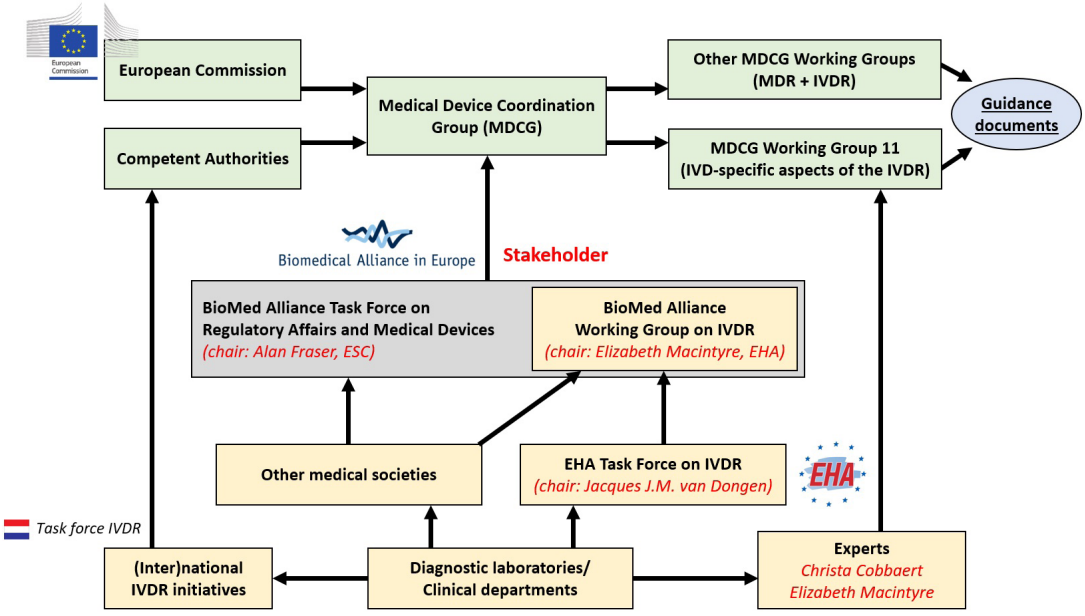

Figure 7. The IVDR implementation process. A main task of the Medical Device Coordination Group (MDCG), which is composed of members from the European Commission and national competent authorities, is to draft guidance documents that explain specific requirements of the IVDR in more details. In this process, the BioMed Alliance is considered as an important stakeholder from the side of the healthcare professionals, representing 35 European medical societies (including the European Hematology Association; EHA). Similarly, stakeholders from the side of the medical device industry and the notified bodies are involved in this process. In parallel, individual experts are also involved in as part of the more specialized MDCG Working Groups. Finally, many independent initiatives such as the EHA Task Force on IVDR and the Dutch Task force IVDR have been established with the aim to support their followers with preparations for the IVDR (e.g. by publication of informative documents/guidance[3, 20]) and/or to provide advice and raise concerns to the authorities on the national or international level.

In conclusion, in order to optimally benefit from their innovation efforts and to keep maximum control over their assay portfolio, diagnostic laboratories should take the IVDR into account when making decisions about innovation, IP management and collaboration with industry. Acting as a collective can be beneficial because of the stronger negotiation position and the possibility to share work, knowledge and experiences. Diagnostic laboratories, individual or as a collective, play a crucial role in the process of making high-quality, well-validated IVDs available to the diagnostic community.

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