Working together to untangle IVDR

The European Union's *In Vitro* Diagnostics Regulation (IVDR) replaces the *In Vitro* Diagnostic Medical Devices Directive (IVDD), completely overhauling the regulations regarding pre- and post-market requirements for IVD devices. This has implications for the entire supply chain, from manufacturers with responsibilities for design, development and commercialization, to agreements between manufacturers and key economic operators, such as importers and distributors. The regulation also introduces specific requirements and limitations on hospitals and labs developing their own diagnostic tests, which must review and, if necessary, replace in-house assays with commercially available CE-marked, IVDR-certified alternatives to ensure compliance for the chosen application.

The IVDD came into effect more than two decades ago, and a lot has changed since then. There was a clear need for reform to cover the gaps created by new technologies – such as point-of-care and genomics devices – and products targeting personalized medicine, which are not covered by the IVDD. This led the European Union to embark on a major regulatory overhaul to modernize device classification, and address any product safety or quality issues that may have gone unnoticed. The resulting IVDR came into force in May 2017, requiring all existing IVD devices, plus any new devices coming to market, to meet the requirements of the new legislation. The transition period was initially due to end on May 26, 2022 – a tight deadline that was compounded by the COVID-19 pandemic – and so a more progressive roll out was implemented to prevent disruption in the supply of essential healthcare products. While all new IVD devices and Class A non-sterile devices were required to be IVDR compliant from May 2022, a more gradual implementation – between 2025 and 2028 – is now permitted for devices in other classes and in-house assays.

The IVDR contains very specific requirements for analytical and clinical performance, and every manufacturer must demonstrate that its devices meet these standards, as well as the general safety performance requirements for device safety and quality. There is also an increased need for post-market vigilance activities to ensure cradle-to-grave compliance, with clearly defined responsibilities for manufacturers, distributors, importers and authorized representatives to enhance transparency throughout the entire supply chain. The benefits are evident, but what is less obvious is the effect on commercial labs creating their own in-house tests, who are now defined as manufacturers and must therefore comply with IVDR. While it may, in some cases, be possible to switch to a CE-marked test, commercial assay manufacturers are likely to be reluctant to invest significantly in niche products with a limited market.

Ganzimmun Diagnostics in Mainz is one of the largest labs in Germany, serving both primary care doctors and complementary medicine practitioners. It offers a wide variety of genetic, clinical chemistry and immunoassay tests for different clinical indications, some of which have been developed in house. Ganzimmun's PRRC (person responsible for regulatory compliance) Petra Hammer explained the impact of IVDR on her laboratory: "Under IVDR, we are both a customer using third-party assays and a manufacturer of lab-developed tests. We use a range of commercially available assays from Tecan – predominantly saliva diagnostics, but also other endocrinology and immunology assays, as well as complementary tests for integrative medicine – which we run on a Freedom EVO® platform, giving us a complete solution for high throughput analysis. In addition, we use a large number of in-house tests, all of which must be reviewed, and any necessary action taken to comply with IVDR, by the end of 2028."

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Petra continued: “We began by performing a gap analysis to establish the difference between IVDD and IVDR, to see what we needed to do to ensure our existing assays were compliant and could continue to be used. Most of the tests we use are Class B, with a few in Class C. We can’t discontinue in-house tests that are still required by our clients when there is no CE-marked alternative available, so we have to check whether the validation of these assays is acceptable for IVDR. We found that around 20 percent of our assays – generally Class C tests – need revalidating, which will require a lot of time and resources. The biggest challenge for us is that IVDR demands technical documentation of in-house software. As this was not necessary before, and much of the work done in the past is not documented, so we have to establish what was done, when, and how. We are also obliged to perform post-market surveillance now, which consumes further resources.”

Every department at Ganzimmun offers a different range of in-house assays, and it is each team manager’s responsibility, with support from the quality management team, to establish which tests – if any – must be revalidated. “In the past, tests were developed in each lab, with no specific department to guide the process. To overcome this, we recently set up a department with responsibility for assay development. This team supports the individual labs by providing information to help them devise a plan for revalidation, testing and statistical analysis.”

While Ganzimmun is responsible for ensuring its in-house assays are IVDR compliant, for third-party tests the burden falls on the manufacturers, who must work with a Notified Body to achieve IVDR certification for their products. As a result, new tests required to extend the scope of a lab’s services may not be available as soon as they would like; it can be quicker to develop an assay in house, as this does not require a Notified Body. There is much to be gained by clinical laboratories and IVDR-ready manufacturers – such as Tecan – collaborating to ensure that labs have access to CE-marked tests that meet their needs. “Labs need tests that are both suitable for their applications and regulatory compliant. CE-marked tests validated by the manufacturer are IVDR compliant by definition, but we still need to check that they work as expected with our samples and the equipment in our lab. If we are uncertain whether the way we are using a test complies with the manufacturer’s intended purpose, we ask them to help us check that we are performing the assay correctly. The continuous communication between our lab and Tecan gives us the information and practical support that we need, as well as allowing us to provide input about our needs and challenges, with benefits for both parties,” Petra concluded.

For more about Tecan’s IVDR-ready assays, visit
www.tecan.com/ivdr-overview

To learn more about Ganzimmun Diagnostics, go to
www.ganzimmun.de