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Letter to Editor

# In vitro diagnostic medical device regulation (IVDR): the end of laboratory developed tests (LDT)?

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In May 2017 the in vitro diagnostic medical device regulation (IVDR) proposed by the EU was published after the in vitro diagnostic medical device directive (IVDD) [1,2].

What is the difference between a directive and a regulation?

A directive sets certain aims, requirements and results that must be achieved in every member state; it identifies a process that should be implemented by member states. The national authorities should adapt their laws and procedures to meet these aims. On the contrary, regulations are a direct form of EU law; they have a legal force on par with national laws.

From a historical point of view, the IVDR was a response to public scandals regarding implanted medical devices such as hip prostheses and breast implants [3,4]. IVDR was created to enforce transparency in the manufacturing process of medical devices and diagnostic assays.

A notified authority ensuring the quality of the products must review all the devices.

Obviously, this regulation will have a huge impact on test availability and the ability of our laboratories to implement LDTs.

For manufacturers, the previous IVDD required a self-declaration certifying a good manufacturing practice. The IVDR requires conformity assessment by notified bodies [5-7]. The evaluation of the clinical evidence (scientific validity, analytical performance, and clinical performance) of medical devices will be a challenge for many manufacturers, probably too expensive; consequently they may not certify some products resulting in a scarce availability of IVD-certified assays.

But for our laboratories the IVDR could have a worrisome impact. Laboratories will use IVDs marketed by companies which have received CE-IVD certification. However, the possibility of using LDTs remains for laboratories providing specialized assays for pathology, genetics, predictive tests. But for our rigorously validated assays, preferably according to the EN-ISO 15189 procedures, a switch to equivalent commercial alternative will become mandatory. This will require re-validation of new assays, new equipment and at the end this will result in time, efforts and costs.

Moreover, healthcare institutions are obliged to justify for each LDT its use and demonstrate that the specific needs of a patient cannot be met with a comparable IVD device available on the market. The arguments for rebuttal can be technical or clinical and/or the national guidelines produced by scientific societies and the scientific literature. All these items must be

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documented and handed over on request of the competent authorities.
The consequences of IVDR are very important and the time to organize our labs is short; the date of application will be 20 May 2022.
It is advisable that our scientific society envisions the IVDR legislation and expresses an opinion on the consequences.
The Dutch scientific societies involved in this problem (Clinical Chemistry, Pathology, Microbiology, Clinical Genetics, Immunology, Pharmacy) organized a task force and produced a document [8] that served as a basis of discussion with the Health Ministery and consequently with EU healthcare authorities.
A series of questions could be raised and discussed:
How can the EN-ISO15189 support the validation of LDT?
Which and how many are the notified bodies certifying the assays? How much time can pass before reaching an authorization?
Small factories producing assays for niche activities might not have the resources for certification.
What will be the impact on innovation in our labs?
The costs of a certification process for a LDT from a notified body are too high for an academic or a peripheral hospital.
The introduction of article 5.5 of the IVDR will decrease our response to the rapidly evolving needs of our profession.
It might be very useful if SIAPEC-IAP could organize a working group on this topic before it's too late. May 2022 is here.

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