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European Society of Human Genetics

EUROPEAN SOCIETY OF HUMAN GENETICS

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ESHG POLICY STATEMENT

Regulation EU 2017/746 (the IVD directive) is a threat to both precision medicine and crisis management if the Article 5-§5 conditions (d)-(i) are not removed

Conclusion

ESHG strongly recommends that Article 5-§5 conditions (d) to (i) for in-house exemptions are removed from the IVD directive, while conditions (a) to (c) are kept. Failure to do so will increase health care costs and jeopardize our ability to design precise "personalized" laboratory tests (necessary for precision medicine) and to adapt to shifting test needs (like repurposing instruments for covid-19 testing).

Background

Regulation EU 2017/746 on *in vitro* diagnostic medical devices (the IVD directive) will be European law from May 26th, 2022. The intentions of the legislators have been appropriate: to secure quality of all kinds of medical diagnostic tests, and to make sure such tests are performed within the frame of the health care system. An apparently convenient means to obtain this is to demand industry standard CE marking of tests and instruments.

In-house exemption to CE marking

Since CE marking is too cumbersome and expensive for the low-volume specialized tests designed in many diagnostic laboratories, also as part of precision medicine, an in-house exemption to the requirement for CE marking has been made (article 5-§5). Such in-house tests are very common in medical genetics. However, this in-house exemption can only be invoked if several conditions are fulfilled (numbered a-i). One condition is that the laboratory must be accredited according to EN ISO 15189 or a similar nationally approved system. This condition makes much sense since such accreditation automatically implies quality management and risk evaluation (other requirements). More problematic, however, is condition (d): "*the health institution justifies in its documentation that the target patient group's specific needs cannot be met […] by an equivalent device available on the market*". In other words: If a CE marked commercial test exists that gives similar test results, that test must be used – and cost is not an issue.

Precision medicine out of control

So far commercial CE marked tests for rare conditions are exceptional, likely because the "market" is too small, i.e. not worth the investment. This may change when next generation (whole-exome or whole-

genome) sequencing (NGS) is established as the basis for all kind of rare disease diagnostics; companies that now label their sequencing instruments "*for research use only*" may suddenly introduce a CE marked diagnostic "NGS-package" using the same instruments that will return a standardized set of sequencing data for local interpretation, like they have done for NIPT (non-invasive prenatal testing). This will turn in-house laboratory skills into an unaffordable luxury.

Furthermore, it will be too expensive to develop test reagents (like unique FISH probes) since the documentation requirements for non-commercial reagents in the IVD-directive goes beyond ISO 15189. The need for control measures that goes beyond EN ISO 15189 has not been documented as necessary for securing good laboratory quality. Practice in line with the well-established ISO-standard is in our view a sufficient quality control. We are, however, unsure if it is wise to allow national exemptions to this standard, like Article 5-§5 now allows. If Article 5-§5 stays as it is, commercial interests will govern precision medicine, and patient interests will suffer because in-house personalized testing will not be possible.

Let us keep the flexibility and creativity alive

Standardization is fine if you want to mass produce a car, but not if you suddenly need to find a creative solution to novel problems in patient diagnostics (as part of precision medicine) or pandemic control (to enhance covid-19 test capacity). The ability to rapidly repurpose testing was crucial to obtain pandemic control in Europe, and here Europe had an advantage over the more rigorous US system. Let us not lose this capacity because a too rigorous IVD directive becomes EU law. That would really be a threat to public health.

On behalf of the Executive Board of the European Society of Human Genetics

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