European Alliance for Personalised Medicine

Council General Approach on the IVD Regulation
Briefing document, 12 October 2015

The Council has issued a General Approach on the Proposal for a Regulation on in vitro diagnostic medical devices in September 2015. The text, which aims to overhaul the way in which these specific types of diagnostic devices are regulated, will have a significant impact on personalised healthcare. The way in which companion diagnostics are defined, in-house assay exemptions applied, clinical evidence gathered, highly specialised distance-sales regulated, and a transition period decided will profoundly change the structures within which IVDs reach patients in the application of personalised healthcare.

In addressing these points in the new approach, policymakers should avoid creating an overly bureaucratic system that stifles patient access to safe and reliable diagnostics that allow for personalised healthcare. This can only be done by acknowledging that IVDs more broadly, and companion diagnostics specifically, cannot be subject to the same requirements as other medical technology or medicinal products. Instead, all IVDs must be subject to specific assessments and requirements that are appropriate for these technologies in proving their safety and efficiency.

Call to action

EAPM calls on legislators from the European Parliament, European Commission and the Council to:

Ensure patients have access to **safe and reliable IVDs** in a timely manner;
Define companion diagnostics appropriately to reflect the small number of IVDs that play a unique role in choosing patients that are suitable or unsuitable for a specific therapy;
Exclude special treatment for in-house assays except when no appropriate CE-marked product is available and existing loopholes are closed;
Define clear and proportional requirements for IVD devices used for 'Distance Sales'; and
Account for the specificities of companion diagnostics and other IVDs to ensure **appropriate and proportionate requirements** on clinical evidence, transparency, and the transition period.
Maintain an **attractive and competitive environment for innovation in the diagnostic area,** especially considering the future competitiveness of the many European SMEs developing new diagnostic test, platform and providing diagnostic services.

Companion diagnostics

The new legislative text proposes concrete mechanisms intended for the specific control of companion diagnostics, including a unique definition that should allow for their clear identification from among a milieu of 40,000 IVD products. The final definition should only reflect the small subset of devices that act as gatekeepers for advanced therapies . The correct definition is a first step in acknowledging the role companion diagnostics play in personalised healthcare, including their relationship to the patient and a therapy, which is very different from other IVDs.

To ensure the safety of patients undergoing testing with companion diagnostics, it is necessary that once analytical performance has been established, an intermediate assessment mechanism be available to ensure that patients involved in interventional studies are kept safe and that a clear path to market for companion diagnostics is not unnecessarily interrupted. Likewise, it is during these studies that the companion diagnostic demonstrates its clinical validity by determining that the detected biomarker does indeed correspond to the adequate selection of patients. The clinical validity cannot therefore be established before the study.

In-house assays

Development and use of in-house assays constitute critical components in the evolution of innovation and addressing unmet diagnostic needs, as may occur when a new pathogen is identified or in the case of an outbreak necessitating a rapid response. Not unlike other diagnostic tools, these tests also provide key healthcare

information on the patient's condition, and if they are companion diagnostics, they will help to determine the suitability of a patient for a specific therapy.

To ensure that safety risks are not taken when using in-house assays, these devices must also be subject to oversight, and EAPM welcomes proposals to enhance the guarantee of safety. This includes applying special rules for in-house assays only when no comparable CE-marked assay is available and ensuring that appropriate oversight mechanisms are in place for the laboratories performing in-house assays. Laboratories should also only be permitted to use the in-house assay exemption if they are non-commercial.

Distance Sales

Personalised medicine often involves disruptive technologies, which in turn are often based on new business models. This includes an evolution toward centralised laboratories. Successful integration of these promising technologies requires a regulatory framework that offers legal certainty and clarity for all stakeholders involved.

The "Distance Sales" provision (art. 5(2)) of the Council draft is a welcome advance in providing clarity on the regulation of devices used in centralised laboratories. Yet the remainder of the draft text has not been aligned to the provision, either in its language or its requirements. For instance, "Distance Sales" devices are by definition never "placed on the market" as is the case for other IVDs in Europe. As such, they would be excluded from the Regulation under a literal reading of art. 1(1). Furthermore, certain requirements, like those relating to chemical and electrical design, stability, instructions for use, and even CE-marking may be disproportional or inappropriately extraterritorial when applied to devices that are used solely by the manufacturer and never enter the European Union market.

The Regulation should ultimately address the distinct features of 'Distance Sales' devices to ensure clarity and proportional measures for safety and reliability.

Horizontal issues

Transparency – The level of transparency for IVD-related information is contingent on the level of intellectual property and other protections afforded to these types of medical technology. IVDs do not have data exclusivity with regard to study data nor can the target of the study be covered directly by a patent. For instance, a human gene cannot be patented and by disclosing details such as the performance characteristics of the IVD, unprotected trade secrets would be made public. In order to account for the commercial sensitivities, information on IVDs can be stored in the EUDAMED database (registration, UDI, vigilance, notified body certificates, performance evaluation studies, summary of safety and performance), while the full technical file should be stored by the manufacturer.

Genetic testing – The discussion surrounding a possible prescription requirement for certain IVD testing must ensure the right of patients to comprehensive information that allows them to make an informed decisions. However, it should be kept in mind that there are many different types of genetic testing and requirements must be proportionate to risks, which are not the same when testing for inherited and transmitted characteristics as compared to acquired somatic mutations (e.i. tumor mutations).

Freedom of research - IVD development and important research frequently takes place in universities, hospitals and other non-for profit research organisations. This research does not necessarily aim to get a product on the market, certainly not before having enough data to understand whether the test would be of any use to patients. While the introduction to the draft Regulation is very clear about the – in vitro diagnostic medical devices aiming to obtaining a CE mark, the current Council text is more ambiguous. A new recital should be included to clarify that the Regulation only applies for getting products on the market.

Clinical evidence requirements – The new clinical evidence requirements in the proposed regulatory text are greatly increased for all categories of IVDs. These requirements must be made clear, applicable, feasible and appropriate for implementation. They must also be proportionate to the risk posed by IVDs as, for example, most studies on IVDs rely on samples from biobanks and do not require patients to use an IVDs as part of the study. IVDs also never directly impact patient outcomes and as such, applying clinical benefit requirements to IVDs is often not appropriate. When an interventional trial is appropriate for an IVD, it may be necessary to reduce administrative burden through communication with a clinical trial counterpart for a related companion drug.

Transition period – The original five-year transition period proposed by the European Commission is a more realistic target for ensuring all of the new mechanisms of the proposed regulation are in place, particularly when considering that the revision completely overhauls the system and will impact every aspect of the pathway.

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