

Briefing on in vitro diagnostic medical devices for patients' organisations

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1. Introduction

1.1 WHAT IS AN IN VITRO DIAGNOSTIC DEVICE

In vitro diagnostic medical devices (IVDs) include all tests performed to provide a diagnosis by assessing a biological substance provided by a patient in a test tube (e.g. tests to monitor liver enzymes, and levels of electrolytes such as calcium, sodium, or potassium), as well as devices for self-testing (e.g. pregnancy tests, blood glucose monitoring devices for diabetes etc.).

They provide information on medical conditions that may assist doctors with:

- providing a correct diagnosis
- monitoring the progression of an illness
- informing treatment decisions
- determining the predisposition toward a disease

The majority of IVD tests are performed in advanced laboratories and other secure medical environments, but in recent years, many more devices have been developed for point-of care testing and patient self-testing, giving patients and health care professionals better access to information on medical conditions.

1.2 WHY DO THEY MATTER TO PATIENTS?

They are important to the patient community as they play an essential role for the diagnosis of a disease, for population screening, and the monitoring of prescribed treatments. One particularity compared to other medical devices is that they are generally not provoking direct risk or benefit for the patient on their own: the risks or benefits are indirect, based on further actions by the patient or healthcare professionals. Decisions and resulting actions about how to prevent, manage or treat a medical condition can be based on other indicators on top of the information provided by the diagnostic device.

It is important to know these 3 particular types of devices:

device for self-testing: device intended to be used by lay persons, including devices used for testing services offered to lay persons through the internet (article 2 point 4)

device for near-patient testing: device that is “intended to perform testing outside a laboratory environment, generally near to, or at the side of, the patient by a health professional” (Article 2 point 5)

companion diagnostic: “device which is essential for the safe and effective use of a corresponding medicinal product” (Article 2 point 6)

1.3 HOW ARE THEY CURRENTLY REGULATED?

In vitro diagnostics devices were regulated by an EU directive since 1998.¹ Under the Lisbon Treaty, the European Union has a competence to adopt harmonising measures setting high standards of quality and safety for medicinal products and medical devices (Article 168, paragraph 4).² As IVDs are produced and circulated all over the European Union, it is important to have common rules to ensure the devices on the European market are safe for EU citizens.

1.4 WHY A NEW REGULATION AND WHEN WILL IT APPLY?

The European Commission made a new proposal for a legislation in 2012. The aim was to strengthen the safety of devices, improve their surveillance once they are on the market, and improve transparency to the public and information to users. The proposal was debated in the European Parliament and the Council, who reached an agreement in June 2016.³

2. What are the other changes that are important for patients in the Regulation?

2.1 SAFETY AND QUALITY OF CARE

Many healthcare decisions are taken based on the data provided by IVD devices. Ensuring the quality of these devices is therefore essential.

2.1.1 CONFORMITY ASSESSMENT

The Regulation defines a new classification system for IVDs, with class A,B,C, D. Class D encompasses the devices that pose the most risk for public health and patients, for example “Devices intended to be used to detect the presence of, or exposure to, a transmissible agent that causes a life-threatening disease with a high or suspected high currently undefined risk of propagation.”⁴ Conformity of IVDs have to be assessed according to different rules depending on the class the device belongs to (Article 40). As for the medical devices Regulation, there are stronger provisions in relation to monitoring the activities of notified bodies in the new IVD Regulation.⁵

¹ <http://eur-lex.europa.eu/legal-content/FR/TXT/?uri=celex%3A31998L0079>

² <http://eur-lex.europa.eu/legal-content/EN/ALL/?uri=OJ:C:2008:115:TOC>

³ <http://data.consilium.europa.eu/doc/document/ST-9365-2016-REV-3/en/pdf>

⁴ Classification rules are detailed in Annex VII of the Regulation.

⁵ For more details about these changes, see EPF’s briefing on “Medical devices briefing for patients: Patient safety in the new Regulation” pp7-8

2.1.2 SCRUTINY ON IVD MEDICAL DEVICES CLASSIFIED AS HIGH RISK

For class D devices, a scrutiny mechanism has been put in place, which means that when a certificate of conformity (to declare conformity with the Regulation) is issued by a notified body for a class D device, notified bodies⁶ must inform competent authorities⁷. Upon reasonable doubt the competent authority or European Commission can review the work of the notified body, or ask for scientific advice through a panel of experts (Article 42).

2.1.3 CLINICAL EVIDENCE

The Regulation takes measure to strengthen the collection and assessment of clinical evidence in order to assess the conformity of IVDs with the Regulation. All manufacturers have to carry out a performance evaluation, to demonstrate the scientific validity, analytical performance and clinical performance of the device. This is defined as a continuous process in the Regulation (Annex XII Part A). Manufacturers have to draft a performance evaluation report following this assessment.

Manufacturers must carry out a clinical performance study in order to provide clinical evidence for in vitro diagnostic devices, unless it is justified to rely on another source of information to obtain clinical evidence. In a similar way as for clinical investigation, a clinical performance study must be subject to an ethics review with an ethics committee, comprising at least one lay person (Article 2 point 45b), and in particular patients or patients organisations (Recital 43a). Like for clinical investigation, a clinical performance study must be registered (Article 49), and for studies in several member states there is a single assessment procedure (Article 56), and rules around substantial modification of the study protocol and early termination (Article 53 and 55).

2.1.4 VIGILANCE AND MARKET SURVEILLANCE

The IVD Regulation contains measures to ensure that the safety of IVDs is monitored by manufacturers and competent authorities once it is on the market, to prevent serious incidents (Chapter VII), very similarly to the measures taken for medical devices.⁸

⁶ Notified bodies are independent bodies, accredited by authorities of Member States, to verify and certify the conformity of medical devices with the EU directives (or the new Regulation once it is in application). The authorities that accredit notified bodies are National Competent Authorities (also called competent authorities)

⁷ The authorities that accredit notified bodies are National Competent Authorities (also called competent authorities)

⁸ For more details about these measures, see the EPF briefing “Medical devices briefing for patients: Patient safety in the new Regulation”, or chapter VII of the IVD Regulation pp5-6

Manufacturers of class C and D devices must provide a safety periodic update report at least annually (Article 58c) to summarize relevant information gathered as part of post market surveillance activities.

Like for medical devices, the IVDs Regulation requires that Member States take appropriate measures and establish electronic and non-electronic ways of reporting incidents, to encourage reporting by patients and healthcare professionals of serious incidents involving an IVD device, in order to prevent these incidents (Article 64 ba).

2.1.5 IN VITRO DIAGNOSTIC DEVICES SOLD ON THE INTERNET

An important safety issue for the patient community is the reliability of tests sold directly to patients on the Internet. The Regulation makes it clear that devices available online must comply with the provisions of the Regulation, and a competent authority can require the EU declaration of conformity to be provided. A Member state can also ask an internet website which sells IVDs to cease its activities, when this request is to protect public health (Article 5). This was a key concern raised by EPF in its position therefore we welcome these provisions.

2.1.6 IN HOUSE IN VITRO DIAGNOSTIC DEVICES

In its position published in 2013, EPF advocated for the possibility for healthcare institutions to develop, use or modify in-house tests to respond to the needs of specific groups of patients, while ensuring the quality of these tests. The Regulation keeps the possibility for healthcare institutions to develop such in house tests provided it is not on an industrial scale, and that it addresses specific needs which cannot be met by devices available on the market (recital 9,9a, 9b and Article 4 paragraph 5).

2.2 TRANSPARENCY AND INFORMATION TO PATIENTS

The new Regulation on IVDs explicitly highlights the importance of transparency and access to information, to empower patients and healthcare professionals to make informed decisions and maintain trust (Recital 28).

Information to patients and healthcare professionals is essential for in vitro diagnostic devices in order to interpret the results of tests accurately.

The new Regulation sets rules to ensure that patients are provided with appropriate information to give their **informed consent** when taking a genetic test, and that they are provided with **counselling** for tests which provide information on the genetic predisposition for medical conditions and/or diseases which are generally considered to be untreatable according to the state of science. Member States have the responsibility to put in place such provisions (Article 4a). This goes in the right direction, as EPF had advocated for avoiding to

treat all genetic conditions as similar in risk and to draw up guidelines with healthcare professionals at national level to define when genetic counselling is necessary.

The new Regulation also prohibits **false claims**, which means that the device cannot be described as having property it does not have (Article 5a).

The Regulation establishes new requirements for information to be provided to patients, in particular for devices for **self-tests and near patients testing** (Section 17 of Annex I).

For the classes of IVDs that would pose the most risk to patients if the device was failing to provide an accurate result (class C&D), manufacturers should provide a **summary of safety and performance** written in a clear language for the intended user (Article 24), and make it publicly available in cases where it is relevant for patients to have access. The summary will contain information to identify the device and manufacturers, information on risks and undesirable effects, suggested profile and training of users and a post market performance follow up.

Sponsors of clinical performance studies⁹ also need to publish the report of the study at least when the device is registered, and provide a lay summary of the results.

The new Regulation also clarifies provisions related to the **informed consent** for patients/subjects participating in clinical performance studies (Article 48b), as in the medical devices Regulation.¹⁰

For vigilance once the in vitro diagnostics is on the market, Member States have to take measures to **raise awareness** of patients and healthcare professionals regarding the importance of reporting incidents (Article 59 para 3).

Like for medical devices, there are provisions to extend the purpose of the **database** (currently Eudamed) to enhance transparency through providing better access to information to patients and healthcare professionals (Recital 29). The database will provide information concerning the device registration, notified bodies, performance studies, vigilance and post marketing surveillance (Article 25).¹¹

⁹ Clinical performance studies are “undertaken to establish or confirm the analytical or clinical performance of a device” according to the Regulation. They are the equivalent for IVDs of clinical trials.

¹⁰ For more details about these measures, see the EPF briefing “For more details about these measures, see the EPF briefing “Medical devices briefing for patients: Patient safety in the new Regulation” p 7

¹¹ For more information on this, please see our briefing on “transparency and information to patients in the new medical device regulation” pp5-7

2.3 PATIENT INVOLVEMENT

Provisions on patient involvement are similar to those adopted in the Regulation on Medical Devices:

- The competent authorities should take into account, where appropriate, the information provided by and views of relevant stakeholders, including patient and healthcare professionals' organisations and manufacturers' associations (Recital 50a). This means that you can report your concerns regarding safety or quality of devices to competent authorities.¹²
- The views of laypersons, in particular patients and patients' organisations have to be taken into account by ethics committees (Article 2 point 45b).
- Modalities defined in article 78 for the Medical Device Coordination Group also apply for in vitro diagnostics which means that like for medical devices, stakeholders including patients can be invited by the group as observer in relevant subgroups.¹³

The final agreement fails to integrate a proposal from the European Parliament to involve patients and healthcare professionals in the review of instruction for use for in vitro diagnostic devices as advocated by EPF to ensure information is tailored to the needs of users.

3. How can patient organisations contribute to safety and quality of IVDs?

Other than the issues mentioned above, patient organisations can contribute proactively to the safety and quality of in vitro diagnostics devices and ensure the patients' perspective is taken into account in the implementation of the Regulation.

What provision	What action	Which organisation
Summary of safety and performance	Advocate for patient involvement in the decision to define for which IVDs summaries should be written accessibly for patients and to ensure they are effectively provided in a user friendly language	European level organisations

¹² The list of competent authorities is available here: https://ec.europa.eu/growth/sectors/medical-devices/contacts_en

¹³ For more details about this provision , see the EPF briefing “Medical devices briefing for patients: Patient safety in the new Regulation” p9

Ethics committees	Advocate for patient representatives to be involved in ethic committees, and raise awareness of the difference of expertise between a lay person and a patient. As patients bear the risk of clinical investigations, their participation in evaluating and managing risk is a right.	National patients' organisations
Vigilance	Ensuring Member States put in place effective campaigns for patients on reporting of incidents, and that the forms for reporting are accessible and patient friendly	National patients' organisations and European level organisations
Transparency on clinical investigations results	Advocate for patient involvement in the guidelines that will be drafted by the European Commission on clinical investigation report and the summary	European level organisations
Internet sales of IVDs	Report to your competent authority if you have a particular concern regarding the online sale of an in vitro diagnostic medical device in your country	National organisations
database	Advocate to ensure patients have appropriate access to information on in vitro diagnostics devices through the database, in a clear and easy to understand language	European level organisations
Instruction for use of self-tests for patients	Provide feedback to your national competent authorities if patients face issues with information provided to them on self-tests devices	National organisations

4. Conclusion

The European Patients' Forum will continue to inform its members and monitor implementation of the Regulation on in vitro diagnostics medical devices, to ensure patients have access to quality information about IVDs and to quality, reliable devices.

5. Resources

Agreement of the Council and the European Parliament on the Regulation on in vitro diagnostic medical devices of 15 June 2016 (awaiting final publication at the official journal): <http://data.consilium.europa.eu/doc/document/ST-9365-2016-REV-3/en/pdf>

EPF position of September 2013 on IVDs: <http://www.eu-patient.eu/globalassets/policy/medicaldevices/ivd-epf-position-statement-sept13.pdf>

EPF position of November 2014 on IVDs: <http://www.eu-patient.eu/globalassets/policy/medicaldevices/epf-recommendations-council-ivd-nov14.pdf>

European Commission (DG Growth) webpage on medical devices: https://ec.europa.eu/growth/sectors/medical-devices_en

List of national competent authorities for medical devices: https://ec.europa.eu/growth/sectors/medical-devices/contacts_en

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