EPF Position Statement on the European Commission's proposal for a Regulation on In Vitro Medical Devices

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Introduction

In Vitro Diagnostic medical devices 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 (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, or, in some cases, 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.

They are important to the patient community as they play an essential role for the diagnosis of a disease, for population screening, the monitoring of prescribed treatments, and for HTA purposes. One particularity compared to other medical devices is that they are generally not provoking direct risk or benefit for the patient on their own: it is 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 may be based on several indicators of which the data provided by a single diagnostic test is only one part.

In September 2012, the European Commission issued two proposals for Regulations, on Medical Devices, and In Vitro diagnostic Medical Devices, as well as a Communication on safe, effective and innovative medical devices and in vitro diagnostic medical devices for the benefit of patients, consumers and healthcare professionals, available here.

While EPF has been involved in the debate on medical devices[1], this is our first contribution as regards in vitro diagnostics medical devices. EPF chose to do a separate statement as while a significant part of the Regulation is similar to the Medical Device proposal, this piece of legislation also raises issues related to genetic testing and patient safety that are important for the patients' community.

[1] http://www.eu-patient.eu/Initatives-Policy/Policy/Medical-Devices/

1. Scope and definitions (Chapter I)

1.1. SCOPE (ARTICLE 1)

EPF supports the proposed changes to clarify and extend the scope of the IVD Directive[2] to include:

- high-risk devices manufactured and used within a single health institution,
- tests providing information about the predisposition to a medical condition or a disease (e.g. genetic tests)
- tests providing information to predict treatment response or reactions (e.g. companion diagnostics), which are considered as in vitro diagnostic medical devices
- medical software

1.2. DEFINITION OF IN VITRO MEDICAL DEVICES (ARTICLE 2)

EPF supports the definition of in-vitro medical devices, and the drawing up of the categories for **near patient testing devices** and **self-testing devices** to encompass those devices that are not used in a laboratory environment. We also welcome the specific provisions to ensure a stricter assessment of these devices even when classified as lower risk (Article 40).

EPF is very concerned by the growing trends towards direct-to-consumergenetic testing and profiling services- we believe that this growing market needs to be regulated by the EU:

Direct to consumer sale of genetic tests[3]

Direct-to-consumer sale of genetic test is an important concern for the patient community, in particular given the presence of unreliable tests on the market. We support the principle of high-quality information and advice to all patients who consider taking such a test.

While there is currently no clear consensus amongst our member patient organisations on whether better regulation or an outright ban on direct-to-consumer sale to would be the most appropriate strategy, a majority of those who responded to this question favours better regulation, for the following reasons:

1) A ban would hamper the development of devices that encourage self-care and empowerment of patients as regards chronic diseases prevention and management in the future (from diagnostics to monitoring of diseases by the patient themselves).
2) This might have the unintended consequence of encouraging sale of direct-to-consumer tests illegally over the Internet. There is a demand from patients for such direct-to-consumer tests for various reasons, such as issues around access to specialised centres in remote areas, or fear of stigma.
3) A ban on Direct-to-consumer tests, which are mostly sold over the Internet and often originate outside the EU, would be impossible to enforce.

[2] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:1998:331:0001:0037:EN:PDF (Article 1 para 1b)
[3] The statement below is not supported by Alzheimer Europe, which supports ban of genetic testing.

4) The wording "persons admitted to the medical profession" chosen by the Rapporteur is too restrictive: It does not take into account the development of new skills in certain healthcare professions, such as nurses and pharmacists, clinical genetic scientists, and genetic counsellors.

Appropriate regulation should from the patients' perspective include the following elements: High-quality, peer- reviewed information to patients; including on success rates and with appropriate communication of risks as regards results, and advice to consult with healthcare professionals. Tests provided to patients should have undergone a strong conformity assessment, as applied to the highest-risks devices, to ensure their clinical validity.

However, one patient organisation of those that responded strongly supports the ban proposed by the rapporteur on the grounds that:

1) Certain tests provide information on susceptibility or risk to develop a disease, but it is not explained to the patient that a negative result does not mean one will never have the disease, while a positive result does not mean the patient will necessarily develop the disease; this lack of information may have dramatic consequences for the patients, their carers and their family.
2) Providing information to patients on a leaflet would not be sufficient, as understanding genetic information and taking decisions based on this information requires a high level of health literacy. A ban would ensure that patients receive genetic counselling before taking the test and when receiving the results.
3) A ban should be accompanied by strong advice to patients against illegal offers.

We call on the European Parliament to take action on this issue as part of the Regulation, as we believe there is a need for a coordinated solution at European level. Stakeholders, including patient organisations, need to be involved to ensure patients in Europe have access to high-quality genetic tests, while ensuring the safety and quality of services, and empowering patients to make informed health decisions. EPF is undertaking further work with its membership on this issue.

Genetic testing and self-testing devices

The Regulation should refer to the Additional Protocol to the Convention on Human Rights and Biomedicine concerning Genetic Testing for Health Purposes developed by the Council of Europe[4], which developed **key principles regarding the quality of genetic testing services** and providing high-quality information[5] to consumers of such services.

The Regulation should ensure that patients and consumers are provided **with high-quality, reliable, non-promotional information** about genetic testing devices, regarding their use and how to interpret the results: one example of such information is the FAQ developed by

[4] http://conventions.coe.int/Treaty/en/Treaties/Html/203.htm
[5] http://www.coe.int/t/dg3/healthbioethic/Source/en_geneticTests_hd.pdf

the European Genetic Alliances Network (EGAN) on genetic testing and biomedicine.[6] Guidance and descriptions of possible results, including positive and negative outcomes, should be included as well as information on the clinical validity of the device (e.g. its success rate) and advice on where patients can find support and medical advice.

Guidelines for professionals on how to communicate results appropriately should be developed with the input of patients' associations.

All self-testing devices[7] should be developed with the aim to empower patients: the clear expectation is that the use of these devices should improve diagnosis and potential outcomes at an acceptable cost, while giving patients further treatment choice.

Categorisation of devices

We welcome the requirements for cooperation between Member States on the regulatory status of devices- we strongly believe that classification and categorisation of device should be the same across Europe. We also welcome the possibility for the European Commission to adopt an implementing act to determine if a product or category of product is an in vitro device. We believe it is essential to have appropriate framework for companion diagnostics, especially in the context where personalised medicines are likely to develop – ensuring appropriate cooperation to ensure safety and quality of these products is paramount.

2. Making available of devices, obligations of economic operators, reprocessing, CE marking, free movement (Chapter II)

2.1 LABEL AND INSTRUCTION FOR USE (INFORMATION TO PATIENTS)

Annex I section 17 details the information that manufacturers are required to provide. For self-testing and near patient testing devices, further information is required, including:

- Advice to the user on action to be taken (in case of positive, negative or indeterminate result), on the test limitations and on the possibility of false positive or false negative result. Information shall also be provided as to any factors that can affect the test result (e.g. age, gender, menstruation, infection, exercise, fasting, diet or medication);
- a statement clearly directing that the user should not take any decision of medical relevance without first consulting the appropriate healthcare professional;

[6] http://www.biomedinvo4all.com/en/research-themes/medical-genetics
[7] This includes non-genetic tests such as blood glucose monitoring devices for Diabetes

- For devices intended for self-testing used for the monitoring of an existing disease, the information shall specify that the patient should only adapt the treatment if he has received the appropriate training to do so.

We welcome information required by Annex I section 17 - and particularly the specific information for near patient testing devices but we believe this information should be reviewed by users (both patients and healthcare professionals) to ensure it is understandable and reliable. Compulsory check of the information provided to patients should be foreseen and patients' involvement required as already exists for medicinal product. Patients have a fundamental and legitimate right to access information on all aspects of their health and their treatments, including high-quality, non-promotional, unbiased, comparative and validated information on the safety, efficacy, clinical validity, utility, implications for daily life, clinical follow-up, HTA outcomes, product availability and costs of medical devices.

Information and health literacy is key for patients to become effective co-managers of their disease, and to empower them to contribute actively to their healthcare and to patient safety. As stressed by the conclusions of the medical devices exploratory process[8] , patient empowerment is necessary to optimise clinical decision-making, treatment adherence, self-care and self-management of chronic diseases.

2.2 IN-HOUSE EXEMPTION

Devices which are manufactured by healthcare establishments and only used on their own patients are exempt from the requirements of the medical device regulations (that is the so-called in house exemption). The proposal for a regulation strengthens the requirements for this kind of device, who will have to comply with the ISO standard EN ISO 15189. Further, it removes the exemption for the highest risk in vitro diagnostics.

EPF welcomes these new rules that will ensure better quality of in-house in vitro diagnostics. Experience from patient organisations indicate that currently quality of lab test can vary.

Regulators need however to ensure that appropriate exemptions are in place to ensure that health institutions can continue to design test for rare genetic diseases. Class D[9] device also include CE-marked tests which need to be modified to be able to provide a diagnosis. One example is that laboratories often receive too inadequate a sample volume to be able to make a diagnosis with a CE-marked test[10]. Smaller sample volumes, such as a spot of dried blood, give healthcare professionals access to segments of the population which are at risk of infection with HIV and HCV but are reluctant to seek contact with medical care. To be able to diagnose with this smaller sample volume, laboratories modify one component of the CE-marked test under the in-house exemption. Rules must provide for enough flexibility

[8] http://ec.europa.eu/health/medical-devices/files/exploratory_process/final_report_en.pdf
[9] Classifications rules are explained on p6 and annex VII (p117-119)
[10] Source: European Commission working group on in vitro diagnostics

to continue carrying out such tests to reach out to vulnerable groups, and for public health purposes.

3. Identification and traceability of devices, registration of devices and of economic operators, summary of safety and clinical performance, European databank on medical devices (Chapter III)

3.1 IDENTIFICATION AND TRACEABILITY

EPF welcomes measures to improve identification of all devices. Traceability is essential for vigilance and post-market surveillance purposes, in cases where the product presents a risk and needs to be recalled. For more information please see our position on medical devices.

3.2 SUMMARY OF SAFETY AND PERFORMANCE (ARTICLE 24)

In the case of devices classified as class C and D[11], the manufacturer shall draw up a summary of safety and performance. It shall be written in a way that is clear to the intended user. The Commission will set out the form and the presentation of the data elements to be included in the summary of safety and performance.

EPF strongly welcome this obligation. However, we believe it should be clarified that the summary must be made understandable, always, for both categories of users: patients, and healthcare professionals, as they have different information needs. EPF recommends that the Commission set clear standards for what elements the summary needs to contain – These standards should be developed with the involvement of civil society, and in particular intended users including patient organisations. The article should also stipulate clearly that this summary will be made publicly available on the database for medical devices. It is important that clinicians have access to the right information so that they can make more informed decisions about the devices available on the market.

3.3 EUROPEAN DATABANK ON MEDICAL DEVICES (ARTICLE 23 AND 25)

As for the Medical Devices Regulation, this draft Regulation proposes to develop a new publicly accessible central database. It will contain integrated electronic systems on a European UDI, on registration of devices, on clinical investigations, on vigilance and on market surveillance and relevant economic operators and certificates issued by notified bodies.

[11] Classifications rules are explained on p6 and annex VII (p117-119)

The Commission will lay down the modalities necessary for the development and management of this database through implementing acts.

We welcome that the public will have increased access to information on in vitro medical devices, and we believe the Commission should draft an access policy with patient organisations, healthcare professionals and researcher, to ensure appropriate access to information. For further details please see our position on medical devices.

4. Notified bodies (Chapter IV)

For this section we refer you to our position on the proposal for a Regulation on Medical Devices.

5. Classification and conformity assessment (Chapter V)

5.1 CLASSIFICATION

The proposal introduces a risk-based classification system for in vitro medical devices, composed of 4 groups going from A to D[12]- for each of these groups the conformity assessment becomes stricter with higher risks devices, and more clinical evidence is required for higher risk devices.

EPF welcomes the new risk based classification as it is clearer than the current list based system, and can contribute to better patient safety. In our view classification of risk levels for genetic tests should be based not only on the degree of invasiveness of the test and risks associated with this, but also reflect the impact the potential results of the tests could have upon the patient and their family. This is why we believe patients should be involved in reviewing the classification system for in vitro diagnostics, and participate in decision making about borderline cases[13]: they have a different perspective on the risk/benefit balance as end users.

[12] Classifications rules are summarized on p6 of the proposal and explained in detail in annex VII (p117-119)
[13] Borderline cases are products which are at the limit between different categories e.g. medical device/ in vitro device or medicine/in vitro device

5.2 CLASSIFICATION AND CONFORMITY ASSESSMENT FOR SELF-TESTING/NEAR PATIENT TESTING DEVICES AND COMPANION DIAGNOSTICS (ARTICLE 40)

Self-testing and near patient testing devices are subject to specific rules under the Regulation: Depending on their classification, they are subject to supplementary requirements for their conformity assessment. Devices intended for self-testing are classified as class C, except those devices from which the result is not determining a medically critical status, or is preliminary and requires follow-up with the appropriate laboratory test in which case they are Class B. Notified bodies are always involved in the conformity assessment procedure for these devices.

For companion diagnostic intended to be used to assess the patient eligibility to a treatment with a specific medicinal product, the notified body shall consult one of the competent authorities designated by the Member States in accordance with Directive 2001/83/EC on medicinal products for human use or the European Medicines Agency (EMA)

EPF welcomes provisions for further involvement of notified bodies for these devices. Genetic tests can range from simplistic to very complex or with far reaching implication of the outcome – therefore specific rules are justified. Implications of the results for the quality of life of patients need to be taken into account in the way tests are classified.

6. Clinical evaluation and clinical investigation (Chapter VI)

EPF strongly welcome the new requirements as regards clinical evaluation and clinical investigation. While the risk to patient is indirect, having inadequate results can affect the diagnostic and course of a treatment, therefore having sound clinical evidence for in vitro diagnostics is as essential as for other medical devices, and notified bodies need to have relevant expertise to appraise this.

We believe the European Commission needs to be required to set a working group with the meaningful involvement of patients, academia and healthcare professionals to determine appropriate level of access to clinical evaluation data, as well as their format (e.g. appropriate language) for each of these groups (see also point 2.3. European Databank on Medical Devices)

As regards interventional clinical performance studies the requirements are similar to these for clinical investigations on medical devices therefore we refer you to our position paper on medical devices **for this section.**

7. Vigilance and market surveillance (Chapter VII)

As for Medical Devices, EPF is in favour of establishing user friendly means for reporting, and strongly encouraging direct patient and healthcare professional reporting on user errors and incidents with in vitro diagnostic medical devices.

We believe reporting of incidents by healthcare professionals should be mandatory and is part of their role, and we are in favour of providing additional means for patients to report directly an incident.

We also believe stronger cooperation between Member States in this area is paramount to patient safety. **For more details, please refer to our position on the** proposal for medical devices**.**

8. Governance (Chapter VIII and IX)

For this section we refer you to our position on the proposal for a Regulation on Medical Devices.

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