EUROPEAN PARLIAMENT

Briefing

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In vitro diagnostic medical devices

SUMMARY

In vitro diagnostic medical devices are tests used on biological samples to determine the status of a person's health. The industry employs about 75 000 people in Europe, and generates some €11 billion in revenue per year.

In September 2012, the European Commission (EC) published a proposal for a new regulation on *in vitro* diagnostic medical devices, as part of a larger legislative package on medical devices. The proposed legislation aims at enhancing safety, traceability and transparency without inhibiting innovation.

In April 2014, the European Parliament (EP) amended the legislative proposals to strengthen the rights of patients and consumers and take better into account the needs of small and medium-sized enterprises (SMEs).

Some stakeholders consider that a provision for mandatory genetic counselling interferes with the practice of medicine in Member States and violates the subsidiarity principle. Device manufacturers warn that the proposed three-year transition period may be too tight.

In this briefing:

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Glossary

Companion diagnostic: (*in vitro*) medical device which provides information that is essential for the safe and effective use of a corresponding drug or biological product.

***In vitro* diagnostic medical device:** test performed outside the human body on biological samples to detect diseases, conditions, or infections.

Notified body: (private-sector) organisation appointed by an EU Member State to assess whether a product meets certain standards, for example those set out in the Medical Devices Directive.

Introduction

What are *in vitro* diagnostic medical devices?

In vitro diagnostic medical devices (IVD) are tests used on biological samples (such as tissues, blood or urine) to determine the status of a person's health. There is a broad range of IVDs, from self-tests for pregnancy and blood glucose monitors for diabetics, to sophisticated diagnoses performed in clinical laboratories. Other examples of IVDs are HIV tests, blood type identification and cancer screening.

Unlike medical devices or pharmaceuticals, IVDs never come into contact with a person. IVDs do not treat patients, but provide information about the functioning of the body. IDVs do not cause direct harm, but may pose risks if their use leads to incorrect diagnoses.

The European IVD market and industry

There are over 40 000 different IVD products on the European market. Annual spending on IVDs in Europe amounts to under €21 per capita – or 0.8% of total healthcare expenditure. IVDs help reduce healthcare costs by making treatments more precise and efficient.

The European IVD industry generates around €11 billion in annual sales, compared with €100 billion for the entire medical devices industry. The European IVD industry comprises about 3 000 companies – 95% of them SMEs – and employs 75 000 people. 11% of the employees work in research and development (R&D), and an estimated 10 to 15% of the revenue is reinvested in R&D.

EU legislation

Currently, IVDs fall under the scope of Directive 98/79/EC on *in vitro* diagnostic medical devices. The Directive sets out essential requirements based on harmonised standards. Unlike medicinal products, medical devices and IVDs are not subject to pre-market authorisation. Member States must ensure that IVDs are only placed on the market if they conform to the requirements, and must ensure the free movement of such devices in the internal market. Member States designate independent organisations ('notified bodies') which ensure that a conformity assessment[1] is carried out for all devices (except low-risk devices for which manufacturers themselves can certify the conformity). These notified bodies may carry out inspections of manufacturers. Manufacturers must report any incident causing death to, or damaging the health of, a patient to the competent authorities.

Additional related pieces of legislation are Directive 93/42/EEC for medical devices and Directive 90/385/EEC for implantable medical devices.

The European Commission's impact assessment identified the following major problems with the existing IVD legislation:

- regulatory gaps and uncertainties;
- inflexible classification of IVDs and their appropriate conformity assessment;
- unclear legal requirements (and need for adaptation to technical progress).

With regard to the overall medical devices framework, the impact assessment identifies some systemic problems, including oversight of notified bodies, post-market safety, and lack of transparency and traceability.

There are also substantial differences in the interpretation and application of the rules in the Member States, which undermines the main objectives of the Directive, i.e. the safety and performance of IVDs and their free movement in the internal market.

Comparison with US regulation

A study by the Boston Consulting Group found that the time-to-market for medical devices is faster in the EU than in the US, which has a time-consuming centralised approval system. For European patients and doctors, this results in more treatment options, better quality of life as well as cost savings.

Analysts claim that the European approval system enables innovation worldwide, because earlier revenues from the European markets allow manufacturers to finance innovation that could not be financed under the US system where approvals take much longer and are far more expensive.

A systematic review of the impact of the EU and US approval systems for medical devices finds that existing studies recommend policy reforms in both jurisdictions, but quantitative data about post-approval safety outcomes in the two regions are insufficient.

Commission proposal for a new Regulation

On 26 September 2012 the Commission proposed a new Regulation for *in vitro* diagnostic medical devices, as part of a wider legislative package on medical devices. The proposed legislation aims at the highest level of protection for patients, consumers and healthcare professionals. By ensuring that safe, effective and innovative medical devices can be placed on the market and made available to users in a timely manner, it should benefit patients as well as European competitiveness. The Commission initiated the reform in May 2008 with a public consultation to seek the opinions of stakeholders, followed in 2010 by a second public consultation focussed on technical aspects of IVD legislation.

Reform of the medical devices legislation gained urgency in 2011, after it became known that over half a million women worldwide, among them 100 000 Europeans, had received deficient breast implants, revealed to have contained cheap industrial silicone. The French firm Poly Implant Prothèses (PIP) had sold these products for over ten years. PIP had allegedly concealed evidence of their use of this material during checks, announced in advance, by the notified body.

The proposed IVD Regulation shares many elements with the proposal for a Regulation on medical devices. The Commission had considered making only one legislative proposal that would cover both IVD and medical devices, but decided against it. For more detailed information about the reform of the medical devices legislation, please consult the further reading list at the end of this briefing.

Both the proposed new IVD regulation (to replace Directive 98/79/EC) and the proposed medical devices regulation (to replace Directives 93/42/EEC and 90/385/EEC) clarify the scope, aim to improve market surveillance, strengthen notified bodies, and ensure the transparency and the traceability of products. All parts of the supply chain (suppliers, manufacturers, importers, distributors) will have increased obligations with regard to compliance and vigilance. A new expert committee (Medical Device Coordination Group) would play a central role in achieving harmonised interpretation and practice.

The role of notified bodies would be strengthened, including an obligation to carry out unannounced factory inspections. Stricter criteria would also be applied for the designation of notified bodies.

Manufacturers would be required to report serious incidents and corrective actions that reduce the risk of recurrence. This information would be kept in a central database and automatically forwarded to the national authorities. The proposal reinforces the rights and obligations of the competent national authorities to ensure effective coordination of their market surveillance activities.

The proposed IVD regulation aims to strengthen patient safety without inhibiting innovation. The proposal extends the scope of the rules to high-risk devices manufactured and used within a single health institution, tests providing information about 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), and specific medical software. Manufacturers would be required to designate a 'qualified person' responsible for regulatory compliance. There would be stronger provisions for the identification and traceability of devices along the supply chain, and registration of devices and of economic operators in a central European database.

The proposal introduces a new risk-rule-based classification system, based on GHTF principles.[2] IVDs would be divided into four classes from A (lowest risk) to D (highest risk), with appropriate conformity assessment procedures and proportionate clinical evidence requirements for each of these four device classes.

European Parliament

The European Parliament resolution of 14 June 2012 on defective silicone gel breast implants called on the Commission to develop legislation to ensure the safety of medical devices, and urged immediate measures based on current legislation. In September 2013, the Commission adopted measures to tighten the designation and surveillance of notified bodies, and requiring notified bodies to perform unannounced factory inspections.

According to the EP's appraisal of the Commission's impact assessment, some social impacts have not been addressed, notably safety, health and well-being of medical staff and people living close to patients, and employment in the medical devices sector. The impacts on public finances and health insurance schemes have not been assessed, and the impact of the proposal on SMEs is neglected. The EP appraisal notes a lack of quantitative data and external studies.

On 4 April 2014, the outgoing Parliament adopted legislative resolutions on the proposed IVD regulation and the proposed medical devices regulation. The EP resolution on the IVD regulation (rapporteur Peter Liese, EPP, Germany), amends the Commission proposal as follows:

- The scope of the in-house exemption (i.e. devices which are developed and used in-house by a single health institution) would be widened to include Class D IVDs, provided that certain conditions are met.
- A device might only be used for a genetic test if the person concerned has given free and informed consent, after having received appropriate information on the nature, significance and implications of the genetic test. In the case of minors, the informed consent of the parents or legal representative or minors themselves would be obtained, in accordance with national laws.
- Genetic counselling would be mandatory before using a device for predictive and prenatal testing and after a genetic condition has been diagnosed. Such counselling shall include medical, ethical, social, psychological and legal aspects and would be carried out by physicians qualified in genetic counselling.
- Clinical performance studies should be carried out only after a positive assessment by an independent ethics committee. The time limits are slightly extended to give the ethics committee and the authorities the time necessary to assess the proposal.
- In order to alleviate the burden for SMEs, it would be possible, for example, to provide some information electronically, and the information accompanying a product should be provided in an official EU language and not in any other language.
- Certain devices would require a medical prescription, particularly high-risk devices (Class D) and Class C devices for genetic testing and companion diagnostics. Direct-to-consumer advertising of prescription-only devices would be prohibited.
- The new regulation would become applicable three years after its entry into force, whereas the Commission had proposed five years.

The EP resolution on the proposed medical devices regulation would require high-risk medical devices to be assessed by 'special notified bodies' with higher competence requirements, designated by the European Medicines Agency. Devices should be reusable by default, unless explicitly designated as single-use devices. The EP amendments restrict hazardous substances in medical devices. However, the plenary rejected provisions for a marketing authorisation procedure that were contained in the Environment Committee's report (rapporteur Dagmar Roth-Behrendt, S&D, DE)[3] and supported by the European consumer representation, BEUC.

Expert analysis and stakeholder positions

The British Standards Institution (BSI) advises IVD manufacturers to start planning ahead to meet the requirements of the proposed legislation, in particular to be prepared for the three-year transition period that has been called for by the EP. Otherwise they risk having to take devices off the market. It emphasises that 80 to 90% of IVDs will require a notified body under the new rules, compared to only 10 to 20% under the current IVD Directive. Experts recommend that companies plan and budget for the changes, invest in qualified persons and quality management systems, start identifying and generating the clinical data required, and ensure that notified bodies have enough capacity to deliver new certificates in time before the old ones expire.

The Council discussed the proposed legislation on 20 June 2014 and is aiming to agree its position in the autumn.

IVD manufacturers point out the peculiarities of producing clinical evidence for IVDs, and recommend taking these into account in the legislation.

The European Patients' Forum generally welcomes the Commission's IVD proposal, and insists on providing patients with high-quality, reliable, non-promotional information about genetic testing devices.

An alliance of European health associations urged new Commission President Jean-Claude Juncker to leave the responsibility for medical devices and medical technology with the Health Commissioner (rather than move them to the Internal Market and Industry Commissioner).

Reactions to Parliament's amendments

The European Commission indicated its position on the EP amendments and made a number of comments. It considers that the proposed three-year transition period does not give operators enough time to adapt.

The European Diagnostic Manufacturers Association (EDMA) welcomed the plenary vote but is concerned that a three-year transition period is not sufficient for adapting to the new legislation, which introduces a new classification system and requires new clinical studies to produce the necessary clinical evidence, citing experiences from Australia which is implementing a similar system.

The European Society of Human Genetics (ESHG) considers that the amendment regarding genetic counselling restricts the rights of doctors and patients to essential genetic testing and is incompatible with the different ways in which medical practice is organised and delivered in Member States. The ESHG position is supported by a legal analysis which finds that the amendment violates the principle of subsidiarity, contradicting an earlier legal opinion commissioned by the European Parliament's EPP group. Similar reservations about mandatory genetic counselling are expressed by the presidents of National Human Genetic Societies and the Eurogentest network.

The European Public Health Alliance (EPHA) is in favour of mandatory genetic counselling where testing goes beyond routine procedures. EPHA generally welcomes the revisions to the legislation and hopes that the new regulations will overcome the shortcomings of the current legislation.

The PHG foundation, a genomics and health think-tank, is concerned that the proposed regulation and the EP amendments focus only on genetic testing for inherited diseases and do not take account of other potential uses.

Further reading

Initial appraisal of a European Commission impact assessment: European Commission proposals on medical devices and in-vitro medical devices / European Parliament, January 2013

Workshop on Medical Devices and *In Vitro* Diagnostic Medical Devices / Policy Department A, European Parliament, February 2013

Revision of Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on *in vitro* diagnostic medical devices: summary of responses to the public consultation / European Commission, February 2011

The proposed EU regulations for medical and *in vitro* diagnostic devices / Gert Bos and Erik Vollebregt, British Standards Institution, 2014

The push for safer medical devices in the EU / Peter Mayer, dpa, December 2013

Legal opinion: options for action of the European Union in the area of human genetics and reproductive medicine in the light of the proposal for a regulation on *in vitro* diagnostic medical

devices / Michael Schweitzer and Hans-Georg Kamann, Centre for European Law at the University of Passau, January 2013

The competence of the European Union to legislate in relation to certain amendments endorsed by the European Parliament in connection with a Commission proposal for an *in vitro* diagnostic device regulation / Lawford Davies Denoon & Axon Lawyers, February 2014

Endnotes

[1] The notified bodies issue a certificate of conformity that allows the manufacturer to use the EU-wide 'CE' mark which should be recognised by all Member States.

[2] The Global Harmonisation Task Force (GHTF) was a voluntary group of representatives from medical-device regulatory authorities and trade associations from Europe, the United States of America, Canada, Japan and Australia. The GHTF no longer exists, but its work is continued by the International Medical Device Regulators Forum (IMDRF).

[3] In the eighth parliamentary term, Glenis Willmott (S&D, UK) is the EP rapporteur for the medical devices regulation. Peter Liese remains the rapporteur for the *in vitro* medical devices regulation.

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