Obligation of Economic Operators, Traceability, Vigilance and Market Surveillance of Medical Devices as foreseen by the EU Commission Proposal for a Regulation of Medical Devices of 26 September 2012: Comparison with Existing Requirements and Evaluation

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List of Abbreviations

AFSSAPS: Agence Française de Sécurité Sanitaire des Produits de Santé

AIMDD: Active Implantable Medical Devices Directive 90/385/EEC

CE: Conformité Européenne (European Conformity)

CEN: European Committee for Standardization

CENELEC: European Committee for the Electrotechnical Standardisation

CTD Common Technical Document

EEA European Economic Area

EFPIA: European Federation of Pharmaceutical Industries and Associations

EFTA: European Free Trade Association

EN: European Norms

ENVI: Committee for Environment, Public Health and Food Safety

Eucomed: European Medical Technology Industry Association

EUDAMED: European Database for Medical Devices

FSCA: Field Safety Corrective Action

FSN: Field Safety Notice

GHTF: Global Harmonisation Task Force

GMDN: Global Medical Device Nomenclature

GS1: Global Standard One

HIBCC: Health Industry Business Communications Council

IFU: Instructions for Use

IMDRF: International Medical Device Regulators Forum

IVDD: *In Vitro* Diagnostic Devices Directive 98/79/EC

ISO: International Standard Organisation

MDCG: Medical Device Coordination Group

MDD: Medical Devices Directive 93/42/EEC

MDR: Medical Device Regulation

MEDDEV: Medical Devices Guideline

MEP: Member of the European Parliament

MEP: Member of the European Parliament

MHRA: Medicines and Healthcare Products Regulatory Agency

OJ: Official Journal (of the European Union)

PIP: Poli Implant Prothèse (Manufacturer)

PMA: Premarketing Authorisation

SCENIHR: Scientific Committee on Emerging and Newly Identified Health Risks

UDI: Unique Device Identification

UDID: UDI Database

1 Introduction

Together with medicinal products, medical devices are products that have widespread use in the healthcare sector, due to their broad range of types, intended purpose and modes of action [1].

However, they differentiate themselves from medicinal products by the mode of action with which they achieve their intended purpose.

While medicinal products achieve their intended purpose by pharmacological (e.g. activation or antagonism of a receptor by a particular molecule), immunological (e.g. by evocating a immunological response) or metabolic (e.g. releasing a biologically active substance following metabolism) means, medical devices have different modes of action (e.g. physical means) to achieve their intended purpose.

In some cases, however, the borderline between medical devices and medicinal products is difficult to define and in these cases it is very important to determine what the principal purpose is [2].

In the European Economic Area, the regulatory framework for medical devices currently consists of three basic Directives:

- The **Active Implantable Medical Devices Directive (AIMDD)** 90/385/EEC**,** published in 1990, which covers all medical devices that are implanted into the human body and need to use a source of energy that is neither gravity nor energy from the body,
- The **Medical Devices Directive (MDD)** 93/42/EEC**,** published in 1993, which covers the majority of medical devices, and
- The ***In Vitro*** **Diagnostic Directive (IVD)** 98/79/EC**,** issued in 1998, which covers all those products used *in vitro* for examination of specimens from the human body and those used as diagnostics to provide information [3].

These Directives are based on the "New Approach", a legislative pathway based on Article 95 of the European Council Treaty. According to the "New Approach", manufacturers must demonstrate compliance of their medical devices to the essential requirements described in the applicable directive. The conformity assessment is performed either by the manufacturer himself (in case of low risk products) or by independent commercial organisations called notified bodies (for medium and high risk products). Once these associations have verified and ascertained the conformity, manufacturers are allowed to appose the mandatory conformity mark ("CE") on their products. Once products bear this mark, they can be marketed in all Member States in the states of the European Economic Area (EEA) and other countries that recognise the above mentioned directives for medical devices (Switzerland and Turkey) [4].

Apart from smaller amendments, the first two Directives were comprehensively amended in 2007 with the adoption of Directive 2007/47/EC of the European Parliament and of the Council of 5 September 2007.

In May 2008, the European Commission launched a public consultation to collect opinions from stakeholders on a revision, or "recast", of the legal framework for medical devices. The feedback received demonstrated the need of a revision of the current Directives as regards the performance of the notified bodies, the commercial organisations in charge of the conformity assessments and as regards improving the traceability of devices, to give two examples. Moreover, it was deemed important to have cooperation between the authorities of the different Member States [5].

The publication of a proposal for a revision of the three directives was planned for the beginning of 2012. However, the safety issues resulting from the incidents of high rupture rate of breast implants manufactured by the French company Poly Implant Prothèse (PIP) triggered the need of a more stringent regulatory framework and the need for a uniform application of requirements throughout all Member States. In the case of the breast implants manufactured by PIP, the silicon filling actually used for the production of the implants was not that declared in the technical documentation, as the manufacturer had deliberately and fraudulently used a cheaper kind of industrial-grade silicon oil instead of the approved medical grade silicon [6].

Thus, this scandal was taken especially by politicians to call for a more stringent regulatory framework for medical devices in Europe, especially as regards device traceability throughout the supply chain, transparency, harmonisation of requirements and the need of better vigilance and surveillance processes [7].

Two proposals from the European Commission were eventually published on 26 September 2012 with the aim to replace the current Directives. One proposal, the Medical Devices Regulation proposal (MDR proposal) covers requirements for both medical devices and active implantable medical devices, the second covers *In Vitro* Diagnostic Devices.

Among the most important changes introduced are:

- The introduction of a new body of European experts, which would ensure coordination between Member States and their supervision,
- A scrutiny procedure for the highest risk devices, which empowers this new body to request more data before a Certificate of Conformity is issued,
- The introduction of a Unique Identification System to improve traceability, and
- More functions to be included in the current European Database on Medical Devices (EUDAMED).

Both proposals are in the form of **Regulations,** in order to make them directly applicable in the same way in all Member States and without the need, like in case of Directives, to transpose their content into national law.

The Commission proposals are, for the time being, being examined by the other two parties involved in the ordinary legislative procedure, the **European Parliament**, which represents the Union's citizens and by the **Council of the European Union**, which represents the respective governments of the Member States.

On 16 October 2012, the German Member of the European Parliament (MEP) **Dagmar Roth-Behrendt** was appointed as Rapporteur of the leading Committee for Environment, Public Health and Food Safety (ENVI) to prepare a report with an evaluation of, and amendments to, the MDR proposal.

A draft position of the Rapporteur, which proposed radical changes to the Commission Proposal, was published on 15 April 2013. In this document, Ms Roth-Behrendt highlights the need of a premarket approval procedure for the highest risk and implantable devices rather than a conformity assessment procedure. For innovative devices, these should be a centralised procedure like that applicable for certain medicinal products, for other high risk devices, the Rapporteur proposed a procedure between Member States, similar to the decentralised procedure. The current conformity assessment procedure would still be used for low-risk devices [8].

The 13 May 2013 was the deadline for MEPs to submit their proposed amendments, after which the Parliament Committee for Environment, Public Health and Food Safety (ENVI) will discuss these amendments to finalize the European Parliament report by July 2013.

A vote of the plenary is scheduled tentatively in September 2013.

If the Council approves the Parliament's position, the act will be adopted at first reading and come into effect in 2014 at the earliest.

If the Regulation is not published by the middle of 2014, the election of the new European Parliament could cause delays in the publication of the final Regulation.

After publication of the final legislative acts in the Official Journal of the European Union, there will be a 3-year transition period for the new Regulation to be fully applicable.

2 Aim of This Thesis

The aim of this thesis is to give an overview of the current legislative framework in Europe for medical devices (Chapter 3) and to analyse the progress of the on-going legislative procedure (Chapter 4) and the most important changes introduced by the EU Commission's Proposal for a Regulation of the European Parliament and the Council on medical devices published on 26 September 2012 (Chapter 5).

Furthermore, this thesis has the aim of assessing some of the important proposed changes of obligations for economic operators (Chapter 6) and the variations brought in, namely:

- Traceability requirements (Chapter 7),
- Vigilance and market surveillance (Chapter 8)

in comparison with current requirements.

A discussion and an evaluation by the writer of the suitability of proposed changes to address the weaknesses of the current requirements are provided in Chapter 9.

At the time of writing, the situation is yet evolving and discussions of the European Parliament and of the Council of the European Union are still being held.

Therefore, this work covers the situation and the content of official documents published by the European Commission and European Parliament up to June 2013.

3 Current Legal Framework and Regulatory Process for Medical Devices in the European Union

3.1 Definitions

Medical devices are products of unquestionable importance in the healthcare sector. In the European Union only, about 25000 companies are active in the medical devices market employing over five million people and creating 95 billion Euro annual sales (about 33% of the whole market) [1].

This category covers a heterogeneous range of products, from simple bandages to heart pacemakers, and can rely on diverse actions to achieve their intended purpose. The variety of the risks associated to their use makes it necessary to use different criteria to classify them and to regulate them in a manner that adequately addresses safety and effectiveness concerns. Therefore, a tiered applications of regulatory requirements is necessary according to the device classification [3].

The main difference that classifies a product as a medical device rather than a medicinal product is the **mode of action** to obtain the intended purpose:

- If a product obtains its intended purpose by pharmacological, immunological or metabolic means, it is classified as medicinal product, and, therefore, needs a marketing authorisation from a competent authority before being marketed,
- If the intended scope is obtained by other means (e.g. physical action), the product is likely to be classified as medical device and will, therefore, be subject to a different regulatory framework.

Medical devices can, however, be assisted in their function by substances classified as medicinal products, like in the case of bone cements containing antibiotic, where the intended purpose is achieved mechanically by the cement, but the antibiotic is used to prevent infections (ancillary action) [2].

The entity and the purpose of a product are also decisive factors for its classification: medicinal products are, according to Article 1 of Directive 2001/83/EC, defined as substances (or combinations of substances) only and have the scope of *treating and preventing disease of human beings;* and *which can be administered to a human to restore, correct or modify a physiological function or to make a medical diagnosis.*

A medical device can not only be a substance but also, according to Article 1 of Directive 93/42/EEC, *any instrument, apparatus, appliance, software or other article which is intended by the manufacturer to be used for human beings* and with the **purpose** of *diagnosis, prevention, monitoring or alleviation of disease; diagnosis, monitoring, treatment, alleviation of compensation for an injury or handicap; investigation, replacement or modification of the anatomy or of a physiological process, control of conception*.

Thus, medical devices comprise a wider range of different product groups compared to medicinal products.

3.2 "New Approach"

In the European Union, medical devices are subject to a more flexible regulatory approach than the one applied for medicinal products, according to the so-called "New Approach", a legislative pathway based on the Article 95 of the European Council Treaty. The "New Approach" does not only apply to healthcare devices, but also to other kind of products such as toys, lifts, radio and telecommunication equipment. Products marketed according to the "New Approach" do not need a marketing authorisation, but need to have a Conformité Européenne (CE) (translated from the French: European Conformity) mark affixed on them, which testifies that the products conforms to the essential requirements as specified in the European Legislation. The "New Approach" consists of directives harmonised throughout the EU that allow industry to meet its obligations without the need of a heavy regulatory approval process: Member *States must repeal all contradictory national legislation and are not allowed to maintain or introduce more stringent measures than the ones in the Directives,* although they may include additional provisions which are needed *to apply the requirements more effectively* [4].

Presently, the regulatory framework for medical devices consists of three basic directives:

- The **Medical Devices Directive (MDD) 93/42/EEC,** which was amended in 2007 by Directive 2007/47/EC covers the majority of medical devices,
- **Directive 90/385/EEC (AIMDD),** also amended in 2007, regulates active implantable medical devices and
- **Directive 98/79/EC (IVDD)** covers *In Vitro* Diagnostic Devices.

The three directives are complemented by the EU Commission MEDDEV guidelines, which have been developed by representatives of competent authorities and commission services, notified bodies, industry and other interested parties in the medical devices sector.

The content of these guidelines is, however, not legally binding. A different approach than those outlined in the guidelines is possible, provided legal requirements are complied with [9].

The three directives only define the essential requirements that devices must meet as well as the end results that must be attained, in order to have **only safe devices** on the market that are also **effective for their intended use.**

Key elements of essential requirements cover basic features: safety, effectiveness, risk management, stability, choice of the materials, information supplied by the manufacturer, as well as particular categories of devices (utilising a power source, with measuring function, protection against particular radiation, sterile devices).

Manufacturers must establish and prove conformity of their devices with the essential requirements. The Directives let the manufacturer openness with regard to the methods and/or solutions applied to meet the essential requirements as well as for conformity assessment

procedures, although the use of harmonised standards is recommended and is the preferred method to establish conformity.

Compliance with essential requirements allows application of the "CE" mark of conformity to the devices, which is a mandatory requirement to put them on the market in the European Union and to put them into service according to their intended purpose. The mark demonstrates that a product has sustained a conformity assessment procedure according to the applicable directives and meets the essential requirements. If the devices receive CE designation in one Member State, they can be sold in all Member States and circulate freely in the EFTA countries and in Turkey [3] [4] [11] [10].

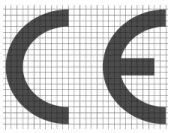

Figure 1 - CE Mark

The CE mark may be accompanied by the identification code of the body that has carried out the conformity assessment according to the Directives. These external parties are called "notified bodies". They are inspection and auditing organisations that are designated by the Member States to perform particular conformity assessment procedures [11] [12]. They must demonstrate that they are competent to perform compliance assessments and *can also offer their services outside the Member State where they are located. Notified bodies constitute the interface with regulatory bodies for medical device manufacturers* and may be designated for specific types on devices only (e.g. bandages and wound dressings or dental materials) [13].

Their task is to assess manufacturers' compliance to the European Medical Device Law by issuing compliance certificates and performing audits periodically to monitor their compliance.

The Commission maintains an updated list of available notified bodies sorted by categories of products [12] [14] .

3.3 Classes of Devices

The level of controls needed for conformity depends on the risk that the use of the device may pose and thus to its classification. The manufacturer must first classify its product according to the criteria and the rules according to Annex IX of the MDD. The device will be classified according to criteria such as degree of invasiveness, mode of action, impact on the body. Then the 18 classification rules will be applied to classify the device into one of four categories: classes I, IIa, IIb and III [11].

According to the class to which a device belongs, regulatory requirements are diverse. For example, although provision of clinical data is needed for most medical devices, according to the requirements outlined in the directives, these data might not be required for some Class I devices (e.g. medical thermometers). *The provision of clinical data in support of conformity with the requirements of the directives does not necessarily mean that* clinical investigations

must be conducted, but the manufacturers can also present evaluations of scientific literature or clinical data that is already existing, *which can be also based on studies on an equivalent device, provided that* equivalence is demonstrated. *In the case of implantable devices and class III devices* the manufacturer must justify that it is sufficient to rely on existing clinical data if he does not conduct clinical investigations [16].

The verification of compliance with essential requirements also depends on the classification of the devices: the manufacturer itself makes a self-declaration of conformity in the case of Class I (lowest-risk) devices, unless they are sterile or have a measuring function. In the other case of higher-risk devices belonging to classes IIa, IIb and III, the notified body performs the conformity assessment and inspects design and manufacturing of the device to ensure that the CE mark can be affixed. In the case of the riskiest devices, Class III devices, the notified bodies will make a thorough evaluation of the product design and will audit the quality system. Requirements for inclusion in the technical documentation used by the manufacturer to demonstrate compliance with the essential requirements also vary according to the classification of the device [14].

3.4 Use of Standards

As mentioned in Chapters 1, 3.2 and 3.3, the three basic directives mandate compliance to the essential requirements, but leave some flexibility on the methods used by the manufacturers to fulfil them.

Thus, the use of standards is recommended (but non mandatory) and, as stated in Article 5 of the MDD and of the AIMDD, *Member States presume compliance with the essential requirements in respect of devices in conformity with the relevant standards*. The list of reference standards in periodically published and updated in the Official Journal of the European Union, once the Commission has determined that those standards are fit for the purpose. Standards included in the list can be used to demonstrate conformance with the essential requirements stated in the medical device directives.

At European level, standards are developed via the European Committee for Standardization (CEN) or, in case of electrical standards, via the European Committee for the Electrotechnical Standardisation (CENELEC). These committees have been mandated by the European Commission to develop those standards that are prepared as draft with input of industry associations, circulated to the member bodies and finalised as European Norms (EN) via a voting system. Standards can also be developed at a global level via the International Standard Organisation (ISO) or the International Electrotechnical Commission (IEC), always through a voting procedure. If no international standards exist, manufacturer can make reference to national standards.

The most important standard for medical devices is the EN ISO 13485: 2012 “Medical Devices-Quality Management Systems Requirements for Regulatory Purposes”, which has the purpose to determining an harmonised model to quality management systems requirements that is compliant to international medical device regulations [11].

4 Revision ("Recast") of the Medical Device Directive and Consequences of the "PIP" Scandal

4.1 The "Recast"

On 8 May 2008, a public consultation was launched to get stakeholders' views on a possible revision ("recast") of the legal framework for medical devices. Responses underlined the need to revise some specific aspects. The Commission received 200 responses from further stakeholders. Moreover, in 2010, the Commission launched a public consultation targeted on issues related to *in vitro* diagnostic devices [5].

The issues for which a feedback was requested were, among others: risk-based classification, implantable/invasive devices for aesthetic purposes, revision of the "New Approach", essential requirements, elimination of specific national requirements, improvement of the work tightening of designation of notified bodies, increased transparency via EUDAMED, improved exchange of information and transparency between notified bodies and competent authorities as well as among authorities, safeguard clause, possible extension of the European Medicines Agency and possible devices for which the EMA could participate in the evaluation process, related procedural aspects; improvement of the vigilance system, implementation of EUDAMED to include all information needed for market surveillance [5].

In November 2011, the European Commission published the roadmap for revision of the medical device directives. This document highlights the factors that have triggered the Commission to simplify and at the same time strengthen the legal framework:

- The need of consolidating the existing texts,
- Key elements having suffered in terms of coherence and uniformity in the interpretation and implementation of legal requirements in the single Member States (Market Surveillance, Vigilance, notified bodies, Clinical Evaluation and Transparency),
- Other national variations (e.g. in the areas of borderline and classification) having hindered the uniform implementation of the directives,
- The need to assess new and emerging technologies,
- The need of aligning the European Llgislation to the Global Harmonization Task Force model to keep European industry competitive in a global market.

Three policy options were under consideration:

1. No EU action, i.e. no change to the current regulatory framework,
2. Fundamental change of legal approach with a shift to a marketing authorisation system and the assignment of the assessment of safety and performance of medical devices to a national competent authority,

3. Reinforcement of the current regime while keeping the same approach, entailing a revision of the three main Directives and addressing the weaknesses identified. This option would also imply a number of individual actions as regards scope, legal form and alignment with other legislation, premarket phase, postmarket phase, management of the system [17] [18].

4.2 The PIP Scandal

Publication of the revised directives was planned at the beginning of 2012. However, the issues on safety of breast implants manufactured the French Poly Implant Prothèse (PIP) company raised some important concerns.

At the end of 2009, the then **French Health authority AFSSAPS** noticed that PIP Breast implants experienced an unexpected high short-term implant rupture rate [7]. This incident triggered an inspection from the French Authority, conducted in March 2010, which demonstrated the use by the French manufacturer of a non-medical grade silicone for the filling of its implants, different to the one declared in the technical documentation. As a consequence, AFSSAPS suspended the marketing and the use of the silicon implants manufactured by PIP on 29 March 2010. The inspection was followed by a detailed series of analysis, between June and beginning of September 2010, of implants taken from PIP premises, with the aim of characterising raw materials and mixtures used in the filling, to ascertain the strength of the prostheses and to evaluate the tolerance of biological tissues in contact with the silicon gel. The analyses conducted confirmed that the filling was not satisfying the quality requirements of a silicon gel intended to be used in breast implants [6].

According to available data, PIP silicone breast implants were available in most EU Member States and approximately 87000 women had been implanted with them especially in Germany, France, United Kingdom and Spain. Moreover, it is reckoned that around 400000 PIP silicone breast implants have been sold worldwide[19].

The so-called “PIP-scandal” was not the only one in the field on medical devices: in September 2010, the metal-on-metal hip replacements manufactured by DePuy, a subsidiary of Johnson & Johnson, were withdrawn from the market in the United Kingdom. These implants had shown a failure rate of 12 to 13 per cent and had given problems because of the frictions between the metal ball and cup, which was the reason for small metal parts to break off, leak into the bloodstream and cause inflammations. Moreover, there were concerns that the fragments could slowly poison the nervous system, lungs and heart. The British competent authority MHRA requested orthopaedic surgeons to contact every patient who had received the two models concerned and make sure that the patients would be monitored. However, the British Orthopaedic Association (BOA) has expressed that not all the concerned patient, but only over one third of those who were implanted with the DePuy hip implants, had been contacted [20].

4.3 SCENIHR Evaluation and Consequences for the Recast

In January 2012, the EU Commission requested the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) to conduct an assessment of safety of PIP silicon breast implants and to determine whether they were more prone to failure than those of other manufacturers and to establish the consequences to health from PIP implant failure. The Committee found it reasonable to conclude that the migration of low molecular weight components of the silicon might have weakened the shell of the implants and that components can have leaked into the surrounding tissue. As regards toxicity test findings, an in vivo test for irritancy was positive, thus suggesting that further investigation was required to better establish and manage any health risk. Tests for cytology and genotoxicity were negative. However, there were a few case reports that broken breast implants may be associated with a higher incidence of swollen and painful lymph nodes in the axilla, the groin, the neck and the mediastinum [19].

After publication of the SCENIHR report, the **European Commission** announced, on 2 February 2012, that further in-depth studies were requested to better evaluate the potential health impact of faulty breast implants. Scientists from SCENIHR concluded that data available at that time was not sufficient to draw concrete conclusions regarding the risk associated with PIP implants. Moreover, the Commission announced that it would be necessary to discuss with Member States on how to strengthen surveillance of medical devices and safety controls of devices already on the market within the existing legislative framework. In that occasion, the then EU Health Commissioner John Dalli declared that they would *take into account the lesson learnt from this case and take them on board in redrafting our legislation, in particular with regard to market surveillance, vigilance and functioning of notified bodies*. The possibility to enhance surveillance of medical devices would be consolidated within the current legislative framework, e.g. including the possibility of conducting unannounced inspections, increasing the control on notified bodies and performing additional sample testing on products already on the market [7].

On 26 April 2012, the **European Parliament** announced with a press release that the Environment and Public Health Committee had unanimously passed a resolution proposing some measures to prevent recurrence of such case. The resolution clearly acknowledges that transposing Directives into national laws *has not avoided this health fraud.*

According to the Members of the European Parliament (MEPs), the PIP case had demonstrated the **insufficiency of cooperation both at European and national levels**, a lack of traceability of raw material used for manufacturing of medical devices, as well as a failure of the current system of certification of compliance and of the controls of the notified bodies by national competent authorities. The European Parliament's press release also highlights the need for improved traceability of implanted devices and of market surveillance.

Traceability of implanted medical devices needs to be improved both on manufacturers and on users/hospital level and between Member States, as well as the reporting system for serious side effects or damage occurred. Furthermore, MEPs stressed that patients and health care professionals should be given the opportunity to report all adverse and harmful effects without having to face excessive bureaucracy hurdles, according to the MEPs.

A breast implant **register** should be introduced in each Member State, and each register should be interconnected and enable exchange of information in cases of defects in implants.

MEPs also called for increased **transparency and information sharing on adverse effects for** an improved **device traceability and follow-up**. A single database should be established in order to collect information on marketed medical devices, on registered economic operators, vigilance, market surveillance, clinical investigations and EC certificates issued in the EU.

The resolution adopted by the Parliament was published on 14 June 2012 [21] [22].

5 EU Commission Proposals of 26 September 2012

5.1 Weaknesses of the Current Medical Devices Directives

The two awaited proposals for a Regulation on Medical Devices [COM (2012) 542 final] and on *In Vitro* Diagnostic Medical Devices [COM (2012) 543 final] were eventually published on 26 September 2012 by the European Commission, with the view of replacing the current regulatory framework: MDD and AIMDD by the first mentioned Regulation, IVDD by the latter one [23].

The two proposed Regulations address the weaknesses of the current legal framework, the most important of which are:

- **Differences between notified bodies throughout Europe:** currently, around 80 notified bodies are designated to perform conformity assessment procedures with regard to medical devices. Significant differences are reported as regards their designation and monitoring, as well as the quality of the conformity assessment performed by them. This exposes patients to varying levels of protection, which is an issue of concern from a public health perspective.
- **Unclear obligations and responsibilities of manufacturers and comparable stakeholders** (in the MDR proposal defined as economic operators): they need to be understood from requirements mentioned in the Annexes and are not comprehensibly stated in the body of the Directives. No minimum criteria exist for authorised representatives, distributors and importers, which are not mentioned at all in the current Directives. A Quality System is not clearly required for Class I manufacturers.
- **Insufficient information available to Member States as regards post-market safety:** Member States do not have necessary information available whenever the marketing of a medical device is restricted or banned from the market because of safety issues or if the CE marking is illegally affixed to a product. After incidents have been reported to national competent authorities, Member States should inform each other on measures taken to avoid repetition of such incidents by exchanging National Competent Authorities Reports (NCAR). The number, however, varies considerably among Member States (40% NCARs has been exchanged by Germany, 20% by the UK, while other Member States have submitted very few reports). Furthermore, national competent authorities react differently to the same problems (e.g. after a report of an incident with an insulin pump, in one Member State the product was recalled, in other Member States the manufacturer has been requested to provide additional information), thus not ensuring a uniform level of patients' protection throughout the European Union.
- **Lack of transparency:** for the time being, there is no central depository of information and no accurate data on number, type and approval status of medical

devices marketed in the EU, although in some Member States (e.g. Italy) national electronic registration tools are in place. The existing European Database for Medical Devices (EUDAMED) is not available to the public and its scope is limited to information on low-risk device manufacturers/authorized representatives, certificates, vigilance reports and clinical investigations. National competent authorities, which in some cases have to implement their own systems for collection of their national data, have the task of uploading the information in the database.

- **Lack of traceability:** no requirement on the traceability exists in the Medical Device Directives, although some traceability requirements through a Unique Device Identification (UDI) have been required in few Member States (e.g. Spain). Traceability across borders is, however, not possible as national systems are not compatible with each other.
- **Lack of coordination and cooperation among Member States:** no legal basis in the current Directives can ensure overview of the situation at EU level with regards to vigilance and surveillance. Each Member State has its own national requirements and this leads to a lack of uniformity. Provisions taken in a Member State following an incident in its territory are often not communicated to other States where the device is marketed.
- **Classification of products and regulatory uncertainties**: certain products like those manufactured with non-viable human tissues/cells, implantable/invasive products without a medical purpose are not regulated. Uncertainties also exist for reprocessing of single-used devices and, in the case of IVDs, diverging interpretations in the EU pose problems for genetic tests and "in house" tests.
- **No existing coordination for assessment of multi-national clinical investigations**: similarly to multinational clinical trials on medicinal products, medical device manufacturers have to submit applications to each Member State. The assessments by different national authorities might also have led to different outcomes for the same medical device. Moreover, patients participating in the same multistate clinical investigations are subject to different safety levels.
- **Lack of involvement of external experts:** manufacturers, healthcare professionals and regulators have expressed the need of advice of scientific and clinical experts (e.g. healthcare professionals, academics), as discussion on regulatory or safety issues always involve regulatory authorities and manufacturers, unless an opinion on a specific issue is requested to the SCENIHR
- **The IVD Directive,** adopted in 1998 and, since then, **not yet amended**: the recent technological, scientific and regulatory developments are not reflected in the current Directive. Moreover, current IVD classification in the EU is not in line with international guidelines [24] [17].

5.2 Possibilities to strengthen the Provisions

The two policy options envisaged in the EU Commission Roadmap published in November 2011, which is either no EU Action or a possible fundamental change implying a marketing authorisation of medical devices, were not deemed appropriate.

The option "no EU action" had been rejected, because current weaknesses would still exist, and not cease problems for public health, which would still be even more at risk, possibly with a recurrence of facts like the PIP scandal.

A **possible introduction of a marketing authorisation system for medical devices**, similar to the one of medicinal products, **had also been refused by the Commission**, as no evidence exists that the existence of a marketing authorisation system would *have prevented fraudulent practice from the manufacturer* like in the case of PIP, which was rather the consequence of an insufficient post-marketing surveillance system and a criminal act, respectively. Furthermore, none of the European marketing authorisation procedures would be ideal: a decentralised procedure would imply having diverse national marketing authorisations, which would hinder access to other Member States, thus *having a negative impact on the internal market;* a centralised procedure at EU level would involve the establishment of a public institution with qualified staff to assess marketing authorisation procedures for medical devices, similar to the Food and Drug Administration (FDA) Centre for Devices and Radiological Health (CDRH), which assesses marketing authorisation procedures for marketing of medical devices in the United States. This would inevitably have a huge impact on budget and administrative burden for both the EU and manufacturers, who would also have to deal with additional costs for regulatory compliance and with considerable impact on time to market.

A comparison of the Eucomed response of 3 July 2008 to the public consultation, published on 2 December 2010, and the EFPIA's report entitled "The pharmaceutical industry in figures", issued in 2010, shows that the R&D costs to bring a new medicinal product to the market were estimated, at that time, at around 1 b €, while the cost for the development of a new medical device were estimated at around 10 m €, hence demonstrating that the price for obtaining a marketing authorisation similar to those of medicinal products would be excessive compared to the cost for obtaining a CE marking.

The option of **reinforcing the current regime while addressing the weaknesses was the one preferred**. Three general objectives were determined: *ensuring a high level of protection of human health and safety, ensure smooth functioning of the internal market, provide a regulatory framework which is supportive for innovation and the competitiveness of the European medical device industry. Individual policy options were also decided to allow an evolution of the current regulatory regime,* they cover specific objectives: uniform control of notified bodies, enhanced legal clarity and coordination in the field of post-market safety, solution in determining the regulatory status of borderline cases, enhanced transparency and traceability regarding medical devices on the EU market, improved

involvement of external scientific and clinical expertise, clear responsibilities of economic operators, management of the regulatory system [17].

The first important introduced change is the **kind of legislative act proposed:** instead of directives, which would have involved the additional step of implementing them into Member States' national laws, with the possibility of having differences among Member States, the proposed text would now be **regulations,** thus they will be directly applicable and uniformly binding in all Member States. Once these Regulations are applicable, there will not be the danger of diverse Member States implementing a Directive in different ways and different timeframes, therefore, the harmonization of requirements in the European Economic Area is ensured.

5.3 Main Changes

The main changes identified by the European Commission in the proposed Regulations are, as expected from the current weaknesses (see 5.1):

- The **scope** of the legislation will become wider and clearer to include implants for aesthetic purposes (e.g. contact lenses) and products with non-viable human tissues/cells (e.g. collagen injections), and clarified as regards medical software and genetic texts. A thorough assessment of their safety and performance will be conducted before they are placed in the market. However, some products containing or consisting of biological substances including living microorganisms will be excluded from the scope.
- **Notified bodies** will have more powers and obligations, e.g. they will conduct unannounced inspections and sample testing to constantly monitor manufacturers, but they will also be strongly supervised by national authorities. They will follow uniform standards and criteria throughout Europe in the assessment of medical devices. For designation, they will have to satisfy stricter requirements: their designation will only occur for assessment of categories for which they can actually demonstrate knowledge and competence. In addition, they will have to publish a statement demonstrating their impartiality, and will have to enter all issued certificates of assessment and amendments into EUDAMED.
- Clearly established rights, tasks and responsibilities for manufacturers, authorised representatives, importers and distributors (now defined in the draft texts as **economic operators**), including diagnostic services and Internet sales, for which a dedicated chapter exists. New definitions have been added for economic operators now reflect the content of the "Blue Guide" to the implementation of directives based on the "New Approach". A qualified person responsible for regulatory compliance will be mandatory.
- The current **database on medical devices** will be revised and will provide comprehensive information on medical devices marketed in the EU. Key information will also be available to patients, the public and healthcare

professionals, who will be provided with information on benefits, risks and overall risk/benefit ratio, and will be supported in making the right use of devices for treatment of patients.

- The **traceability throughout the supply chain** will be improved, thus allowing an effective response to safety concerns (e.g. enabling recalls). The post-market safety of medical devices will be improved with the introduction of a Unique Device Identification (UDI) system, which is also being developed in parallel in the United States by the FDA and internationally by the International Medical Device Regulators Forum (IMDRF) and which will also play an important role in reducing medication errors and counterfeiting.
- Rules for **clinical investigation of devices** and for **data for premarket and continuous post-market assessment** have been reinforced to ensure patient safety. Multi-national clinical investigations will be conducted under a simplified approval process. Clinical investigations can start after approval of the concerned member states (in case of higher risk devices implantable or long term invasive devices) or in any case after 35 days if no refusal is given by member States because of public health/safety issues.
- The **general health and safety requirements,** including labelling provisions, have been adapted to the technological and scientific progress e.g. the adaptation of safety and performance requirements applicable to new health technologies (e.g. software and nanomaterials used in healthcare).
- **National surveillance authorities** will be coordinated to ensure that only safe devices are marketed in their territory and to communicate to other authorities about incidents in their jurisdictions with medical devices also marketed in other countries to prevent recurrence of other incidents.
- A new entity, the **Medical Device Coordination Group (MDCG)** will be established. This will be composed of members from national competent authorities who will ensure coordination of Member States with regards to clinical investigations, vigilance and market surveillance. The MDCG will also support them in assessing and overseeing notified bodies. It will also have a fundamental task in the newly introduced scrutiny procedure, as defined in Article 44.
- The European Union will be more aligned to **international guidelines,** e.g. *In Vitro* Diagnostics will be divided into four different classes according to the guidelines issued by the former Global Harmonisation Task Force (GHTF).
- **Vigilance** will be stricter: manufacturers will have to report serious incidents and corrective actions in a EU portal that will be accessible to competent authorities, Commission and notified bodies. In case a similar or the same incident occurs in more than one Member States, a coordinating authority will analyse the case and will inform the responsible notified bodies. Rather than individual incident report, manufacturers will be able, in some cases, to submit **periodic summary reports.**

Manufacturers will also update their technical documentation with vigilance data and inform notified bodies accordingly.

- A new definition has been added for **reprocessing** of single-use devices.
- For higher risk devices, a **scrutiny procedure** has been proposed, according to which notified bodies would inform the MDCG before issuing a Conformity Assessment for Class III Device. The MDCG would then decide whether further information is needed from the manufacturer before the certificate is issued.

The rules for medical devices manufactured in the EU will also applicable to medical devices produced in third countries and imported into the Union [24] [25].

The proposed regulation on medical devices covers both medical devices **and** active implantable medical devices. Once applicable, it will replace the two existing Directives. Provisions of the two Directives have been merged and AIMD will be classified as Class III devices, to align to the classification at international level by the GHTF, and as it already happens in some member states [17]. It is a very extensive document: 194 pages, and contains an explanatory memorandum, 71 Recitals, 10 chapters with Articles and sixteen annexes. Eventually, an appendix with 50 definitions is available at the end of the document.

As regards **conformity assessment** manufacturer will not apply to more than one notified body in parallel for the same conformity assessment. Notified bodies will have to inform both the Commission and the MDCG of applications and outcomes of any scientific advice for every class III device. Notified bodies will also enter all issued certificates and amendments into EUDAMED. Conformity assessment will also be needed for custom-made devices.

5.4 Consequences: Changes in the Medicinal Products Directive and in the Application

Another existing legislative text is affected: Medicinal Products Directive 2001/83/EC with regards to **drug/device combinations**. There is a new obligation to include conformity assessment results of the device parts in the marketing authorisation dossier of the combination product, even if they are regulated as medicinal products. According to Title 9 of the MDR proposal, the Directive on medicinal products should be amended to reflect the changes proposed with regards to medicinal products having a medical device as an integrating part. For these products, an adequate assessment of their compliance with general safety and performance requirements should be ensured in the context of a marketing authorisation. Moreover, the exchange of information on vigilance cases should also be ensured.

Although no amendments to the legislation have been made for the time being, the European authorities have already started requesting some basic information on the **device that is part of a medicinal product.** On 15 April 2013, the European Commission

published the amended **application form for medicinal products** for human use in Volume 2B of the Notice to Applicants. The use of this amended version became mandatory **as of 3 June 2013.**

The revised application form now includes some new Sections (2.2.4 to 2.2.4.4) on medical devices or active implantable medical devices incorporated as an integral part.

Applicants must fill in:

- Information on **economic operators** (manufacturers or authorised representatives),
- **Device identification** (name of the device, serial number or other indications to identify the device incorporated),
- Whether the device has a **CE marking (**the manufacturers declaration of conformity must be included in module 3.2.R of the EU Common Technical Document),
- Whether the device is covered by **certificates issued by a notified body** and contact information of the institution that has released the relevant certificates, **which must be added in module 3.2.R** of the EU CTD [27].

5.5 Implementing and Delegated Acts

The MDR proposal still leaves many open ends, as the European Commission will be empowered to adopt some upcoming decisions by means of delegated or implementing acts, as specified in the final provisions.

Implementing acts and delegated acts are new categories of legal acts that were introduced by the treaty of Lisbon:

- **Implementing acts** are needed to ensure the uniform implementation of European measures and are defined in Article 291 of the Treaty on the Functioning of the European Union as published in the Official Journal on 9 May 2008, which states that these acts confer implementing powers on the Commission.
- **Delegated acts** are needed to complement the regulatory framework over time, e.g. specify some technical details, and are defined in Article 290 of the Treaty [28].

Once finalised, the regulation will completely replace Directives 90/385/EEC and 93/42/EEC, which will cease to exist after the Regulation becomes applicable.

5.6 Criticism from the British Press to the Notified Body System

In October 2012, the result of a "secret shopper exercise" was published.

This exercise was conducted by journalists of the British Medical Journal and of the Telegraph to test the CE certification process in use.

The journalists contacted 14 notified bodies to get approval of an imaginary large diameter metal hip implant modelled on one that was previously recalled for having high failure rates and for releasing metal ions into the blood. They eventually submitted a dossier to one

notified body, which confirmed that it would approve the device if provided with manufacturing documents and a visit to the factory. The investigation found that n*otified bodies competed on price and speed of certification, accepting low levels of evidence on safety and effectiveness of medical devices* [29] [30].

A response from the British Agency MHRA immediately followed these findings, in which the competent authority recognized that *improvements to the regulation on medical devices need to be made* and that they specifically recommend *improving oversight on the notified bodies, improved surveillance of post-market events and the better collaboration between national regulatory bodies* [31].

5.7 Reaction from European Medtech Industry

On 30 January 2013, Eucomed, an association representing medical technology industry in Europe, published a position paper to recommend additional measures to be incorporated in the MDR proposal. Although the industry recognizes that some of the proposed improvements are necessary, it proposes a "systematic control procedure" as an alternative to the proposed scrutiny procedure.

The scrutiny procedure as proposed in Article 44 is found to be inappropriate and would imply a *duplication of reviews and checks* without ensuring necessarily the achievement of the patient safety because of its random mechanism [32].

5.8 Public Hearing of the European Parliament's Environment, Public Health and Food Safety (ENVI) Committee on 26 February 2013

On 16 October 2012, the German MEP Dagmar Roth-Behrendt was appointed as Rapporteur of the ENVI Committee.

On 26 February 2013, a public hearing with stakeholders was held at the European Parliament.

The Rapporteur raised concerns on the facts that the current system does not ensure the safety of patients, that high-risk devices should undergo a clinical evaluation before being put on the market and that a real premarket authorization procedure should be set up, at least for higher risk devices.

During the public hearing, concerns were also raised on the number and the expertise of the notified bodies: the existence of eighty notified bodies is not justified and the fact that they are commercial organisations living on the fees they charge to manufacturers creates a competition among them on the price charged for a procedure to manufacturers and speed at which they can give the conformity assessment. Many of them cannot ensure having the resources, the expertise and the knowledge needed for assessment of many kinds of devices.

Moreover, notified bodies often employ personnel who can provide expertise on technical issues on mechanics and materials, but not always they have at disposal health

professionals who can have expertise on the clinical performance and on the safety of the devices.

Therefore, it was insisted on the fact that a certification procedure and a supervision procedure for notified bodies are needed [33].

5.9 European Parliament: Draft Report with the Rapporteur's Suggested Amendments

On 15 April 2013, Dagmar Roth-Behrendt, European Parliament Rapporteur, published her draft report with her amendments to the MDR proposal.

The most significant change, as expected, is the introduction of a **premarket authorisation system for medical devices with highest potential risks**, which do need a more stringent procedure than the current conformity assessment, i.e.: class III devices, those incorporating a substance considered to be a medicinal product, intended to administer a medicinal product, or utilizing non-viable tissues or cells or their derivatives, as well as implantable devices. The marketing authorisation would also be required already on the European Union market at the date into entry of the Regulation, as of the expiry date of the validity of their certificate.

A centralised procedure, involving the European Medicines Agency, should be introduced for innovative devices with the above characteristics, while a decentralised procedure, involving national competent authorities, should be introduced for devices with the above characteristics, but that are not innovative. The report does not, however, define what is meant with "innovative".

The marketing authorisation, like in the case of medicinal products, would normally be valid for five years and then would need a renewal on the basis of a re-evaluation of the risk-benefit balance.

For all other kinds of devices, the current conformity assessment procedure would still be applicable.

The controversial clause on the scrutiny procedure, Article 44 of the MDR proposal, has been deleted and has been replaced by the abovementioned PMA.

Clinical trials with medical devices should only start after a positive evaluation by an independent ethics committee and should include randomized clinical investigations in the appropriate target population. If those investigations are not carried out, companies should provide a justification. All Member States should be informed in case of early termination of the trial, so that they can inform sponsors that conduct similar investigations.

According to the Rapporteur, public and healthcare professionals should have an adequate level of access to EUDAMED.

To better be able to determine whether an incident has been caused by the use of the device or by the device itself, incidents and **Field Safety Corrective Actions** should be reported

with mention **of date and place of incidents** to ensure a fast tracing back of all aspects surrounding the incident.

The Rapporteur also proposed new provisions on **notified bodies,** a manufacturer should inform the national competent authority of the Member State where it is registered if he wishes to apply for a conformity assessment procedure to a notified body established in another Member State.

The classification of medical devices into four classes according to the level of risk is considered appropriate. However, rule 21 in Annex VII is considered inappropriate. According to this rule, class III is assigned by default to all **devices** made of substances intended to be ingested, inhaled or administered rectally/vaginally and that are **absorbed by or dispersed in the body**, is considered disproportionate. The rapporteur proposes, therefore, deletion of this rule.

It is also proposed that only devices explicitly labelled as reusable should be reprocessed, but not those labelled as single-use devices [8].

The deadline for Members of the European Parliament to suggest amendments was 13 May 2013, followed by internal discussions in order to prepare the final report of the leading ENVI committee (expected in the late summer 2013). The European Parliament's final plenary vote is due in November 2013.

In the European Union, the ordinary legislative procedure (previous Co-decision procedure) foresees the publication of a proposal (COM Document) from the European Commission to both the Council (representing the Member States at ministerial level) and the European Parliament (which represents the citizens of the European Union and are directly elected by them). The Parliament considers the proposals and other submitted options and adopts its position. The Council may approve the Parliament's position and, in this case, the act is adopted at first reading. If the Council does not approve this position, it will adopt its own position and forward it to the Parliament.

6 Obligation of Economic Operators

In this chapter, an overview will be given on the current status with regard to definitions on economic operators and their obligations they have to fulfil to bring medical devices on the market.

6.1 Current Obligations according to the MDD to bring Medical Devices to the Market

Currently, Article 1 of the MDD only defines the **manufacturer** as a person *with the responsibility for the design, manufacture, packaging and labelling of a device before it is placed on the market under his own name.* The obligations to be met by manufacturers also apply to other parties that perform operations like assembling, packaging, full refurbishment or labelling of the device with the intention of placing them on the market under their name.

The **authorised representative** is defined as a person who is established in the Community and that, after explicit designation of the manufacturer, takes the manufacturer's obligations in the Community and may be addressed by competent authorities and notified bodies.

The manufacturer has the obligation to define the **intended purpose** of the device, i.e., according to the definition in Article 1 of the MDD, *the use for which the device is intended according to the data supplied by the manufacturer on labelling, instructions and/or promotional materials.* The intended purpose, as mentioned in Chapters 1 and 3, is fundamental to determine first of all whether a product is a medical device and to identify the Directives that apply to it.

If the product falls under the definition of medical device, it is very important to **classify** it in one of the four existing classes according to the list of classification criteria in Annex IX of the MDD and then choose an adequate conformity assessment procedure to follow as stated in Article 11 of the MDD:

- **Class III Devices:** procedure relating to the EC declaration of conformity according to Annex II (Full quality assurance system) **or** a procedure according to Annex III (EC Type examination procedure). In the latter case, coupled with
    - Procedure set out in Annex IV (EC verification procedure), or
    - Procedure set out in Annex V (production quality assurance).
- **Class IIa devices:** Full quality assurance **or** EC declaration of conformity (Annex VII). In the latter case, coupled with:
    - Procedure according to Annex IV (EC verification)**,** or
    - Procedure according to Annex V (production quality assurance), or
    - Procedure according to Annex VI (product quality assurance).
- **Class IIb:** Full quality assurance **or** procedure according to Annex III (EC Type examination procedure). In the latter case coupled with:

- Procedure according to Annex IV (EC verification), or
- Procedure according to Annex V (production quality assurance), or
- Procedure according to Annex VI (product quality assurance).

After having implemented a quality system, manufacturers will be audited by a notified body. To implement a full quality system, manufacturers can choose to follow the international standard ISO 13485, which presumes conformity with the essential requirements. The manufacturer will then create a technical file or design dossier (for class III devices) accordingly and apply to a notified body, who will audit the quality systems, review the technical documentation and test the devices to ensure that the manufacturer is compliant to the essential requirements. If the audit or testing is successfully passed the notified body will issue an EC certificate of conformity, which demonstrates that the company is compliant to the applicable directive. Once the EC certificate of conformity is obtained, the manufacturer can prepare a declaration of conformity, a legally binding document that is signed by then authorized person within the company [34].

- **Class I:** in this case, the manufacturer shall follow the procedure set out in Annex VII and draw up the declaration of conformity himself before placing the device on the market. The intervention of a notified body is needed in case the Class I device is sterile or has a measuring function [34]**.**

6.2 The MDR Proposal

6.2.1 A New Dedicated Chapter

While obligations and responsibilities of economic operators are not stated clearly enough in the current Directives, but must be understood by a careful reading of the different chapters throughout the documents [24] [17], the proposed Regulation includes a dedicated chapter (Chapter II, Articles 4 to 22).

The term “economic operators” has been introduced in recital 23 of the MDR proposal to define manufacturer, authorised representative, importer and distributor, in line with the definitions of the “Blue Guide”, which covers all legislations under the “New Approach”.

The proposal stresses the importance of **a strict supply chain control mechanism** and imposes autonomous obligations at different stages of the supply chain. Each link in the supply chain has to look back to check whether the previous links are in compliance with the applicable requirements.

6.2.2 New Definitions

According to the definitions in Chapter 1, Article 2 of the MDR proposal, a **manufacturer** is any natural or legal person who manufactures or fully refurbishes a device, or already has a manufactured or fully refurbished device and markets it under his name or trademark. According to Chapter 3 of the “Blue Guide”, which defines the responsibilities of the

different parties, a manufacturer is *a person responsible for designing and manufacturing a product with a view of placing in on the Community market in his own behalf.*

For the purposes of the MDR proposal, any economic operators shall assume the obligation of a manufacturer if they perform "manufacturer-like activities" like:

- Making available a device under his name, registered trade name or registered trade mark,
- Changing the intended purpose of a device already on the market,
- Make modifications to a device already marketed that affect compliance of the product with the applicable requirements.

The last point is particularly important because it is made clear that if changes are made to the device already covered by the CE Mark of a manufacturer (e.g. a change of the plug), the device is not covered by the original CE mark anymore.

> *The **authorised representative** is any natural or legal person established in the European Union who has received and accepted a mandate from the manufacturer to act on his behalf in relation to specified tasks with regard to the latter's obligations under the Regulation.*

There are not many differences from the old "authorised representative" definition, i.e. any natural or legal person established in the Community who, explicitly designated by the manufacturer, acts and may be addressed by authorities and bodies in the Community instead of the manufacturer with regard to the latter's obligations under this Directive.

The definitions for importer and for distributor are not included in the AIMDD and in the MDD. According to the definitions in Chapter 1 of the MDR proposal:

> ***Importer** means any natural or legal person established within the Union who places a device from a third country on the union market.*

Chapter 3 of the "Blue Guide" also states that importers must ensure to provide the market surveillance authority with the necessary information regarding the product if the manufacturer is not based in the Community and has no authorised representative.

> ***Distributor** means any natural or legal person in the supply chain, other than the manufacturer or the importer, who makes a device available on the market.*

According to the "Blue Guide", the distributor is considered as a person in the supply chain taking any subsequent actions after the product has been placed on the market and who has to act with particular care not to place non-compliant products on the market. Furthermore, he will have to be able to demonstrate that to the surveillance authorities.

The responsibilities will be as follows:

Importers will take on new duties and stricter autonomous responsibilities, as they must ensure that the manufacturer in the third country has

- carried out a the appropriate conformity assessment procedure,

- designated an authorized representative according to Article 9, if the importer is not also designated as such,
- drawn up the EU declaration of conformity and the technical documentation.

Furthermore, they will have the responsibility to check and ensure that the device

- bears the CE Marking correctly,
- is labelled correctly by the manufacturer and accompanied by the required instructions for use and declaration of conformity,
- has been assigned a Unique Device Identification according to the new requirements on traceability (Article 24 of the MDR proposal),
- is registered in the relevant electronic system managed by the Commission.

They also

- must identify any economic operator, as well as any health institution or healthcare professional to whom they have supplied a device for at least five years and any economic operator who has supplied them with a device,
- make sure that the label of the device reports their contact details,
- take, autonomously, adequate corrective actions and not only when it is agreed by the manufacturer,
- engage in postmarket surveillance activities such as report complaints,
- must refuse to import devices whenever they have reasons to think that the products are not in conformity with the applicable requirements.

Distributors will have the responsibility to ensure that

- the manufacturer and, where applicable, importer, i.e. all parts upstream, are in compliance,
- the products are accompanied by the appropriate information, provided by the manufacturer, and bear the CE conformity mark.

Furthermore, they have to

- make sure that the device is labelled with their contact details,
- take autonomously corrective actions (e.g. undertake recalls and reports to the authorities),
- engage in postmarket surveillance activities and inform the other relevant economic operators if a device presents a risk or if an incident is reported.

They will have to make an evaluation on whether the device is conform and, if not, bring it into conformity, withdraw or recall it [35].

6.2.3 A New Mandatory Requirement: the Qualified Person

A **new requirement** has been introduced by the MDR proposal for manufacturers and for authorised representatives to have available a **qualified person responsible for regulatory compliance.**

As outlined in Article 13 of the MDR proposal, the qualified person must have expertise and knowledge in the field of medical devices, to be demonstrated by either a university degree, or an equivalent study, in a relevant discipline plus at last two years of professional experience in regulatory affairs or quality management systems relating to medical devices, or five years of professional experience in regulatory affairs or quality management systems.

This requirement will not apply to manufacturers of custom-made devices that are microenterprises.

The qualified person will be, at least, responsible for ensuring that

- the conformity of the products is adequately accessed before the batch is released,
- both technical documentation and declaration of conformity have been prepared and kept up-to-date,
- all reporting obligations regarding vigilance are fulfilled according to Articles 61 to 66,
- the signed statement is issued, in case of investigational devices, to confirm that the device, apart from the aspects covered by the clinical investigation, complies to the general safety and performance requirements, and that the possible precaution has been taken to endure the protection of the subject's health.

7 Traceability and Unique Device Identification

The MDR proposal provides for strengthened new obligations for economic operators with regard to traceability provisions. These are outlined in Chapter VII of the MDR proposal.

7.1 Present Situation and ISO 13485: 2012 General Requirements

The current Medical Device Directives do not establish provisions on traceability of medical devices. This has urged some Member States (e.g. Spain) to impose national or regional device identification requirements to manufacturers [17].

Having different traceability systems among countries does not allow transparency among member states, as national systems are not compatible with each other and, therefore, traceability among Member States is not possible [36]. Moreover, manufacturers marketing their products in different Member States are subject to an huge administrative burden as they have to enter data in diverse national – or sometimes even regional – databases, follow different sets of national rules and adapt their products to each mechanism to satisfy the requirements of all Member States where they wish to market their products [17].

Although the current Directives do not address traceability requirements, a general requirement for traceability is provided in **Standard EN/ISO 13485:2012** [37]:

- According to Section 7.5.3.2.1 of the Standard, *the organization shall establish documented procedures for traceability*, which *shall define the extent of product traceability and the records required. Where traceability is a requirement, the organization shall control and record the unique identification of the product.*
- Section 7.5.3.2.2 covers particular requirements for active implantable medical devices and implantable medical devices and states that the organization *in defining the records required for traceability, shall include records of all components, materials and work environment conditions,* if these could be a cause for which the *medical device does not satisfy its specified requirements.* The organization will also mandate *its agents or distributors to maintain records of the distribution (….) to allow traceability. These records must also be available for inspection.*

According to Section 4.2.4 of the Standard, records must be retained *at least for a period equal to the lifetime of the product defined by the organization,* in any case *no less than two years from the date of product release* [38].

Although some provisions are mentioned in the Standard, the definition of specific requirements is in any case left to the manufacturer and no provisions are legally mandated in the European Union.

The MDR proposal, therefore, provide for the establishment of a Unique Device Identification (UDI) System that is harmonised at European level, which is seen as the best means for effective identification of devices. The texts also provide for an enhanced

traceability of devices throughout the supply chain by increasing the responsibilities of the economic operators. Furthermore, there will be additional measures for an improved response to incidents and in improved transparency among Member States.

Provisions are treated in Chapter III (Articles 23 to 27). Requirements outlined in this chapter do not apply to custom-made and investigational devices.

7.2 The UDI as Tool for Effective Traceability

7.2.1 A New Requirement

The new requirement for a UDI is found in Article 24, Paragraph 3, which states that manufacturers *shall assign a Unique Device Identification (UDI) to their devices* before placing them on the market.

According to Definition 13 in Article 2 of the MDR proposal, the Unique Device Identification is *a series of alphanumeric characters created through internationally accepted device identification and coding standards and that allows unambiguous identification of specific devices on the market*.

Article 24 of the proposal states that *the UDI shall consist of* two identifiers:

- **A device identifier,** manufacturer and device model specific, which shall provide access to some information like *expiration date or manufacturing date, name and address of manufacturer and trade/brand name. The information is listed in Part B of Annex V.*
- **A production identifier**, *which identifies data related to the unit of the device production.*

According to Article 24.4 of the MDR proposal, the UDI will appear in the technical documentation provided by the manufacturer to the notified bodies and on the declaration of conformity. It will also be used in serious incident reporting and to report FSCAs.

The manufacturer will have the obligation of allocating an UDI to a device, to place it on its label (or on the implant card in case of implantable devices) and to archive it electronically. Furthermore, all economic operators will have to store and keep all UDIs (device and production identifiers) of the devices they have supplied or they have supplied with.

The system for assignment of UDIs will be operated by one or more entities (i.e. organisations with legal personality) designated by the Commission. The system must be capable of allowing identification of the devices throughout its distribution. This legal entity will be in charge of giving access to the system to all interested users according to *transparent terms and conditions*. It will operate its system for minimum three years after the designation remaining *in compliance with the criteria and terms of designation.*

The electronic system on UDI will be set up and managed by the Commission in cooperation with the Member States. This system will collect data elements of the UDI

device identifier as listed in detail in part B of Annex V, i.e. basic information on the manufacturers and device models. This information will be available to the public.

The UDI system will be an integral part of the revised EUDAMED database.

No provisions are given in the MDR proposal for the following, but the Commission will have the authority, be means of delegated acts, to

- decide which devices, groups or categories of devices the UDI system will apply and timelines for the implementation, which will be gradual and, as mentioned, will begin with devices belonging to the highest risk-class,
- adapt requirements on what data must be included in the production identifier and which varies according to the risk class,
- adapt the information in Part B of Annex V to reflect technical progress,
- define obligations of economic operators, health institutions and professional users with regards to the use of UDI: allocation of alphanumeric characters, placement of the unique identification on the label, archiving of the information in electronic systems, and use of UDI in documentation and reporting.

7.2.2 UDI implementation in the United States and globally

The U.S. FDA has already started developing the UDI system earlier than the European Commission: a draft rule was published in July 2012 and a draft guidance document is due by the end of November 2013, according to the priorities for 2013 of the FDA Center for Devices and Radiological Health [39].

Similarly to the European Commission, the FDA defines the UDI as *a unique numeric or alphanumeric code that acts as a key to certain basic identifying information about a device, such as the name of the manufacturer and the type of device, and may represent certain other information about the device, such as its expiration date and batch or lot number. This information will be contained in a publicly available UDI database, and no identifying patient information will be stored in this device information center* [40].

7.2.3 The Proposal of the Global Harmonisation Task Force

At international level, work has also been progressing since 2008 when, under the auspices of then GHTF, an a*d hoc* working group was set up. A first guideline on UDI was released in 2011, foreseeing the UDI requirement for medical devices to carry the identifier. Eucomed, the European association representing the medical technology industry, released a Technical Information Sheet in April 2011. Although the association recognised the introduction of the UDI as an innovation that would bring many benefits and improve efficiency, they also raised some concerns *inter alia* regarding the costs that manufacturers *would face in altering production and labelling lines* [41].

The mission of the GHTF ended in December 2012 and the group has been replaced by the IMDRF. IMDRF, successor to the GHTF, is a voluntary group, consisting of medical

devices regulators only (industry is no longer involved), who have come together to build on the work of the former GHTF. This group includes authorities from Australia, Brazil, China, Canada, European Union, Japan and the United States. Authorities from Mexico and Russia are observers.

A long-awaited draft version 2.0 of the proposal was eventually released by the IMDRF UDI Working Group on 10 April 2013. The document has the purpose of providing a framework for those regulatory authorities that intend to develop their own UDI systems in a way that they are implemented without national or regional differences and can contribute to achieve common globally harmonised UDI system requirements. The aim is to obtain a global exchange of data on devices and to *reach the goal of a globally harmonised UDI system*.

Although the guideline provides non-binding recommendations, it is expected that regulatory authorities will follow it in the development of their own UDI requirements.

The document sets up the basic principles that a harmonised UDI system should include and establishes *that all stakeholders involved in the distribution and use of a device will be required to capture and store the UDI. This should assist in recalls and in preventing the proliferation of counterfeit medical device products.*

Ideally*, the identifier should be globally unique to the particular device to which it is affixed or otherwise associated, and should not be changed unless the device is re-processed, re-manufactured, or re-labelled as a new medical device.*

The IMDRF identifies three existing systems as acceptable for labelling use:

- The Global Standards One (GS1),
- Health Industry Business Communications Council (HIBCC), and
- The International Council for Communality in Blood Banking Automation (ICCBBA) standards.

According to the IMDRF proposal*, they all meet the criteria of the UDI and manufacturers will be permitted to choose which system they wish to use.* In particular GS1, a non-profit organisations issuing the majority of bar codes used globally in the devices industry, has established a global network of devices industry and healthcare professionals to develop specific standards for UDI [41].

The identifications will be affixed to the device and to the higher levels of packaging (except the shipping containers). Specific requirements will also be applicable for diverse device types, e.g. *In Vitro* Diagnostics, implantable devices, reusable devices, software, and kits [42].

7.2.4 The EU Commission Recommendation of 5 April 2013

On 5 April 2013, the Recommendation from the European Commission on a common framework for a Unique Identification System was published in the Official Journal of the

European Union to complement the provisions for traceability and identification contained in the MDR proposal of 26 September especially as regards the new UDI requirements and to *pave the way to a mandatory implementation of an internationally compatible UDI system in the Union* [36].

This Recommendation also defines

- the device identifier as "**static information**"**,** as it does not differ between two devices of the same model. This will be the information that will be stored in the UDI Database (UDID),
- the Production Identifier as "**dynamic information**". *This identifier will differ according to the way the production process is controlled (by expiration or manufacturing date, lot/batch number or serial number).*

This document outlines not only further details on the future identification system to reflect some international provisions, but also gives more clarifications on the requirements to be fulfilled in the European Union by economic operators, health institutions and professional users to ensure accomplishment of the objectives of the UDI system.

According to the fifth chapter of the Recommendation, while developing their own national UDI mechanisms, economic operators and healthcare institutions should make sure that both **device identifiers** (static information) and **production identifiers** (dynamic information) have been allocated to their product and store them.

The static information would be first stored in the national UDI Databases and then, as soon as the new version of the European Database is set up, it will be centralised and collected via an European UDI system, which will be a part of the EUDAMED database. It is therefore recommended that Member States that decide to develop, in the meantime, own UDI systems, do take EU recommendations into considerations and ensure that their systems are made compatible with each other and with the future system in the EU [36].

The dynamic information would neither be entered into the national UDI databases nor, at a later point, in the European UDI system, but will only be stored at the economic operators and health institutions.

The information in the production identifier should vary according to the different risk classes of the device, although a manufacturer may choose a product identifier applicable to a higher class than the device in question:

- **Class I:** expiration and/or manufacturing date,
- **Class IIa** and **class IIb:** lot/batch number,
- **Class III:** lot/batch number or serial number.

Member States who wish to establish their own systems should implement them gradually and follow a risk-based approach in accordance with the classification of the device. Highest risk device should be the first to reflect the condition to carry an UDI [36].

Member States will have the responsibility to monitor that differentiation between classes is based on the type of production identifier (dynamic information).

The Commission Recommendations also specifies that the UDI should appear in both human readable format and in a format that can be read by an AIDC (Automatic Identification and Data Capture) technology and conveyed via a carrier, whereas a carrier is the way in which the UDI is conveyed.

As a general rule, it should be applied to every package level for all classes of devices.

Health institutions and, where feasible, professional users should use this information in their reporting of incidents, to allow a more efficient action in case of recall or withdrawal of products [36].

7.3 New Tasks for Economic Operators with regards to Traceability and UDI

Article 23 of the MDR proposal assigns to economic operators the obligation to be able to identify all economic operators who supplied them and to whom (including health institutions or healthcare professionals) they have supplied a device for a period of at least five years (15 years in the case of implantable devices) after the last device covered by the declaration of conformity has been placed on the market, *i.e.* a period specified in Article 8(4). Economic operators must also be capable to inform authorities thereof upon request.

The European Commission Recommendation of 5 April 2013 provides further details and clearly outlines the principal steps that diverse economic operators should follow with regards to the UDI allocation and storage.

Manufacturers will

- **allocate** both **identifiers** to the device they manufacture,
- **enter the data elements** in the UDI Database according to the Annex of the Recommendation,
- **modify the existing labelling** by printing on the UDI code on the label and on all levels of packaging,
- **record** both identifiers **electronically**,
- **record electronically** all economic operators, health institutions and health professionals they have supplied each specific product with.

Authorized representatives should be able to obtain access to the record of both UDI identifiers of the products for which they are appointed. A manufacturer that does not have a registered place of business in a Member State should designate one authorised representative at least for all devices of the same model by a manufacturer.

All economic operators downstream (**importers and distributors**) should check that the UDI has been previously correctly allocated by the manufacturers and, in case they believe

that it is not the case, they should refuse to place the device into market or making it available.

Furthermore, they will not remove or change the UDI, as any change or removal would hinder traceability.

Importers should, furthermore, check whether devices have already been registered in the national UDI database of the Member State where the device is on the market:

- In case they have been registered, the importer is, however, responsible for checking that the device identifier on the products and that in the UDI database are corresponding.
- In case the devices have not yet been registered, it is the importer who should register the device identifier.

Importers and manufacturers should then also record electronically:

- Both identifiers (static and dynamic information),
- Economic operators from whom they have received a device,
- Record all economic operators, health institutions or professionals to whom they have supplied a device [36].

7.4 The EUDAMED Database

7.4.1 Current Situation

The Commission MDR proposal foresees the establishment of new functions and extension of the scope of the existing **EUDAMED database**.

EUDAMED is a secure web-based portal the use of which is mandated by Article 10b of the AIMDD, Article 14a of the MDD and Article 12 of the IVDD. The European Commission Decision 2010/227/EU of 10 April 2010 established its mandatory use by Member States national authorities since May 2011.

At present, access to the database is not available to the public, patients or healthcare professionals, but only **to Member States national authorities and the Commission**, which use it as a central repository for information exchange between them with the aim to reinforce market surveillance and transparency between these parties. However, the regulatory pathway of medical devices is still considered opaque by other stakeholders like Health Technology Assessment Bodies, insurers and third countries, as they have no access to the data regarding the characteristics, the clinical assessment and the conformity assessment procedures of devices [17].

Currently, the database contains data entered by Member States on devices on the European market, manufacturers/authorised representatives, data relating to certificates issued, modified, supplemented, suspended, withdrawn or refused, data obtained in accordance with the vigilance procedure and data on clinical investigations.

The tool presenting the best practice for the purposes of EUDAMED is the Global Medical Device Nomenclature (GMDN), developed by CEN for the purpose of regulatory data exchange, then further developed by the GMDN maintenance to be regularly updated web-based. Data entry is, however, also possible without providing a GMDN code [43].

At present, the competent authorities of the European Economic Area, Switzerland and Turkey have to set up an own system to collect the data and then upload it in EUDAMED. This causes a heavy administrative burden to the agencies [17].

7.4.2 New Functions and Extension of the Scope of EUDAMED

As listed in Article 27 of the MDR proposal, integral parts included in the new European database will be the following electronic systems on:

- Unique Device Identification,
- Registration of devices and economic operators,
- Information on certificates issued by notified bodies,
- Clinical Investigations,
- Vigilance,
- Market Surveillance.

Data will not only be entered by Member States authorities and the Commission, as it is at present, but also by notified bodies, economic operators and sponsors, who will have precise obligations with regards to provision and maintenance of data.

Access to available information will be extended to the notified bodies, economic operators, sponsors of clinical investigations and, to some extent, to the public.

Sponsors of clinical investigations will also enter data and comply with the new requirements set out in Chapter VI of the proposal with regards to clinical investigations conducted in more than one Member State and manufacturers will enter data to comply with information obligations as set out in Chapter VII with regards to vigilance and market surveillance.

It is assumed that the optimisation of coordination between Member States can only be ensured successfully at Union level, therefore it is the Commission that should develop the database and will be considered the controller of EUDAMED and its electronic systems.

Moreover, an electronic system on clinical investigations would constitute a tool for sponsors that would submit, on a voluntary basis, a single application for several Member States and to report serious adverse events.

An electronic system on vigilance could facilitate reporting by economic operators of serious incidents connected to the use of a marketed device, as well as a coordinated assessment by the national authorities. It would also be a good tool for national agencies to exchange the information on actions taken by them on actions following the reporting of a serious event and other significant events reported by the concerned economic operators.

Personal data will be available in the database only to the extent that is needed for the electronic systems forming integral part of the EUDAMED and listed in Paragraph 2 of Article 27.

These data will allow identifications of the subjects for no longer than at least five years (15 in case of implantable devices) after the last device has been placed on the market.

However, Member States and Commission will ensure that data subjects can exercise their rights to object and to ensure that data subjects can access data relating to them.

Provisions to establish a pan-European central database as outlined in Article 27 of the MDR proposal will then ensure that a high level of transparency is achieved among the different countries, as well as do away with national different registration systems that have been implemented over the years and that have increased the burden and the costs for economic operators.

The new structure is expected to improve the overall transparency, enable a better communication between Member States, the relevant economic operators, notified bodies, and the Commission. In this case, there would be an optimization of resources, as duplication of reporting would be avoided.

7.5 Electronic System for Registration of Devices and Economic Operators

Another integral part of EUDAMED as mandated by the MDR proposal will be an **electronic system for the registration of devices on the market and of economic operators.** The system will be set up and managed by the Commission in collaboration with Member States.

As provided for in Article 25 of the MDR proposal, the **manufacturer or authorized representative** will submit, before placing the device on the market, some basic information needed for identification and description of the device and for identification of the manufacturer (or, where applicable, authorised representative and importer) in this electronic system. **Importers** will have to submit the information **within one week** after placing the device on the market.

This includes information, e.g., on

- **economic operators:** role, name, address, contact details, person in charge to submit information, in different from the economic operator;
- **device:** UDI identifier or data elements as listed in part B of the Annex, risk class, Member States where the device is or has been available (or will be available, in case of Class II and III devices), country of origin in case of imported devices, status (marketed, withdrawn, recalled);
- **certificate:** type, number, expiry date, name or identification number of the notified body that has issued it,

- **summary of safety and clinical performance** for class III or implantable devices, as described in Article 26. It will be written in a language that must be understood by the intended users, will be included in the documentation provided for conformity assessment and will be validated by the notified body. Data elements to be included and their form and presentation will be decided by the Commission via implementing acts;
- **presence of products, of other entities, if used separately, and differently regulated:** medicinal product name medicinal products derived from human blood or human plasma, human tissues or cells, or their derivatives, and name of the substances.

Details of the **information to be provided** by the manufacturers are listed in Part A of Annex V in the MDR proposal. The Commission is enabled to adopt delegated acts to amend the list of elements in part A of Annex V to reflect the experience gained and the technical progression.

The information provided in this electronic system **will be available to the public.**

Economic operators must confirm the exactness of the data no later than two years after the first submission of the above information and then every second year. If a change occurs to the information, the relevant economic operator must accordingly amend the data in the system within one week of the change.

8 Post-Marketing Surveillance

This chapter first compares the current requirements with regards to vigilance with the changes proposed by the European Commission for the new Regulation.

The same comparison is done for new proposed requirements for market surveillance.

8.1 Principal Mechanisms

The post-market performance of medical devices in their everyday use is monitored with these principal mechanisms established by the current Directives:

- **Vigilance** originates from the requirement to inform the competent authorities if an incident associated with the use of the device or a recall occurs and is a "reactive" process following a report that a device can potentially, or has already caused, some harm.
- **Post-market surveillance** is the proactive review, done by **manufacturers,** of the post-production phase experience and the implementation of means to apply corrective actions.
- **Market surveillance** is a process where **authorities** are involved to detect anomalies or non-compliance to the essential requirement and to make sure that the products on the market do not constitute a danger to public health [44].

8.2 Medical Devices Vigilance: Current Requirements

8.2.1 Medical Device Directives

The principal purpose of vigilance is to improve the protection of health and safety of patients, users and others by reducing the likelihood of reoccurrence of incidents related to the use of a medical device.

Therefore, the Medical Devices Directives mandate that adverse incidents are evaluated and, where appropriate, information is disseminated in the form of a National Competent Authority Report (NCAR) with the objective of preventing repetition of such incidents through the adoption of appropriate Field Safety Corrective Actions (FSCA) [45] .

A FSCA is defined as *any action taken by a manufacturer to reduce the risk of death or serious deterioration of health associated with the use of a marketed device.* These actions should be reported via a Field Safety Notice, which manufacturers send to customers or users [46].

Requirements with regards to vigilance of medical devices are outlined in Article 10 of the MDD and Article 8 of the AIMDD, which define, respectively, the task of Member States *to take the necessary steps to ensure that any information brought to their knowledge (...) regarding the incidents (...) is recorded and evaluated centrally.*

The above-mentioned Articles also define incidents as

- *any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labelling or the instructions for use which might lead to or might have led to the death of a patient or user or to a serious deterioration in his state of health* and as
- *any technical or medical reason in relation to the characteristics or performance of a device for the reasons referred to in the above subparagraph (...), leading to systematic recall of devices of the same type by the manufacturer* in the case of medical devices and *reasons resulting in the withdrawal of the (...) device from the market* for active implantable medical devices.

The use of EUDAMED allows the action of coordinating the central registration and the evaluation of incidents. The database enables the sharing of information and data among competent authorities. Ideally, national authorities may decide to disseminate information with the scope of preventing incidents [44].

The **Medical Devices Vigilance System** consists of all the criteria and procedures in use by manufacturers, authorities and other interested parties to notify incidents, corrective actions and recalls [44]. To establish a procedure to review experience gained from devices in the postproduction phase and to keep the procedure updated is part of the manufacturer's application for the EC declaration of conformity, according to Paragraph 3.1 of Annex II of the MDD and of the AIMDD. An additional requirement to present *an undertaking to implement appropriate means to apply any necessary corrective* action as part of the EC Declaration of conformity application can be found in Paragraph 3.1 of Annex II of the MDD and in Annex 6 of the AIMDD as a requirement for custom-made devices.

Furthermore, Paragraph 3 of Annex IV of the MDD and Paragraph 4 of Annex IV of the AIMDD define the obligation of the manufacturer to notify the competent authorities of incidents as a part of the EC verification, i.e. the procedure where a manufacturer/authorized representative ensures and declares that its products conform to the type described in the EC type-examination certificate and meet the applicable requirements. The same requirements apply to the procedures (both production and product quality assurance) for the EC declaration of conformity.

8.2.2 MEDDEV Guidelines

The Directives are complemented by the MEDDEV guideline 2.12-1 "Guidelines on a Medical Devices Vigilance System", which aims to facilitate the application and the Medical Devices Vigilance System requirements outlined in the Directives.

The scope of this document applies to all incidents occurring following the use of CE marked devices in the EEA, in Switzerland and in Turkey, as well as to incidents that apply to devices that do not bear the CE marking, but lead to a corrective action relevant to CE-marked devices [44].

The manufacturer must **report the following incidents** to the competent authorities:

- Those resulting in death,
- Those resulting in a serious deterioration of the state of the health (of users, patients or other person),
- Those that might have lead to death or serious deterioration of health or to death, but did not thanks to fortunate circumstances or intervention of healthcare personal.

Generally, the criteria for reporting an incident are:

- An incident has occurred.
- The device is suspected to be a cause of the incident.
- The event has lead (or might have lead) to death or serious deterioration of death [47] [48].

Incidents must be reported immediately, i.e. without any unjustifiable delay, to the competent authority in the country where the incident occurs. Some authorities, like the German Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte - BfArM), publish the appropriate forms online for manufacturers (Incident Report Form, FSCA) to help manufacturers with the administrative procedure and provide national reporting requirements and principles. Other national authorities mandate electronic reporting [44] [49]. Templates are also available at the MEDDEV webpage where all guidelines are published [9].

The report should contain the elements listed in Annex 3 of the MEDDEV Guideline and should be made by the manufacturer or the authorised representative. The initial report can also be made orally, but should always be followed by a written report.

The MEDDEV guideline provides for the timeframes according to the seriousness of the incident:

- If the incident foresees a serious threat to public health: immediately and, in any case, no later than **2 calendar days** after awareness of the incident,
- In case of death or serious deterioration in state of health: immediately after the manufacturer has become aware of a link between the incident and the use of the device but in any case no later than **10 calendar days** after becoming aware of the incident,
- In other cases: immediately after having established a link between the use of the device and the incident, but no later than **30 days** following awareness of the incident.

After the reporting, an investigation starts, usually performed by the manufacturer, after which it will be decided whether it is needed to perform

- no further action,
- further surveillance or follow-up in case of devices still in use,
- corrective action on future production only,

- a Field Safety Corrective Action /recall (for medical devices) or withdrawal (for active implantable medical devices).

The outcome of the investigation will be sent as a report to the same authorities where the initial incident had been previously reported.

Should the manufacturer be incapable of performing the investigation of an incident for any reason (especially on some cases where access to the concerned device may modify it in a way that might impact subsequent analysis), the authority should be informed thereof as soon as possible. The authority will then be involved or may initiate an autonomous investigation, as much as possible in consultation with the manufacturer. In this case, after the evaluation, the national authority performing the evaluation will inform the manufacturer of the result [44] [48].

A competent authority **might** also take other actions, such as making recommendations to the manufacturers on how to improve information provided with the device, consult with the notified body if the matters refer to conformity assessment, inform the Commission and other authorities when a device is recalled or other actions are taken, consult with the Commission if a re-classification is needed.

Furthermore, if an incident occurs in more than one member state and is reported to more than one competent authority, there **might** be designation of a single authority assuming the role of coordinator.

Authorities might as well, at their discretion, take the decision to circulate among other authorities information on the incidents reported in their territory of competence. This is done via a competent authority report, of which the manufacturer receives a notification.

Moreover, authorities might decide to circulate some information to medical device users, usually practitioners and medical facilities and, in some circumstances, to the public [44] [47] [46].

Reasons for a FSCA can be

- malfunctions or deterioration in characteristics or performance of the device,
- inadequacy of Instructions for Use (IFU)

that might cause or have caused death or serious deterioration of health.

In assessing the need for a FSCA the manufacturer is recommended to use the criteria reported in the International Standard EN ISO 14971:2007 “Medical Devices-Application of Risk Management to Medical Device”, although the text is not mandatory.

In its Annex 1, the MEDDEV guideline provides some examples of incidents and FSCA that the manufacturer should report.

FSCA can also be taken in consequence of an incident occurred in third countries that are involving medical devices covered by the MDD.

In case a FSCA (systematic recall/withdrawal) is the outcome of the evaluation, the manufacturer must send:

- **Field Safety Notice (FSN)** to customers, copying the competent notified body involved in the conformity assessment, the competent authority where the manufacturer has its registered place of business and the notified bodies involved in the conformity assessment,
- **A FSCA Report** listing all technical or medical reasons that caused the FSCA, to authorities in all countries where the action is carried out and to the competent authority responsible for the manufacturer. A copy of the Filed Safety Notice should be submitted with the report.

The detailed content and format of the FSCA report to competent authorities is available in Annex 4 of the MEDDEV guideline.

The manufacturer should normally **allow 48 hours** for receipt of comment on the FSN, unless there is a serious for public health.

Once the FSCA is completed, the manufacturer should inform the coordinating competent authority with information on the effectiveness of the action per country [48].

The MEDDEV guideline also requires the manufacturers to perform **trend reporting**, i.e. to report to the concerned competent authorities whenever an increase occurs of events that are not considered incidents according to the criteria listed in Chapter 5.1.3 of the guideline.

A form for trend reporting is available in Annex 7 of the guideline [44] [48].

An alternative reporting regime is the **Periodic Summary Reporting,** which is agreed between the manufacturer and the national authority in case of similar incidents with the same device/device type if the root cause is known or if a FSCA has already been implemented.

In this case, the manufacturer and the authority agree on the content and the periodicity. A form for these reports is available in Annex 6 of the guideline [48].

Although involvement of **users** is of outmost importance, no legal requirements currently require users to report incidents or other events. However, manufacturers are encouraged to develop a relationship with the customer and to encourage them to report all adverse events as soon as possible, to use reporting forms that may be provided by national authorities and to provide their contact details.

Field Safety Notices can also be a mean not only to provide updated information on the device to the users, but also to request their feedback. Guidance for manufacturers when involving users in the vigilance system is provided in Annex 11 of the MEDDEV guideline [48].

8.2.3 Role of EUDAMED

The **EUDAMED** databank has a fundamental role in the European Medical Devices Vigilance System as it provides European authorities with online information on vigilance data, among others. The information, however, is not publicly available and is entered by the competent authorities only.

Its use allows transparency and coordination of enforcement of postmarket requirements between authorities. Entering data in EUDAMED has been mandatory for competent authorities since May 2011 [44].

8.3 Commission Proposals on Medical Devices Vigilance

8.3.1 Tasks of Competent Authorities, Implementing Acts

In the Commission's MDR proposal vigilance and market surveillance have a dedicated chapter (Chapter VII) and are treated respectively in the first (Articles 61 to 66) and in the second section (Articles 67 to 75).

The proposals of the European Commission aim to include in the legislative act some requirements that were previously only included in the MEDDEV guidelines, and therefore to make these requirements mandatory, and enforce the introduction of a EU portal where to report incidents and corrective actions and where the concerned authorities receive the information. The assessments between competent authorities will be coordinated to avoid duplication of work and to share the expertise.

A strengthened coordination between authorities is also foreseen for market surveillance activities.

The development of **EUDAMED** will also involve vigilance and market surveillance, as it will contain integrated electronic systems on a European UDI, on vigilance and on market surveillance.

The content of the Commission's MDR proposal reflects some requirements of the MEDDEV guideline on medical devices vigilance that are not included in the current Directives. Not being part of a legislative act, the content does not yet provide for mandatory requirements.

According to the Commission' provisions, it would be the **manufacturers** who will have the responsibility to **report directly through EUDAMED**, and not anymore to the national competent authorities, any serious incidents or any FSCA they have undertaken, including FSCA undertaken in third countries in case of devices also made legally available on the Union market.

It will be only in case of custom made devices that manufacturers will have to notify national competent authorities of the Member States where the device is marketed.

Manufacturers shall report **no later than 15 days after they become aware** of the event and of the causal relationship with their device.

Article 61 of the MDR proposal states that *the time for reporting shall take account of the severity of the incident*, although, according to Article 61, no differentiated timescales are specified like in guideline MEDDEV 2.12. (2 days following the awareness of the incident for serious public threat, 10 days in case of death or unanticipated deterioration of the state of health, 30 days in all other cases). However, the Commission may, by issuing an implementing act, adopt modalities and aspects necessary for implementation of Article 61 as regards timelines according to which manufacturers must provide a report.

Not only will manufacturers enter reports on **serious incidents** (see 8.3.2) and **FSCAs** in the electronic system, but also **periodic summary reports,** field safety notices and trend reports.

Field safety notices will be available not only to the users of the concerned devices, but also to non-users, i.e. to the public.

Upon receipt of a notification, reports will be **automatically transmitted** to the concerned national competent authorities, i.e. all Member States where

- the incident occurred,
- FSCA is being or must be commenced,
- manufacturers have their registered place of business,
- the notified body that issued a conformity assessment certificate is established, if applicable.

Article 63 states that Member States will also make sure that their competent authorities evaluate, possibly together with the manufacturer, any information regarding serious incidents or FSCAs, they shall then carry out a risk assessment, evaluate the adequacy of the FSCA envisaged or undertaken by the manufacturer and the possible need and kind of other corrective action.

Furthermore, they will monitor the manufacturer's investigation of the incident. After having performed the assessment, evaluating authorities will inform, via EUDAMED, the other involved competent authorities of any corrective actions taken, envisaged by the manufacturer or imposed to him to minimise the risk of recurrence. Meanwhile, the manufacturer shall ensure that users of the device are informed without delay via a field safety notice of the corrective actions taken. Manufacturers will also enter field safety notice in EUDAMED, so that it will be available to the public.

One important new requirement of the MDR proposal is the fact that **one authority will be nominated to coordinate** the assessments of FSCA or serious incidents in case the same incident (or a similar incident) has occurred in more than one Member State. The proposal also specifies that, unless otherwise agreed between national authorities, the **coordinating**

authority will be the one of the Member State where the **manufacturer has his registered place of business.**

In the past, there was no obligation to designate a coordinating competent authority. The requirement currently in Paragraph 6.3.1 of guideline MEDDEV 2.12 only mentions that national competent authorities should, under particular circumstances, determine it.

Now this requirement will be mandatory and it is clearly stated which authority will be the coordinator.

The coordinating authority will be provided secretarial support by the Commission to perform the following tasks listed in Article 63.7:

- Monitor the investigation done by the manufacturer and the subsequent corrective action,
- Consult with the notified body on a possible impact of the incident on the certificate of assessment,
- Agree with the manufacturer on content and frequency of periodic summary reports,
- Agree on FSCA with the manufacturer and other concerned authorities,
- Inform the other authorities on progresses and result of its assessments.

National authorities will still have the right to perform additional assessments and adopt further safety measures in the interest of patient safety and public health. They will, however, need to inform the coordinating authority and the Commission on any further measures taken.

The Commission may adopt **implementing acts** defining modalities and procedural aspects with regards to typology of serious incidents and FSCA in relation to specific devices or categories of them and on with regards to timelines for incident/FSCA reporting.

8.3.2 Definition of "Incident" and "Serious Incident"

The MDR proposal contains two different definitions for "incident" and "serious incident", while in the MDD and AIMDD there is not such a differentiation.

According to Article 2, Definition 43, an **incident** is thus defined as *any malfunction or deterioration in the characteristics or performance of a device made available on the market, any inadequacy in the information supplied by the manufacturer and* ***any unexpected undesirable side-effect***. The term incident thus includes not necessarily those that can potentially cause the death/ deterioration of health of the patient (...), but **all undesirable side effects.**

According to Article 2, Definition 44, a **serious incident** is defined as *any incident that directly or indirectly* ***led****, might have led or* **might lead** *to death of a patient, user or other person, temporary or* ***permanent serious*** *deterioration of the patient's, user's or other person's state of health,* ***serious public health threat*** thus reflecting the criteria of a

reportable incident according to the content of the MEDDDEV guideline (changes in the text are reported in bold).

8.3.3 Content and Access to Vigilance Information in EUDAMED

Although an upcoming implementing act will exactly define to what extent, economic operatory, notified bodies and users will also have access to the information stored in the EUDAMED database. As already reported, not only authorities, but also notified bodies, economic operators and sponsors of clinical investigations will have access and will have to enter information.

The database will contain the following information on vigilance:

- Manufacturers' reports on serious incidents and FSCAs,
- Manufacturer's Periodic Summary Reports
- Manufacturer's reports on trends,
- Manufacturer's Field Safety Notices,
- Reports by authorities on serious incidents,
- Information to be exchanged between Commission and national concerned authorities as stated in Article 63.4: corrective actions taken or envisaged by manufacturers, or imposed on him to minimize recurrence of serious incidents, information on progress and outcome of assessments.

The MDR proposal does not lay down provisions, but states that the Commission might adopt modalities and procedural aspects by means of **implementing acts** for harmonized reporting forms for manufacturer's reports and harmonised forms for exchanging information between authorities.

8.3.4 Mandatory Trend Reports for Highest Risk Devices

It will be **mandatory** for manufacturers **of higher risk devices (Classes IIb and III**) to enter in EUDAMED any statistically significant increase in the frequency or severity of

- non-serious incidents or expected undesirable side effects with a significant risk-benefit analysis,
- expected undesirable effects that affect the risk-benefit analysis the use of which have caused or might have caused *an unacceptable risk to health or safety of patients or other persons weighted against intended benefits.*

To establish whether this increase is significant, it will be compared *to the foreseeable frequency of incidents or to the expectable side effects of the devices in question during a specific timeframe specified in the conformity assessment.*

Manufacturers will also update the technical documentation of the concerned device with vigilance data and make this notification available to notified bodies.

8.3.5 Involvement of Users

Although no obligation for users is clearly stated in the MDR proposal, Article 61 mandates **Member State authorities** to *take all the appropriate measures to encourage healthcare professionals, users and patients to report (…) suspected serious incidents.*

The authorities will then collect the reports at national level and will make sure that the manufacturer is informed of the incident so that he will ensure that a follow-up is initiated as appropriate.

According to Article 61, national authorities will also coordinate themselves with regards to the structure of web- based forms for incident reports by users.

8.3.6 Evaluation of proposed changes on Vigilance

Although most of the Commission proposals on Medical Device Vigilance reflect the content of the MEDDEV guideline 2.12, thus making the content mandatory, it is clear that the Commission aims to have more effectiveness and more transparency in the Medical Devices Vigilance System.

Having a coordinating authority, which is currently not a mandatory requirement, supervising the assessment and the monitoring of actions after an incident report that could affect the same device in more than one Member State, or if the same FSCA is undertaken in one than more Member State, would ensure a better **effectiveness**. The involvement of a coordinating authority was previously only foreseen as a possibility, but not as a requirement. The proposal also states which authority will be the coordinator.

The extension of access to EUDAMED and the obligation for manufacturers and notified bodies to enter relevant information under their competence would also ensure a better effectiveness, as it would make work sharing possible. Furthermore, the extended access to the database would increase the transparency and would make data on incidents and recalls available not only to authorities, but also to the final users.

Finally, the involvement of **users** ensured by the national authorities would then enhance the possibilities of reporting an incident, which is fundamental for an efficient performance of the vigilance system.

8.4 Market Surveillance

Postmarket surveillance arises from the requirement for manufacturers to implement a systematic procedure to gain and review postproduction phase device experience, to monitor the performance of the device and implement appropriate means to apply any necessary action to protect public health and safety. According to the current Directives (AIMDD and MDD), postmarket surveillance data are also to be used to update the clinical evaluation report document [44] .

According to a document of the GHTF entitled “Review of Current Requirements on Postmarket Surveillance”, no definitions exist in the current European Directives, however

- "**surveillance"** in the European Union means an active collection of information on medical devices,
- "**market surveillance"** indicates *the tasks carried out by the authorities,*
- *"***postmarket surveillance"** *refers to activities carried out by the manufacturers* [46].

There is a short description on the **aim** of surveillance in Annexes II, V and VI of the MDD, i.e. *to ensure that the manufacturer duly fulfils the obligations imposed by the approved quality system*.

8.4.1 Current Requirements

The "Blue Guide" on implementation of directives based on the "New Approach" states that all authorities involved in market surveillance activities should have the *appropriate resources to run the tasks to monitor products on the market and, in case of non-compliance, to take appropriate action to enforce conformity.* This includes visiting the premises of economic operators, organizing random and spot checks, taking samples and requiring all necessary information. *Corrective actions depend on the degree of non-compliance and, thus, must be in accordance with the principle of proportionality* [46].

Competent authorities can also detect through market surveillance other anomalies like devices that have not been evaluated with the appropriate Conformity Assessment Procedure (e.g. class I devices with a measuring function without an intervention of a notified body, devices that have been given an intended use that is different from the one intended by the manufacturer, devices without a labelling in the appropriate language).

Depending on the Member State, some further requirements can be applied to increase the market control, e.g. licences for manufacturing activities, notification of distribution activity or regulation of publicity.

According to the "Safeguard Clause" outlined in Article 8 of the MDD and in Article 7 of the AIMDD, Member States can take all measures they deem appropriate to withdraw devices from the market *or prohibit or restrict their being placed on the market or put into service* if they ascertain that the products can compromise health and safety when *correctly installed, maintained and used for their intended purpose.*

The Member State also have to inform the Commission immediately of the taken measures, of their reasons and, in particular, *if non-compliance with the applicable Directive is due to the failure to meet essential requirements, incorrect application of the standards or shortcoming in the standard themselves.*

However, other Member States are not mandated to apply similar measures [44].

EUDAMED also plays an important role in market surveillance, as it provides authorities information on manufacturers, authorised representatives, devices, certificates vigilance and clinical investigation data. It helps to achieve an uniform application of the directives and it allows coordination between authorities [44].

8.4.2 Commission Proposals on Market Surveillance

While in the current Directives there is no definition, the MDR proposal now defines **Surveillance,** as the whole of the activities performed by **authorities** to proactively check the characteristics and performance of marketed devices according to the definition of Article 2 (48) *to ensure that products comply with the requirements set out in the relevant Union harmonisation legislation and do not endanger health, safety or any other aspect of public interest protection.* Surveillance is covered by the MDR proposal in Section 2 of Chapter VII.

Competent authorities have the task of performing checks by reviewing the appropriate documentation and make checks on some samples.

Member states will have to check the functioning of their surveillance activities at **least every four years,** when they will also make a summary of results accessible to the public.

According to the MDR proposal, national authorities **shall** cooperate with each other and coordinate their activities, thus, if needed, agree on work sharing, share information and also cooperating with competent authorities of third countries, when needed.

According to Article 68, all information related to surveillance will be stored in EUDAMED, the electronic system, i.e. information on the following:

- **Non-compliant devices** that present a risk to health and safety, if non-compliance is not restricted nationally. The procedure to apply in these cases is described in Article 70 and 71 of the MDR proposal. In case of non-compliance, the national authority must immediately inform the relevant economic operator and require that he take all appropriate actions to end non-compliance. Non-compliance must also be communicated **without delay to the commission and other Member States** also on evaluation, actions required and any additional information on non-compliance of devices. If the operator does not take the adequate corrective action, the authority will prohibit or restrict the marketing of the device. Member States can also raise objections against a measure taken by another national authority. In case of urgency, the Commission can also adopt implementing acts with immediate effect.
- **Compliant devices that, however, present a risk to health and safety**: identification, origin/supply chain of the device, finding and correspondent finding of the Member State's evaluation, nature of risk and of measures taken. A procedure is described in Article 72 of the MDR proposal. Member States will have to report all these data immediately to other Member States and to the Commission and request the relevant economic operator to take measures to ensure that the medical device will not present the risk anymore. The Commission can decide if the measures are justified.
- **Products presenting formal non-compliance,** i.e. products bearing a CE Marking in violation of formal requirements, devices without appropriate marking, or in

case of CE marking assigned to product not covered by the Regulation, missing or incomplete declaration of conformity, products without or with an not appropriate labelling, products for which the technical documentation is not available or not complete. According to procedure described in Article 73, the Member State concerned can prohibit the product or insure that is recalled or withdrawn. Other Member States and the Commission must be informed via EUDAMED without delay.

- **Preventive health protection measures:** the system will also serve as mean by the concerned Member State to inform the Commission ad other Member States and store information on provisional measures taken by Member States once they have identified a **potential** risk related to a device/category of devices.

The information listed above must be immediately transmitted to the concerned national authorities and also be accessible to the member states and the Commission.

The procedures to follow by concerned member states are described in Articles 70-74. The Commission can assess national measures taken and decide whether they are justified with implementing acts. If there are grounds of urgency, the Commission can also issue implementing acts that are immediately applicable.

The Commission can also take, by means of implementing acts, measures to ensure protection on health and safety in case it decides that measures taken by the concerned member states cannot contain adequately the risk to health and safety emanating from a device (Art. 71.2) for all devices, that still present a risk to health and safety.

According to Article 75 of the MDR proposal, before any measure is adopted, the economic operator will have the opportunity to make submissions. As soon as the economic operator can demonstrate that he has taken corrective actions, the measure will be immediately withdrawn.

8.4.3 Evaluation on Proposed Changes on Surveillance

Like in the case of the EU Commission proposals on vigilance within the envisaged MDR, the most of the requirements are not completely new but there are more detailed definitions on what non-compliance is. Like in most of the proposed measures, the Commission highlights the need of a coordinated approach to surveillance activities, as well as on harmonised requirements throughout member states.

There is also harmonisation to the provisions that can be taken by member states on the economic operators whenever a vigilance or market surveillance issue arises, while it is currently defined nationally.

The commission will have the power to issue implementing acts to if national measures are justified or not and in urgent cases adopt acts with an immediate effect.

All the rules in Chapter VIII, which put a strong emphasis on transparency, harmonisation of requirements and coordination between authorities, have the aim of avoiding health

scandals like those caused by the PIP breast implants or the DePuy metal-on-metal hip replacements.

9 Conclusions and Discussion

The main issues regarding the weaknesses of the current regulatory framework for medical devices have been considered since the launch of the public consultation on a recast of the current Directives in 2008.

Stakeholders had already identified some inadequacies that would be, a couple of years later, concurrent causes of the so-called "PIP scandal":

- Insufficient requirements for traceability (especially in case of implantable devices),
- Inadequate communication and cooperation among national authorities (which also caused a loss of effectiveness due to work duplication),
- Lack of transparency among authorities with regards to occurrence of incidents and corresponding recalls and corrective actions,
- Lack of oversight of notified bodies.

Although the same device bearing a CE marking can be sold in all the EEA, in Switzerland and Turkey, a harmonisation of requirements with regards to registration of devices, traceability provisions and reporting requirements in case of incidents or recalls among all the concerned states has not been yet reached.

The MDR proposal from the European Commission has some basic features in common with two other important legislative proposals regarding the healthcare sector currently being discussed in the European Union, i.e. the one for a Regulation for Clinical Trials and the parallel proposal for *In Vitro* Diagnostic Devices:

- The elimination, as far as possible, of national differences in favour of a harmonised system,
- An increased transparency between countries, and
- The cooperation of Member States to share expertise and avoid duplication of workload.

In several of its parts, the MDR proposal mandates a significant improvement of harmonisation of requirements at European level and even (like in the case of the Unique Device Identification System) at global level, of transparency and of cooperation not only between authorities, but also involving the Commission, economic operators and notified bodies.

The form of a regulation will be appropriate to make all requirements directly applicable at the same time in all the concerned states, thus resolving the problem of having different national requirements. The differences in the implementation of the directives in the member states has proven to be a burden for companies dealing with marketing of their products in more than one European country, as well as a cause of different level of protection for patients throughout Europe.

Although the European Commission and the European Parliament seem to agree on the above provisions, they have also expressed divergent opinions on other aspects, the most important of which is certainly the kind of procedure for access to market of the highest risk devices. While the Commission is proposing a scrutiny procedure, the Parliament would rather introduce a mandatory marketing authorisation for devices, similarly to the system in use by the FDA in the United States. The two alternatives, scrutiny procedure and premarket approval, give no evidence of bringing safer and more efficient devices on the market. However, both systems would certainly increase the burden on manufacturers and competent authorities, with the risk of causing a significant delay in making devices available on the market and with obvious disadvantages for patients or users. According to Eucomed, *lifesaving and life-enhancing medical technologies are available to European patients three to five years earlier (on average) than those in the United States* [32]. Furthermore, the European health authorities should institute a new division with expertise on medical device, which would have some cost, which would be critical at these times of economic crisis in Europe.

Even if most efforts of this legislative procedure are aimed at achieving a regulation that is effective to prevent incidents like the one occurred in the "PIP scandal", it should not be forgotten that this scandal is the consequence of a fraudulent behaviour of the manufacturer, who deliberately used an undeclared component in the manufacturing of his products.

A more stringent regulatory pathway to bring medical devices on the market would not necessarily prevent a manufacturer from breaking the law, but what could help in detecting whether a device is manufactured in compliance to the applicable requirements and to the information declared in the technical file would rather be more stringent controls.

For this purpose, a provision planned by the MDR proposal, e.g. the right and duty for notified bodies to perform unannounced inspections, could already be an efficient measure to detect whether non-compliant devices are manufactured or brought to the market and then, if needed, take appropriate actions in due time.

The other provisions from Chapter IV of the MDR proposal with regard to the criteria for designation and monitoring of notified bodies are also appropriate to ensure more stringent control of the operations performed by them and to ensure that only the appropriate conformity assessment bodies are notified to the Commission, namely only those who satisfy the requirements set out in Annex VI, as mentioned in Article 33 of the MDR proposal. The notified bodies system has been identified as one of the most significant weaknesses of the current regulatory framework for medical devices by stakeholders and by the press, especially due to their fact that they are commercial organisations, and their better designation and monitoring is one of the aspects where the two European institutions agree that changes to the current system are needed.

The requirement for the manufacturer to have available a qualified person responsible for regulatory compliance would be a further way to ensure that only compliant medical devices are marketed.

The provisions on vigilance and market-surveillance also aim at harmonisation of requirements and to strengthen the cooperation among authorities, especially in case serious incidents happen. The strengthened provisions will increase the possibilities that an incident is detected and reported. The mandatory trend reports for highest risk devices and the increased involvement of users would also increase the possibilities that a follow-up is initiated as appropriate.

The use of EUDAMED not only by authorities, but also by manufacturers, and to some extent by the public, would increase the transparency with regard to information on devices and would make it easier for all authorities to detect whether a device on the market in their territories can be concerned by vigilance or surveillance issues.

There is an urgent need of harmonised requirements on traceability, as there are currently national differences and different national systems that are not compatible with each other. Therefore, provisions on a harmonised system and common identifier as well as the proposal of having a card for implantable devices are appropriate to track devices during their lifecycle.

In conclusion, almost all provisions envisaged on the MDR proposal would be effective to address the weaknesses of the current regulatory framework. The MDR proposal, however, still has many open ends that, as specified in the text of the MDR proposal, will be covered by successive delegated acts or implementing acts.

To keep bringing safe and effective devices on the market and make them available to patients or users without any unnecessary delay, it is also important that manufacturers are not excessively burdened with requirements that would not bring any improvement to the safety and effectiveness of the devices, but that the right balance is found.

Once strengthened provisions on notified bodies, traceability, vigilance, market surveillance, and responsibility of economic operators are in place, once authorities can coordinate themselves effectively and once a better transparency between states is achieved, the need of a marketing authorisation or of a scrutiny procedure would not be needed to market safe and effective medical devices.

10 Outlook and Latest Developments

At the time of writing (June 2013), the situation regarding the development of a Regulation for Medical Devices is still far from being defined: the Parliament's leading Committee (ENVI) has proposed 907 amendments (of which 145 are from the Rapporteur) suggesting changes to the Commission proposal. On 18 June 2013, another Committee of the European Parliament, the Internal Market Committee (IMCO) adopted its draft report on the MDR proposal and will provide it to the ENVI, which will then vote on the adopted IMCO amendments along with the tabled 907 ENVI amendments [50].

The Council of the European Union has also started reviewing the MDR proposal: the EU's Council of Employment, Social Policy, Health and Consumer Affairs (EPSCO) Ministers met on 20-21 June 2013 [51] at the 3247th Council meeting, where a presidency progress report was presented on the two proposals of Regulation on Medical Devices and *In Vitro* Diagnostics [52].

According to the progress report, in the examination of the proposals some issues have emerged. The Working Party on Pharmaceuticals and Medical Devices discussed the possibility of splitting the proposals and giving priority to certain important provisions. The Working Party had also discussions on the scrutiny mechanism as provided for in Article 44 of the MDR proposal and delegations have shown different opinions: some deem that it should be deleted, some accept it as it is in the MDR proposal and other delegations are of the opinion that it should be systematically employed with binding outcomes. Moreover, the Working Party is of the opinion that the difference in responsibilities of member states and the Commission in the designation of notified bodies has yet been clearly outlined in the MDR proposal.

Some concerns were also expressed regarding the provisions in Chapter VI of the MDR proposal regarding clinical trials with medical devices, especially regarding the time limits for authorisation of clinical investigations, which are deemed to be too short, regarding the provision of "tacit approval" and regarding the lack of explicit mention of the role of ethics committees in evaluating applications for clinical investigations [53].

The next step is the final vote of the ENVI on the inclusion of amendments in its final position, foreseen for 10 July 2013. On 9 September 2013 the entire European Parliament will then vote on the final ENVI report. Although changes might still be proposed by political parties for the plenary vote, but usually there are not many at this stage of the procedure, and the adopted report of the plenary will be the position of the Parliament for negotiations with the Council [50].

The act could be adopted at first reading if the Council approves the final position of the Parliament and then come into effect in 2014, but there is still the risk that a delay can occur if it is not published by the middle of 2014, as there will be elections for a new European Parliament.

Once finalised, the Regulation shall enter into force twenty days after being published in the Official Journal of the European Union, after which there will be a 3-year transition period for all provisions of the new Regulation to be fully applicable. According to Article 97 of the MDR proposal, there will be different timelines for some particular provisions:

- Provisions becoming applicable **six months after entry into force** (i.e. six months and twenty days after publication in the OJ): in general, provisions on designation and supervision of notified bodies according to Chapter IV and provisions on the establishment of the Medical Device Coordination Group according to Article 78,
- Provisions becoming applicable **eighteen months after the date of application**: submission of information according to Part A of Annex V in EUDAMED by manufacturers, authorized representatives or importers, and submission of information on certificates by notified bodies according to Article 25 of the MDR proposal.

The Regulation will be binding and applicable in all Member States and EEA States.

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