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Safe innovation: On medical device legislation in Europe and Africa

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ABSTRACT

Objectives: The principal motivation for regulating medical devices is to protect patients and users. Complying with regulations may result in an increase in development, manufacturing and service costs for medical companies and ultimately for healthcare providers and patients, limiting the access to adequate medical equipment. On the other hand, poor regulatory control has resulted in the use of substandard devices. This study aims at comparing the certification route that manufactures have to respect for marketing a medical device in some African Countries and in European Union.

Methods: We examined and compared the current and future regulations on medical devices in the European Union and in some countries in Africa. Contextually we proposed future approaches to open design strategies supported by emerging technologies as a means to enhance economically sustainable healthcare system driven by innovation.

Results: African medical device regulations have an affinity to European directives, despite the fact that the latter are particularly strict. Several states have also implemented or harmonized directives to medical device regulation, or have expressed interest in establishing them in their legislation. Open Source Medical Devices hold a great promise to reduce costs but do need a high level of supervision, to control their quality and to guarantee their respect for safety standards.

Conclusion: Harmonization across the two continents could be leveraged to optimize the costs of device manufacture and sale. Regulated open design strategies can enhance economically sustainable innovation.

Introduction

A medical device can be described as any means of improving or monitoring patient health that acts on the body in a non-metabolic fashion. This wide definition includes electromedical equipment, implantable mechanical devices, diagnostic devices, and even everyday life objects such as band-aids and glasses [1].

Across the world, countries regulate the placement of such devices on the market through legislation that sets the responsibilities of the manufacturers by referring to technical requirements. Technical requirements are usually made available to the manufacturers as documented technical standards or norms. Those documents provide specifications, guidelines or characteristics, including testing methods and acceptance criteria, for the design and manufacturing of medical devices.

Medical device regulations vary greatly across the world, ranging from comprehensive to poor. Moreover, over the past two decades, the number, range, and complexity of medical devices has

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increased resulting in the proliferation of regulatory documents and procedures to encompass these changes. Coupled with this, the differences in regulations between countries oblige manufacturers to prepare a different dossier for each country, which constitutes a lengthy and costly process, leading to a disincentive to medical device companies to sell in some countries. They are also a deterrent to innovation and the development of new products. It has been estimated that developing a medical device from the idea to the market has a cost of around $31 million for a low-to moderate-risk device, and around $94 million for high-risk products [2].

The worldwide market for medical devices is increasing, but access to them varies according to the socio-economic and political status of each country [3]: around one million patients die every year due to the lack of adequate medical equipment [4,5]. Redressing this imbalance is a complex problem, which many African nations are trying to solve [6]. Promoting international standards and streamlining the regulatory process could reduce the legislative burden, lower costs and remove unnecessary delays to new products reaching patients in Africa.

In 1992, the European Union (EU), the United States of America (USA), Canada and Japan conceived the idea of an international partnership between medical device authorities and regulated industry. In 1993, the Global Harmonization Task Force (GHTF) was born with the goal of standardizing medical device regulations worldwide. The GHTF was disbanded in 2011 and the International Medical Device Regulators Forum (IMDRF) was conceived "as a forum to discuss future directions in medical device regulatory harmonization". The IMDRF, which includes medical device regulatory authorities of Australia, Brazil, Canada, China, EU, Japan, Russia, Singapore, South Korea, and USA, with the World Health Organization (WHO) as official observer, is currently developing internationally agreed upon documents related to a wide variety of topics affecting medical devices [7].

The path to harmonization is still far from completion; nevertheless, several African countries have oriented their regulatory processes for medical devices on the EU system. In this paper, after outlining the EU regulatory framework, we will analyse the regulatory landscape in a number of African countries in which at least a representative of the African Biomedical Engineering Consortium (ABEC, http://abec-africa.org) is present. The consortium was founded in 2012 with the mission of pursuing capacity building in Biomedical Engineering for sustaining local healthcare systems. To date ABEC is composed of 16 member institutions from 8 countries. Among these countries, we selected five from different geographical regions, for better describing differences and similarities with EU legislation.

Finally, we will suggest possible solutions for reducing the costs of developing safe, effective and quality medical devices for guaranteeing affordable and equitable healthcare for African citizens.

European regulation for medical devices

In order to place a medical device on the EU market, specific European Directives have to be met. The regulatory processes of medical devices are based on the Medical Device Directive (MDD), which consists of three core directives for safety regulations and marketing of medical devices: the Active Implantable Medical Device Directive (AIMDD 90/385/EEC), the Medical Device Directive (MDD 93/42/EEC) and the In Vitro Diagnostic Medical Device Directive (IVDMDD 98/79/EC) [8].

The new European Regulation was recently published [9]: this new Regulation (EU 2017/745) will substitute the current Directives after a 3 to 5 year transition period.

As proof of compliance to the strict safety requirements of the Directives, manufacturers have to apply a CE mark on their medical devices. The CE mark can be seen as a declaration of the manufacturer that the product is compliant to the relevant legislations including those related to safety. The CE marking consists of several processes that start from the manufacturer's choice of the conformity assessment route, which itself depends on the classification of the medical device [10]. It also addresses the evaluation of intrinsic risk and expected benefit. According to the intended use, length of time used, interaction with the human body and other technical characteristics, the device is considered more or less risky for the patient and therefore classified. By applying the classification rules of Annex IX of the MDD 93/42/EEC all medical devices are individually placed in one of four classes (Class I, IIa, IIb and III, with Class III as the highest risk class). In cases where a medical device or its features can be classified according to several rules, the highest possible class must be applied [11]. While the 4-level classification structure still holds, the new Regulation is even stricter as several new devices are now placed in the highest class (Class III) with respect to their old IIa or IIb positions.

Regardless of the class of the device, all medical devices must be compliant to the Essential Requirements of the directives, intended to enhance patient and user safety and improve device traceability throughout its useful life: some differences between current MDD and future Regulation also apply to the Essential Requirements in as much as a more precise definition has been applied. The core requirement on risk-benefit balance is unaltered but there are new detailed requests regarding validation, clinical proof of benefit and design for the intended user.

Currently MDDs in Europe are enforced by Notified Bodies (NBs), which are independent commercial organizations that provide auditing services for medical devices, and have the ability to issue the CE Mark. There are 50 active NBs in Europe [12], and companies are free to choose the NB amongst those designated to cover the particular class of device under review. After approval, post-market surveillance functions must be provided to the NB [13]. This approach is maintained by the new Regulation, although stricter rules for NBs may lead to a reduction in their numbers in the near future. For all classes, excluding Class I non-sterile devices, the manufacturer has to give proof to a NB that their product fulfils these requirements, e.g. by applying relevant standards. A list of harmonized standards is provided by the European Commission [14]. The new Regulation gives power to the Commission to harmonise standards from international organizations and also to issue Common Specifications where no standards are available. In case of a successful certification procedure, some countries also require that the manufacturer or authorised representative registers the device with the local National Regulatory Authority (NRA), a competent public agency that can enforce legislation. To better understand the Conformity Assessment Routes, Table 1 lists the applied Annexes, and the expected changes in the new Regulation.

Routes for CE marking

To better understand the necessary steps that lead to the assignation of the CE marking, four practical examples are described, each referring to different device class or subclass.

Considering class I Medical Devices, three CE Marking Routes are available as shown in the examples in Fig. 1:

- one for a Class I sterile Medical device (Class Is, e.g. a Personal Protection Kit);
- one for a Class I Medical Device with measuring function (Class Im, e.g. a sphygmomanometer);
- and another one for simple Class I Medical device, not sterile and without any measuring function (Class I, e.g. optical lenses and frame).

Table 1
Comparison between MDD 93/42/EEC and Regulation 2017/745. Note: EC type-examination is the procedure whereby a NB ascertains and certifies that a representative sample of the production fulfills the relevant provisions of this Directive.

	Directive 93/42/EEC	**Regulation 2017/745**
Class III	• Annex II (complete) • or EC TYPE-EXAMINATION (Annex III) and on the following: 1. Verification of conformity to type (Annex IV) 2. Production quality assurance (Annex V)	– Annex IX (complete) OR – Annex X (type) and Annex XI (Product conformity)
Class IIb (implantable)	• Annex II (without Section 4) • or EC TYPE-EXAMINATION (Annex III) and one of the following: 1. Verification of conformity (Annex IV) 2. Production quality assurance (Annex V) 3. Product quality assurance (Annex VI)	– Annex IX (complete) OR – Annex X (Type) and Annex XI (Product conformity)
Class IIb	• Annex II (without Section 4) • or EC TYPE-EXAMINATION (Annex III) + one of the following: 1. Verification of conformity (Annex IV) 2. Production quality assurance (Annex V) 3. Product quality assurance (Annex VI)	– Part of Annex IX (without chapter 2) OR – Annex X (Type) and Annex XI (Product conformity)
Class IIa	• Annex II (without Section 4) • or Declaration of conformity based on the Technical Documentation (Annex VII) + one of the following: 1. Verification of conformity (Annex IV) 2. Production quality assurance (Annex V) 3. Product quality assurance (Annex VI)	– Part of Annex IX (Chapter 2 per family) OR – Technical Documentation referred to Annex I and II + part of Annex XI
Class Is (Sterile)	Declaration of conformity based on the Technical Documentation (Annex VII) + (only for sterility) one of the procedures referred to Annex II, IV, V or VI	– Part of Annex IX (without chapter II) OR – Annex XI (Product conformity)
Class Im (measurement)	Declaration of conformity based on the Technical Documentation (Annex VII) + (only for sterility) one of the procedures referred to Annex II, IV, V or VI	– Part of Annex IX (without chapter II) OR – Annex XI (Product conformity)
Class I	Declaration of conformity based on the Technical Documentation (Annex VII)	Declaration according to Article 19 after drafting the documentation referred to Annex I and II
Custom	Annex VIII	Annex XIII

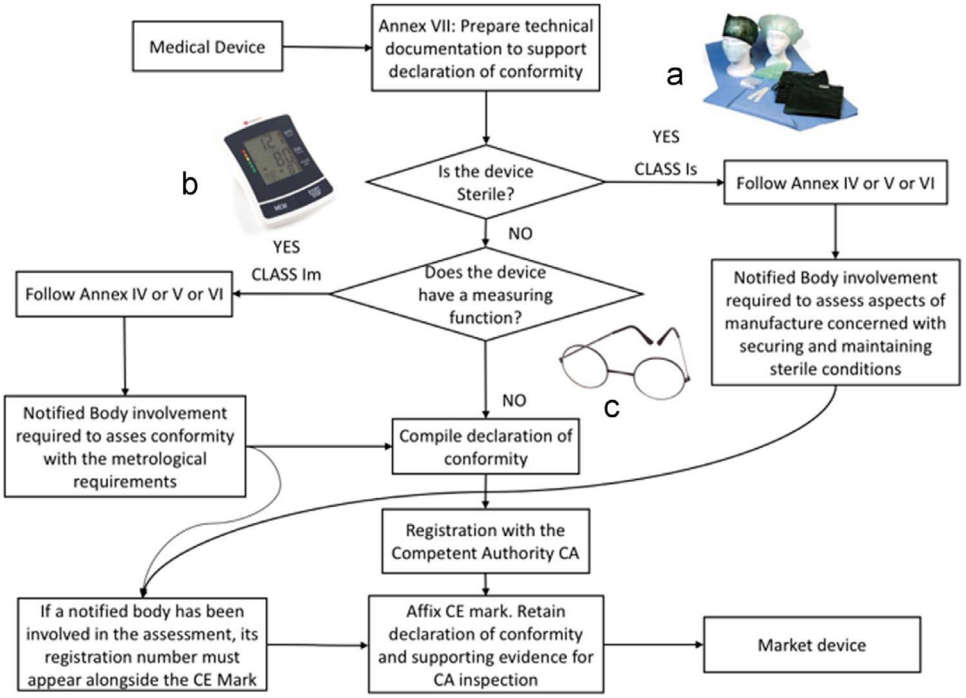

Fig. 1. Assessment procedure for a Class I Medical Device: (a) Personal Protection Kit, (b) Sphygmomanometer, (c) Optical lenses and frame. Adapted from [15].

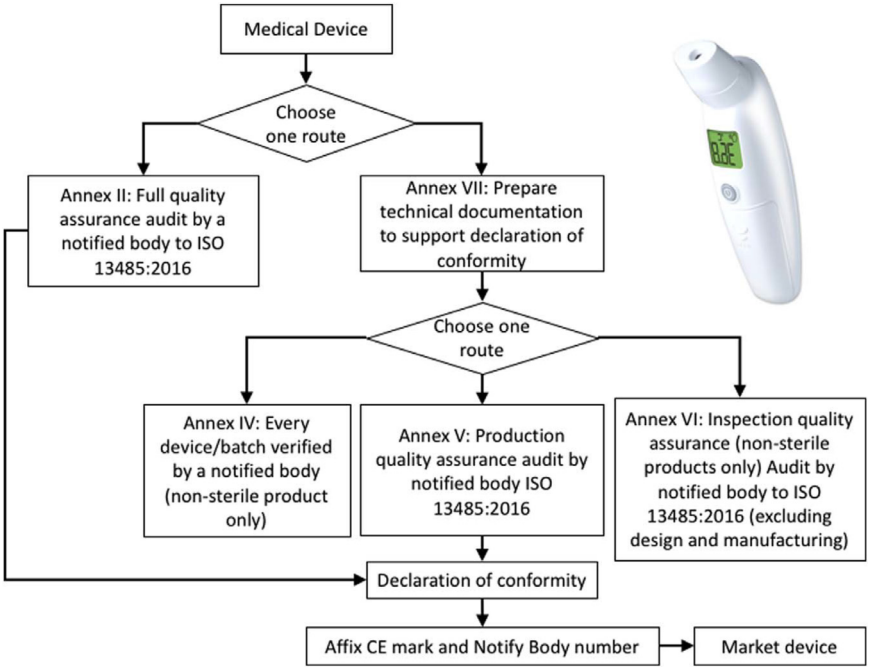

Fig. 2. Assessment procedure for a Class IIa Medical Device, e.g. a Contactless Thermometer. Adapted from [15].

For these devices the route is self-declaration or self-certification as described in Annex VII Module A, EC Declaration of Conformity. The manufacturer ensures and formally declares, via a written statement, that the products meet the applicable provisions of the MDD.

Fig. 2 shows an example of how a Class IIa contactless thermometer arrives on the market. The manufacturer declares conformity with the provisions of the MDD and Regulations (Annex VII) and ensures that the product complies with relevant essential requirements. However, for Class IIa products, this declaration must be backed up in all cases with conformity assessment by a NB using Annex II, IV, V or VI.

The defibrillator is classified as a Class IIb medical device – the assessment route to market is schematized in Fig. 3. Manufacturers of Class IIb devices may also choose the full quality assurance route (Annex II) including assessment of the technical documentation by a NB for at least one representative sample for each generic device group for compliance with the MDD (Annex II Section 7).

Class III includes high-risk devices and those awaiting a proper classification. A hip-joint implant is classified as a Class III medical device and the diagram in Fig. 4 illustrates its route-to-market. Permanent monitoring during the lifetime of high-risk devices is conducted by specialised institutions.

African regulation for medical devices

Brief overview of general situation

In 2005, the WHO performed a study on the presence of NRAs tasked with regulating and controlling medicines, vaccines, blood products and medicine devices in the 46 sub-Saharan African countries. Only 3 of these countries (corresponding to 7%) had an NRA in place, while 29 (63%) had minimal and 14 (30%) no regulations [16,17].

Table 2 lists the current state-of-the-art of medical device regulations in the 8 countries hosting ABEC members, considering the presence of NRAs, directives and laws, how medical devices are classified, the presence of a medical device nomenclature system as well as the existence of policy or guidelines on donated medical devices. All of them except Malawi, where no information is available, have an NRA to regulate and control medical devices.

The names of the NRAs indicate that they are also responsible for food and medicine control, as also happens in some EU countries (i.e. Spain) and in USA with the Food and Drug Administration (FDA), to cite some examples. The GHTF Risk Classification provides a four-tier system, with Class A representing lowest-hazard devices and Class D the highest-hazard device. The European and GHTF Classifications are essentially equivalent, both based on 4 classes: devices are assigned to a class according to their intrinsic potential harm to the patient, intended use and technology [18,19].

Table 2 indicates that ABEC countries orient their regulatory processes on the GHTF system. Furthermore, most of the ABEC countries have implemented or harmonized with European directives in their legislation. It should be noted that despite the fact that most ABEC member countries have already established a basis for medical device regulations, many of them still have limited capacities to do so. The limited capacities might include lack of investment and training to improve and maintain knowledge and skills of personnel [20,21].

African Regulation in five example countries

Describing Africa as a whole means merging a complex and fragmented continent, characterized by different levels of political stability and social situations from north to south, from east to west, into a single entity. This may lead to incomplete or too general descriptions. We illustrate the regulatory landscape in 5 countries with ABEC members in different geographic regions in Africa.

Egypt – North Africa

The Egyptian Ministry of Health (MOH) is responsible for the standardization and coordination of the registration, approval, importation and manufacturing of medical devices [22]. The MOH does this through the Drug Policy and Planning Center (DPPC) and the Central Administration of Pharmaceutical Affairs. The DPPC controls and sets the strategic rules for drug policy but it also regulates the importation and manufacture of medical devices and in-

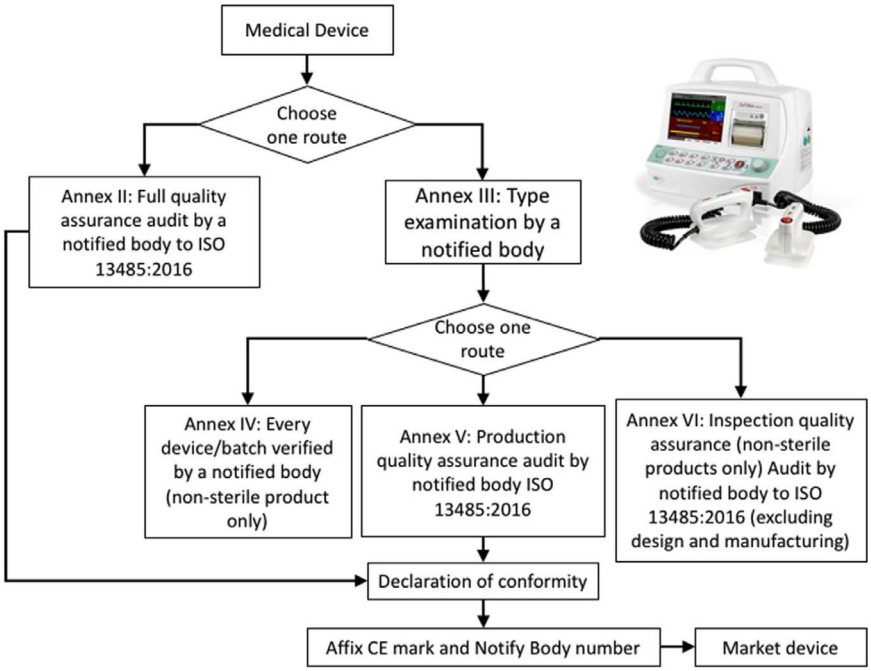

Fig. 3. Assessment procedure for a Class IIb Medical Device, e.g. a defibrillator. Adapted from [15].

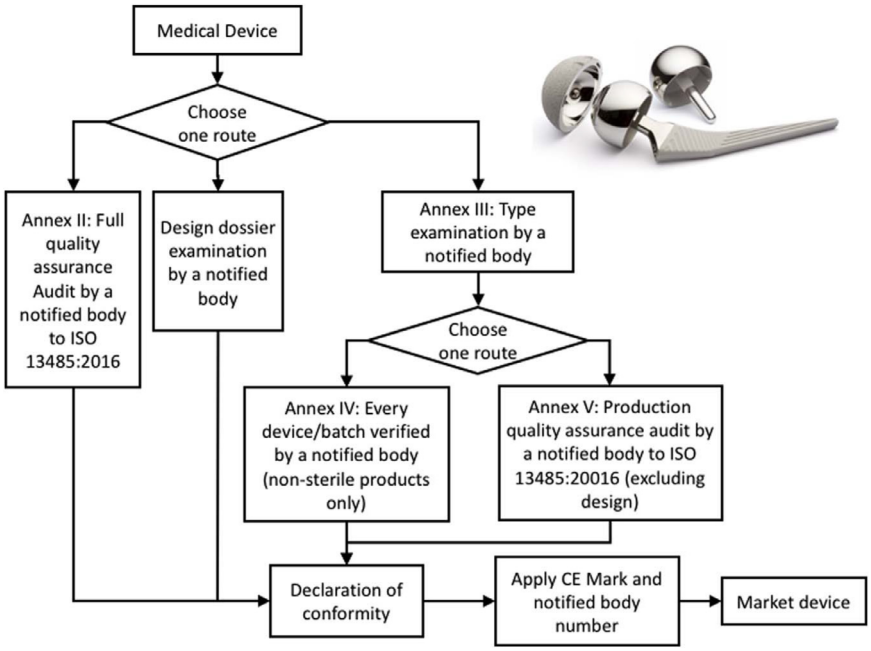

Fig. 4. Assessment procedure for a Class III Medical Device, e.g. an hip-joint implant. Adapted from [15].

struments. It controls the registration of medical devices through a Specialized Committee for Study of Manufactured and Imported Medical Devices and Equipment [23]. As Table 2 shows, Egypt has adopted the definition and classification of Medical Devices according to the European MDD 93/42/EEC. A free sale certificate, and CE Mark or FDA Approval is required to commercialize the medical device in the country. It is important to note that locally manufactured products must also be clearly labelled as such.

Uganda – East Africa

The Ugandan government was able to set up different bodies that are responsible for the regulation of medical devices that, however, present severe limitations [20]. These government agencies have the control on the use and sale of medical devices and ensures that medical devices commercialized within the country's jurisdiction are complaint to international standards. When a device is manufactured in Uganda, the manufacturer must apply for Institutional Review Board clearance before starting clinical testing. This process will usually pass through the medical school at Makerere University or directly at the hospital of choice. Manufacturers must also apply to the National Drug Authority to approve use of the device and the Uganda National Council for Science and Technology for additional ethical clearance. For selling the device, the minimum international standards for medical devices must be obtained, as Uganda does not have local medical device standards. The Uganda National Bureau of Standards (UNBS) does not have

Table 2
Overview on medical devices regulation in ABEC countries.

ABEC Country	National Regulatory Authority	Directives/Laws	Classification of Medical Device	Medical Device nomenclature System	Policy or Guidelines on Donated medical device
Northern Africa					
Egypt	Egyptian Drug Authority (EDA)	93/42/EEC 2007/47/EC	I, IIa, IIb, III	No	Yes
Southern Africa					
South Africa	Department of Health, South Africa Medicines control council (MCC)	No. 101/1965 No. 14/2015 No. 15/1973	A, B, C, D	No	Yes
Western Africa					
Nigeria	National Agency for Food and Drug Administration and Control (NAFDAC)	Cap N1 L.F.N 2004	Compliance to Classification of the country where the device is manufactured	No	Yes
Eastern Africa					
Ethiopia	Food Medicine and Healthcare Administration and Control Authority of Ethiopia (FMHACA)	No. 661/2009 No. 12/2013 No. 9/2012	I, II, III, IV	Nationally developed	Yes
Malawi	No	No info	No info	No	Yes
Uganda	National Drug Authority	Chapter 206_2000	No info	Nationally developed	Yes
Tanzania	Tanzania Food and Drugs Authority (TFDA)	No. 1_2003	A, B, C, D	Based on GMDN	Yes
Kenya	Pharmacy and Poisons Board	Chapter 244_2002	A, B, C, D	Nationally developed	Yes

the laboratory capacity to test the safety and performance of a number of medical devices. Thus two routes must be taken if a device is manufactured outside of the country and a seller would like to market in Uganda:

1. Product Certification - This process requires an assessment of the process of production/manufacturing and testing of the final integrated product. It will be checked for consistency and quality and it will be bench-marked based on the applicable ISO standards (see further in the text) evaluating where the device is manufactured and where clinical trials were performed.
2. Pre-Shipment Verification of Conformity (PVoC) - This certification involves an assessment on whether the medical device complies with the applicable relevant ISO standards through testing, quality assessment and an inspection of a number of sampled devices intending to be exported. A certificate of conformity is issued upon a successful assessment of the examined batch. This process is carried out by pre-shipment agents: in this case, the UNBS entrusts the Société Générale de Surveillance (SGS), the Bureau Veritas and the Intertek International Ltd. This second route is faster.

Kenya – East Africa

Medical device regulation has been a point of contention in Kenya for a while, where different bodies are given the authority for different aspects. Until recently, the Pharmacy and Poisons Board has been implementing and enforcing some aspects of medical device regulations based on a 2002 act of parliament. The Board is responsible for registration of medical devices that enter the market. The Board does not have its own guidelines but adopts those of the GHTF, European MDD 93/42/EEC, AIMDD 90/385/EEC and IVDMDD 98/79/EC, and the US FDA and Australia Therapeutics Goods Act [24]. A new Health Bill is pending and all regulatory bodies have been put on hold. Under the new Health Bill, the Ministry of Health will ultimately be the main regulatory body. The Bill will allow for a unified health system that should coordinate the inter-relationship between the National Government and County Government Health Systems. Moreover, the Bill is to provide for the regulation of health care services and service providers, health products and technologies and for connected purposes, in addition to establishing a single regulatory body for regulation of health products and health technologies. This regulatory body will oversee the licensing of health products and technologies, and the licensing of manufacturers and distributors of health products. It will also regulate contractors for medical devices and physical security for products including radioactive material and biological weapons. Article 31 of the proposed Health Bill looks at the procurement of health products and technologies, which will be undertaken in line with the Public Procurement and Disposal Act [25].

Nigeria – West Africa

The National Agency for Food and Drug Administration and Control (NAFDAC) regulates food and drug products in Nigeria [26]. No medical device can be manufactured, imported, exported, advertised, sold or distributed in Nigeria unless it has been registered in accordance with the provisions of ACT CAP F33 LFN 2004 (Formerly decree 19 of 1993) and the accompanying guidelines. The Standard Organization of Nigeria is responsible for compliance with equipment specification and import standards. Importers of drug products and medical devices must first register them with NAFDAC prior to import. In the case of imported products, the manufacturer must show evidence that they are licensed to pro-

duce medical devices for sale in the country of origin (Certificate of Manufacturer and Free Sale). Such evidence must be issued by the Competent Authority of the country of manufacture, and has to be authenticated by the Nigerian Embassy in that country. In countries where no Nigerian Embassy or High Commission exists, any other Embassy or High Commission of any Commonwealth or West African country can authenticate.

South Africa – Southern Africa

South Africa does not have a comprehensive regulatory framework governing medical devices. However, the market is very sophisticated and it is strongly advisable that the product be FDA approved or even better, carry the CE mark. At present, only electronic products (also known as electromagnetic medical devices or radiation emitting devices) must be registered before they can be sold, leased, used, operated, or applied in South Africa [27,28]. These devices must be registered with the Department of Health, and must have the CE mark. FDA approved electro-medical products without the CE mark are not accepted [28]. The registration of medical devices in South Africa is governed by the provisions and requirements of the Medicines and Related Substances Control Act No. 101 of 1965, and the Regulations and Guidelines published in terms thereof. Compliance with local and international Medical Device Standards and Conformity Assessment Standards can be used to demonstrate compliance with the medical device legislative requirements. The use of these standards is not mandatory, but it is a way to establish compliance with the regulatory requirements. The legislative framework adopts the IMDRF philosophy, and for this reason it adopted the Risk Classification System formulated by the GHTF. The Medicines Control Council is a statutory body that is appointed by the Minister of Health for ensuring that all products that are sold and used in South Africa are safe, therapeutically effective and consistently meet acceptable standards of quality.

Sustainable innovations in the medical device field

Access to new products in Africa can be delayed, sometimes for years, due to complex and costly requirements for regulatory approval in some countries. In order to enable innovations in Africa and in other countries with an immature regulatory system while ensuring a high level of patient protection, as well as giving voice to the citizens and their needs, including those associated with rare diseases, possible alternatives have to be explored. We propose that “Open Source Medical Devices” (OSMDs), designed following collaborative strategies, may help to reduce costs for developing medical devices, respecting the formal regulatory processes, while maintaining at least the same safety levels as European devices.

Creating an OSMD means developing a medical device by sharing ideas and concepts, design files, documentation, source-code, blueprints and prototypes, testing results and all collected data, with other professional medical device designers. Advantages of the open procedure are its accessibility, sustainability, lower costs and, under ideal conditions, improved performance and safety because everyone can review the design dossier [29].

While a couple of years ago, the development of biomedical devices was essentially linked to companies and universities, now several examples of OSMDs have appeared on the web [30], on-line communities share good practices [31], but seldom these medical devices are designed to be compliant with safety standards [32]. Thus, OSMDs are often not yet accurate or safe enough to be used as part of the mainstream clinical routines.

This is mainly due to the fact that the open movement prizes innovation, creativity and ingenuity more than compliance to rules and standards, which are not often fully known and valued, and should be considered from the beginning of the development process. Nonetheless, OSMDs hold great promise because today, thanks to the crowd-thinking and crowd-sourcing paradigms, the design of open products has an intrinsic revision process, driven by a virtual community, composed of a heterogeneous and large population, which has become an active player in the entire process of conception to production [33]. However, biomedical devices do need a high level of supervision, to control their quality and to guarantee their respect for safety standards.

To promote OSMDs and to boost innovation across the EU and Africa, UBORA, a project funded by the EU, aims at developing a Europe-Africa e-infrastructure for open-source co-design of new solutions to face the current and future healthcare challenges of both continents (http://ubora-biomedical.org). According to the project vision, exploiting new ideas and sharing of safety criteria and performance data can be an innovative solution to improve the current state of healthcare in Africa. Examples of biomedical devices under development within UBORA include: coolers for vaccines, systems for the sterilization of surgical instruments, incubators for premature babies, breast pumps with cooling and preservation systems, 4D printed splints (3D printed and then personally modified to suit patients), polymeric devices for treating clubfoot, CPAP devices, preventive methods for malaria [34].

The UBORA platform enables a peer-to-peer evaluation and expert mentorship from Academia and Industry, before submitting the documentation to a NB, for the formal certification route. This double check of the design might then lead to safer medical products because both a large community and a regulatory authority are performing the evaluation.

The projects available for downloading in the UBORA e-infrastructure will be safe and compliant to standards, but will not be defined as a “product”, since manufacturing will require further certification; however production and marketing will be greatly facilitated. An example of this process is the Gamma Cardio electrocardiograph [35], an open source, certified medical device project, which can be placed on the market only by manufacturers who have obtained the certification: each new manufacturer must implement repeatable and approved manufacturing and control procedures and get its own certification.

Standards from the International Standard Organization (ISO) and the International Electrotechnical Commission (IEC) constitute the state of the art, are very widespread and have proven to ensure a minimum satisfactory level of patient safety. For this reason, they probably provide the most preferable reference documents for designing safe medical devices. It can be argued that standards can also be produced and distributed as “open” in the medical device field. The definition of open standards has been widely discussed in the software field [36], with an influential position taken by World Wide Web Consortium, which can be seen as a model for open standards [37].

At present ISO and IEC Standards require a small copyright fee (limiting availability) and their development does not therefore respect the openness requirement. Their widespread use prevents the fragmented development of products that do not work properly with each other and discourages the appearance of new ‘branches’ within old products. The absence of medical device industries in African countries cannot be attributed to the limited access to these standards or to their fees. In fact, relevant standards, such as ISO 13485:2016 Medical devices - Quality management systems - Requirements for regulatory purposes, which addresses the specific needs for quality management systems for organizations in the medical devices industry, costs less than 100€, but their implementation costs are at least three orders of magnitude larger.

Emerging technologies and related standardization challenges

Several emerging technologies are synergic with open source strategies and can facilitate the emergence of a sustainable medical industry and a more socially-responsible way of innovating medical technologies. Additive manufacturing technologies (AMTs) and smartphones and mobile technologies have been successfully applied in the medical field [38,39], however, regulation-related challenges still exist for adequately (and safely) exploiting all their potentials.

For instance, surgical training, diagnostic models, personalized smart prostheses for soft and hard tissue repair and ad hoc ergonomic appliances are already well-established biomedical applications of AMTs [40]. Furthermore, in recent years, in parallel with the expiry of several patents from pioneering companies of the AMTs sector, these technologies are undergoing a "democratization" process and open hardware approaches have reshaped this field, leading to collaborative design environments (e.g. the RepRap wiki, http://reprap.org) and to the development of low-cost AMTs. In turn, this has led to the worldwide expansion of "fab-labs" or digital fabrication laboratories, which support inventors and designers in prototyping and sometimes in manufacturing the final products. These networks of laboratories, if adequately organized, can constitute a powerful tool for promoting a delocalized production of medical devices and for bringing richness to remote regions, helping to shift from mass-production of medical devices to mass-personalization [41]. The teaching-learning implications of these fab-labs, for training a cohort of responsible biomedical engineers worldwide, capable of mentoring (together with medical professionals) the required innovations for the successful future of an open source biomedical industry [42], are also noteworthy. If fab-labs are to provide new alternatives for managing the supply chain and supporting open source biomedical products, or if the hospitals of the future are to count on advanced engineering laboratories for promoting personalized manufacture of medical devices, several regulatory questions arise. Medical device classification does not change if the device is manufactured using traditional methods or AMTs. Rethinking Annex VIII of the MDD with specific guidelines to take into account the relevance of these technological resources will facilitate their custom application to patients, while guaranteeing safety. For instance, an option for promoting AMTs and fab-labs and their synergies with open medical devices is to shift from product-based to a material- and process-based regulation, as it is already happening in the dental sector [43]. For instance, we can cite the recently developed FDA Technical Considerations for Additive Manufactured Medical Devices [44]. The document provides non-binding recommendations for fulfilling current FDA regulations when using these innovative techniques for the development of medical devices. Among the proposed actions, the document gives guidance for: design and manufacturing procedures, both for general and for personalized devices, software-related processes, performing material controls, post-processing steps, final device testing and validation, overall secure data management, labelling and even eco-impact assessment. We envision a similar orientation but with an extended approach, so as to provide an adequate regulatory environment for medical devices developed in a personalized way, taking advantage of open-source approaches and involving global communities of collaborators and manufacturers. Besides, the components, materials and processes should be traceable, for which the use of collaborative development frameworks (such as the Ubora e-infrastructure) may be useful.

Smartphone based medical applications can be simple "apps" advising users to adopt healthier life styles, mainly relying on counting steps and allowing users to introduce information about their calorie intake. More complex "apps" for diagnostic and therapeutic monitoring make use of the smartphone's sensing elements (camera, accelerometers, microphone…), or may, in some cases, be supported by external sensing-actuating kits. They can help users and medical professionals to perform more complex medical tasks [45].

The more complex combinations of smartphones, software and supporting kits, are considered medical devices. Some of these apps may even reach Class III and must comply with available regulations before they are used [46].

The FDA seems to have taken the lead in the regulation of mobile health technologies and of the medical applications of smartphones in general [47], while the EU's new Regulation on Medical Devices plays much attention to medical device software (SW). The harmonized standard IEC 62304 defines restrictive rules on the SW life cycle, for ensuring safety requirements.

Open hardware approaches and the capabilities of mobile technologies, especially of smartphones, can open new horizons in the biomedical field as well as promoting quality healthcare for all. Both Europe, with a user penetration of smartphones already beyond the 64% in 2017 [48], and Africa, with an expected user penetration of mobile phones up to a 76% in 2020 [49], can greatly benefit from the use of medical apps and mobile health technologies for addressing global health issues.

Conclusion

Access to safe biomedical devices ensures equitable healthcare for all and is guaranteed by regulations. However, implementing regulations and complying with them places an economic burden on developers, manufacturers and researchers. In developing countries, poor regulatory control results in the use of substandard devices, and often it becomes a constraint for those wanting to produce, sell, or even donate these devices. Our findings show that African medical device regulations have an affinity to European directives, despite the fact that they are particularly strict. It was observed that most ABEC countries already have a NRA in place to control and medical devices. Most of these states have also implemented or harmonized directives to medical device regulation, or have expressed interest in establishing them in their legislation. Nevertheless they need adequately trained biomedical engineers for consultation, and ABEC was formed in recognition of this need.

As reported in Fig. 5, harmonizing regulations leads to multiple benefits. Regulatory authorities will benefit in terms of improved expertise, collaboration with other regulatory authorities and operational efficiency through sharing of information and recognition of established regulatory authority decisions. Healthcare professionals will benefit through the availability of more treatment options in order to optimise patient management. The biomedical industry will benefit through the access to new markets and the improved ability to comply with regulatory requirements related to devices registration. Patients will benefit through improved supply of devices, access to high quality devices that comply with strict requirements of safety, quality and efficacy and reduced risk of use of unsafe devices. Supranational initiatives, such as the International Medical Device Regulators Forum are currently developing internationally agreed upon documents to facilitate the harmonization of affecting medical devices.

In addition to harmonization, to further save costs and maintain a higher safety level, OSMD might be an option, but they still need certification to be placed on the market. Projects, such as UBORA, are trying to convey the strength of this approach providing a framework to design projects which respect safety standards. They can also be used as a teaching tool for capacity building of future biomedical engineers.

This paper ends with a call to WHO and to all other supranational organizations that are stakeholders in human health and

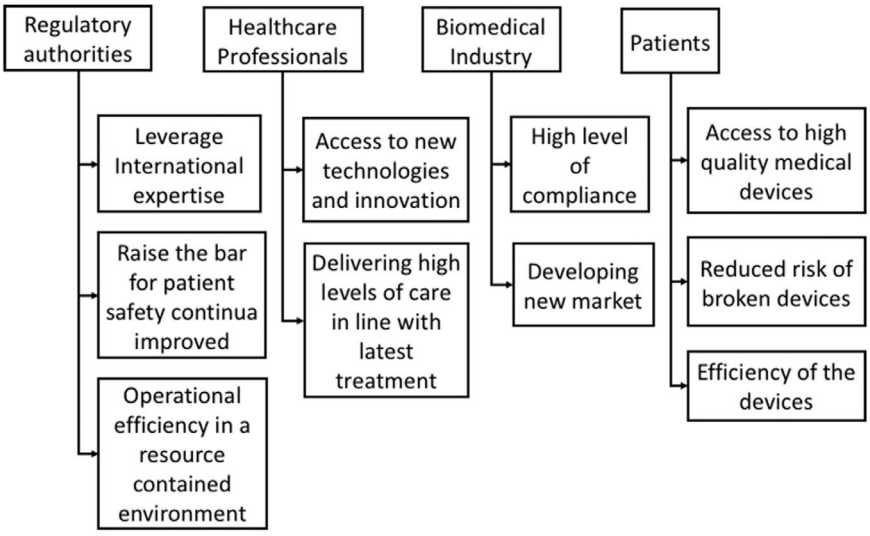

Fig. 5. Impacts of harmonization.

human health improvement, as well to as Standard Development Organizations to provide support, means and expertise to OSMD design for developing economically sustainable, safe and effective healthcare technology.

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Competing interests

Authors have no conflict of interest to declare.

Ethical approval

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