

The need for transparency of clinical evidence for medical devices in Europe

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To use medical devices rationally, health-care professionals must base their choices of which devices to recommend for individual patients on an objective appraisal of their safety and clinical efficacy. The evidence submitted by manufacturers when seeking approval of their high-risk devices must be publicly available, including technical performance and premarket clinical studies. Giving physicians access to this information supplements the peer-reviewed scientific literature and might be essential for comparing alternative devices within any class. Interested patients should be encouraged to review the evidence for any device that has been recommended for them. The new EU law on medical devices states that the manufacturer is to prepare a summary of the evidence for any implantable or high-risk device. Defining its content, however, has been delegated to implementing legislation, which is now being considered. From a clinical perspective, it is imperative that all evidence reviewed by notified bodies and regulatory authorities is disclosed—with the exception, if justified, only of technical specifications that are considered confidential or manufacturing details that are protected as intellectual property—and public access to this evidence must be guaranteed by EU law. From ethical and other perspectives, there are no grounds for less clinical evidence being available to health-care professionals about the medical devices that they use than is already available for new pharmaceutical products. Full transparency is needed; without it, informed decisions relating to the use of new medical devices will remain impossible.

Introduction

The new EU law (Regulation)¹ on medical devices of April 5, 2017, declares at Recital 43 that adequate access to information is essential to enable health-care professionals to make informed decisions. It further provides that the manufacturer should summarise “the main safety and performance aspects of the device and the outcome of the clinical evaluation” (Recital 48), but it restricts this requirement to implantable and class III (high-risk) medical devices.

A key objective of the regulatory reforms is to promote higher levels of evidence before high-risk medical devices are approved in Europe (Recitals 1 and 4). In the past, many devices were authorised without being supported by pivotal clinical trials. Standards of clinical practice relating to medical devices will not improve until detailed clinical evidence is reported publicly.

We review how little evidence has been available concerning the approval of medical devices in Europe when compared with new pharmaceuticals in Europe, and with the approval of medical devices in the USA. We summarise European legislation on access to documents (and thus to freedom of information) and we test the provisions of the Regulation against the need to inform health-care professionals and patients. Finally, we describe what information should be available in the public domain and easily accessible for any new medical device, and we advocate that this information be specified in further legislation.

The need for transparency

All medical researchers have an ethical duty to publish and to disseminate the results of their clinical research. The Declaration of Helsinki² states at paragraphs 35 and 36 that every study involving human participants must be registered in a publicly accessible database,

and that negative and inconclusive as well as positive results must be published or otherwise made publicly available. The EU medical device Directives,³ which have been replaced by the new Regulation, required that “clinical investigations must be carried out in accordance with the Helsinki Declaration” (Annex II, Article 10 c). They also provided, however, that apart from a few exceptions “all the Parties involved in the application of this Directive are bound to observe confidentiality with regard to all information obtained in carrying out their tasks” (Article 20), and concerning clinical evaluation that “all the data must remain confidential” (Annex X).⁴ These provisions were mutually incompatible and contradictory; their net result has been that in Europe no details of the regulatory review of clinical evidence relating to medical devices have been disclosed.

Failure to publish an adequate account of a well-designed clinical trial has been described as a form of scientific misconduct,⁵ yet studies of medical devices are not always reported. Only 13% of 13 327 trials registered at ClinicalTrials.gov and completed between 2008 and 2012, 79% of which concerned drugs and 11% devices, reported their summary results within 12 months after completion.⁶ That is the time limit established by WHO, which described the registration and reporting of clinical trials as a moral responsibility.^{7,8} Only 49% of 177 studies of new cardiovascular devices had been published up to 7 years after their completion.⁹ Publication of a trial for every high-risk device would go a long way towards satisfying the needs of physicians and patients for information about its safety and efficacy, but new medical devices have often been approved before trials have been published⁹ and iterative changes to their design or manufacture have often been accepted without the submission of new clinical evidence.¹⁰

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Panel 1: Information available from the EMA and FDA

EMA for pharmaceutical products

- Trials registered in the EU Clinical Trials Database (EudraCT)
- Summary of product characteristics*
- European Public Assessment Report (EPAR), from the Committee for Medicinal Products for Human Use*
- Divergent expert opinion, published as appendix to EPAR*
- Committee for Medicinal Products for Human Use summary of opinion*
- Conditions of the marketing authorisation*
- European public assessment report summary for the public*
- Summary of the risk management plan*
- Procedural steps taken and scientific information after the authorisation*
- Periodic safety update report single assessments
- Clinical data published at EMA website

Center for Devices and Radiological Health, FDA for medical devices

- Links to relevant trials, all required to be registered at ClinicalTrials.gov†
- Definition and classification of the device†
- List of devices with same product code†
- Summary of safety and effectiveness data, including biocompatibility tests, animal studies, materials and durability testing, with list of relevant standards, and the results of clinical studies with references to their related publications†
- Labelling information including detailed instructions for use†
- Response to premarket approval application, including instructions for conducting postapproval studies†
- Record of all supplementary approvals†
- Medical device recall (for modification of the delivery system)†
- Postapproval studies progress report†
- Postmarket surveillance database²¹

EMA=European Medicines Agency. FDA=US Food and Drug Administration. *Information available from the EMA website confirmed with the use of the example of sacubitril/valsartan (Entresto, Neparvis), initial authorisation Sept 24, 2015.²² †Information available assessed with the use of the example of the Mitraclip device.²³

For more on EudraCT see
<https://eudract.ema.europa.eu/>

For more on EMA see
<https://clinicaldata.ema.europa.eu/>

For more on ClinicalTrials.gov
see <https://clinicaltrials.gov>

In the USA, the US Food and Drug Administration (FDA) website provides a wealth of data about any new high-risk device (panel 1). No evidence suggests that this policy has hindered innovation by industry. Public access to FDA documents has enabled investigators to report that only 31% of 78 premarket approvals of new cardiovascular devices were supported by evidence from more than one randomised controlled trial.¹⁴ Scientific evidence to support the claim of equivalence was publicly available for only 16% of 50 new implantable devices that had been approved on that basis, and for only 3% of their 1105 listed predicate devices.¹⁵ No clinical results had been published for 49% of 92 postapproval studies that had been mandated and completed.¹⁶

Similar studies to assess the EU regulatory system are impossible to do because no central source of information about medical devices exists and information about premarket clinical trials is scarce. A study of field safety notices and medical device alerts¹⁷ and another of the chain of approvals of transvaginal meshes on the basis of equivalence¹⁸ were possible only with the use of data from the FDA website. Clinicians can have difficulty in obtaining sufficient information to understand the

scientific basis for the approval of a medical device (for example, see panel 2). The lack of “even a basic level of transparency” has been judged to be “unacceptable”²³ and suggested to be a major deficiency of the EU medical device directives.²⁴ Access to information about clinical trials has been described as a fundamental component of the right to health, and failure to disclose all trial data as expropriation of the data donated by participants in studies.²⁵

Some cardiovascular devices that had insufficient clinical evaluation before being approved were then associated with serious clinical complications.²⁶ In a well-known case predating current EU legislation, the manufacturer of a heart valve failed to disclose all the data concerning fractures that had been accumulated during laboratory testing;²⁷ later a supervisory panel concluded that comprehensive registries and clear channels for communication with physicians and patients were needed.²⁸ In 2005, delayed disclosure of a risk of battery depletion in a particular model of implantable cardioverter defibrillator was implicated in deaths that might have been avoided,²⁹ and in 2008 delayed reporting of lead fractures was associated with inappropriate shocks.³⁰

Adverse consequences of the paucity of public information about medical devices have been highlighted in many contexts. The European Clinical Research Infrastructure Network concluded that lack of transparency of protocols and results from earlier studies and the limited availability of trial data for secondary analyses are major barriers to doing appropriate randomised trials of medical devices.³¹ In surgery, potential problems concerning the safety or efficacy of approved devices are concealed by the lack of transparency, which means that surgeons cannot make informed choices between different devices; this has contributed to “unstructured, heterogeneous and erroneous innovation”.³² It has been considered to increase the risk of inappropriate remote monitoring of smart medical devices.³³ The lack of transparency of registries of high-risk medical devices has been criticised.³⁴ The European Patients Forum has stressed that patients need access to high-quality information about medical devices³⁵ and others have called for the evidence leading to approval and Conformité Européenne (CE) marking to be publicly available, irrespective of the risk class of the device.³⁶

The EU legal framework

Access to documents (freedom of information)

The right of access to documents in the possession of the EU is provided by Regulation 1049/2001³⁷ and by Article 42 of the EU Charter of Fundamental Rights.³⁸ All EU institutions and all agencies established by the institutions are required to make documents directly accessible to the greatest possible extent.

The European system of standardisation or certification bodies was developed in an EU Council Resolution in

Panel 2: Anticoagulation in a patient with an On-X heart valve

Concern

A 51-year-old woman was anticoagulated with warfarin for prophylaxis of thromboembolism after aortic valve replacement with an On-X mechanical valve. 5 months later she had an embolic stroke, a few days after her international normalised ratio (INR) had been 1.9.

The manufacturer had announced approval and Conformité Européenne (CE) marking for use of its valve in the EU (but at that time not in the USA) with a reduced target range for the INR of 1.5-2.¹⁹ The clinicians wanted to understand the basis for this approval to advise the patient.

Request for information

- The packaging of the On-X valve indicates (adjacent to the CE mark) that it was approved by Notified Body 0459.
- The database of notified bodies²⁰ indicates that 0459 is the Laboratoire national d'essais (G-MED) in France.
- A notified body does not disclose the basis for its decisions to individual physicians.
- The competent authority for notified bodies in France is the Agence Nationale de Sécurité du Médicament et des Produits de Santé (ANSM).
- Two cardiac surgeons reported this event to the Medicines and Healthcare Products Regulatory Authority (MHRA) in the UK. The MHRA contacted ANSM, which contacted G-MED.

- The response received from ANSM was that the approval was appropriate; the MHRA were not permitted to disclose any details.

Presumed basis for the regulatory approval

The basis for the approval was presumed to be the interim results of the PROACT study,²¹ which was done in the USA under an investigational device exemption from the FDA. In the study, patients were excluded if they had any evidence of a prothrombotic tendency and they were eligible only if urinary thromboxane measurements confirmed that they responded normally to aspirin, which was given daily together with warfarin. During the study, the INR was adjusted by home monitoring on average once every 9 days. These vital qualifications for the safe use of reduced anticoagulation were not mentioned in the advertising, and they had not been followed or prescribed in this case. Later, the new anticoagulant target range was the subject of a supplementary approval by the FDA, when the details were disclosed.²²

It is not suggested that the revised CE marking caused the patient's stroke. This case summary is reported merely to illustrate the current difficulties in finding enough relevant information.

1985, as a general response to a perceived need for more harmonisation of standards in all industrial sectors.³⁹ These "notified bodies" are independent commercial profit-making entities that have been delegated by their national competent authorities to assess if products meet EU standards. When the European Economic Community (as it then was) first developed legislation for medical devices in the early 1990s, it adopted the same system. Under the new medical device regulations, the assessment of applications for approval of new devices will remain the responsibility of notified bodies. Although the responsibilities of these independent companies are governed, constrained, and defined in great detail by EU legislation, they are outside the scope of the access rules. The transparency of notified bodies is important not only for clinical reasons but also because they might be vulnerable to conflict of interest with industry.⁴⁰

Transparency of clinical evidence for drugs

The European Medicines Agency (EMA), as an official body of the EU, is bound by the legislation on citizens' rights of access to documents; its policy is to ensure availability to the public of regulatory, scientific, and technical information concerning the authorisation or supervision of medicinal products.⁴¹ This policy was reinforced by Article 81 of the Clinical Trials Regulation of 2014 (to be implemented from 2019), which provides for a

publicly accessible database containing all relevant information about clinical trials submitted through the EU portal, presented in an easily searchable format. The details include the EU trial number, the summary, the layperson's summary, the protocol, the clinical study report, and links to data from other clinical trials, which used the same investigational medicinal product (Annex IV).⁴² Since 2016, the EMA has also implemented an open-access policy for trial databases.⁴³ Much information is now available on any new drug that has been approved (panel 1).

The EU Clinical Trials Regulation does not apply to trials of medical devices.

Medical Device Regulation 2017/745

Under Article 32 of Regulation 2017/745, manufacturers of implantable and high-risk (class III) medical devices must prepare a summary of safety and clinical performance (SSCP) for their device, which is to be publicly available at the EU database on medical devices (Eudamed).¹ The regulation specifies a minimum list of contents and states that the exact form and presentation of the data elements of the SSCP should be defined by an advisory procedure, with the option of an implementing legislative act (Recital 92). A European database will ensure that every clinical investigation is recorded and reported and that a clinical investigation report will be publicly available

(Article 77.7), but this provision applies only to every trial that has been done in the EU. These documents should include “adequate” details to enable informed decisions.

Article 168 of the Treaty on the Functioning of the EU provides that a “high level of human health protection shall be ensured in the definition and implementation of all Union policies and activities”. The EMA aims to protect and foster public health, and the Court of Justice of the EU has held that Article 168 of the treaty provides that a high level of health protection must be “guaranteed”.⁴⁴ If a high level of health protection cannot be guaranteed relating to a given medical device unless evidence concerning its safety, performance, and effectiveness is fully disclosed, then it follows that the publicly available documents should contain all the evidence from clinical investigations.

The clinical evaluation assessment report (Annex IX, Chapter 2, Article 5.1), which is prepared by the notified body, will be accessible in Eudamed, but it and other documents—such as reports of vigilance and postmarket follow-up, and the database of device alerts and field safety corrective actions—are intended for review only by regulators. Since Eudamed will be maintained by the European Commission, its contents will be governed by the EU access rules, although that is not stated explicitly. Instead, Regulation 2017/745 limits transparency by defining limited access or stressing the need for confidentiality, particularly in Articles 12, 73, 92, and 109, and in Annex VII at paragraphs 1.3.1, 2.4, and 3.4.2. Conversely, EMA policy is that disclosure in the public interest always trumps any argument for confidentiality. Three judgments of the General Court of the EU of Feb 5, 2018, dealing with access to market authorisation (MA) data, confirm that EMA policy is supported by the EU rules on transparency in general and by the EU access rules in particular.⁴⁵ These verdicts are not only of relevance to the EMA but also extend by analogy to the tension between transparency and confidentiality in the context of medical devices.

The judgments can be summarised in three points. First, all three rule that there is no presumption in favour of confidentiality for clinical studies,^{46–48} meaning that the burden of establishing the confidentiality of any document, or of information contained in it, lies with the person claiming confidentiality. Second, all three judgments rule that the public nature of a European Public Assessment Report (EPAR) does not mean that information not published in any EPAR is confidential. Third, the judgment in Case T-235/15 (the longest of the judgments) rules that the information contained in an EPAR “cannot in itself satisfy the requirement of transparency laid down in Regulation No 1049/2001. In the field of medicinal products, that requirement of transparency is justified by the need for supervision of the EMA’s activities and, in particular, for supervision, by health-care and research professionals, of the issuing of an MA” (see paragraph 99).⁴⁶

Member states will make information about the inspection of notified bodies publicly available (Article 35.7), but other documents relating to medical device approvals that are retained by a member state and not transmitted to Eudamed are governed by national laws on freedom of information. With diverse national rules and language barriers, these national laws on freedom of information do not solve the problem of general access to clinical evidence.

Clinical evaluation of medical devices

Many consensus statements give details about how to do clinical trials of new drugs, and provide reporting tools that can be used to check that all important aspects of any trial are shared in the scientific literature or in a clinical trial registry. Initiatives such as IDEAL-D⁴⁹ and CONSORT-NPT⁵⁰ have extended those concepts to the assessment of surgical interventions and randomised trials of medical devices. Specific proposals were summarised in a systematic review⁵¹ of 40 publications from regulators and health technology assessment agencies. The IDEAL collaboration has proposed a mandatory registry of all first-in-man interventions, to include both successful and unsuccessful innovations.⁵² Full reporting reduces waste of economic and human resources in research, minimises bias, and prevents unnecessary duplication of research.^{25,53}

Initiatives that are particularly relevant to the reporting of studies of medical devices are listed in panel 3, with some of their major recommendations. The numbers of participants eligible for a study, the numbers included, and the reasons why others did not participate, should be given.⁵⁴ The distribution in a study population of prognostic factors for the disease that is being treated should be reported.⁶⁰ If the use of a particular medical device has a learning curve, then the experience of the operators and the volume of practice in each centre participating in a research study should be reported.⁵¹ Without knowledge of these contextual factors, it is difficult to interpret results and draw generalisable conclusions.

The AllTrials⁵⁶ initiative was launched to ensure that all trials of drugs, medical devices, and other interventions are reported whether their outcomes are positive or negative, and the BMJ has introduced a scheme to publish unreported studies.⁶¹ In the USA, the Final Rule clarifying the Food and Drug Administration Amendments Act of 2007 extended the requirement that results should be reported within 12 months, to device products that are not approved, licensed, or cleared by the FDA; only small clinical trials to determine feasibility and certain clinical trials to test prototype devices were excluded.⁶²

Recommendations on transparency

The most important questions to be considered when implementing transparency under the new medical device regulations are how much information patients need their physicians to know, what information health-care professionals need so that they can choose the best

Panel 3: Collaborations and consensus recommendations relevant to the transparency of clinical evidence for medical devices

STROBE⁵⁴ (2007)

Strengthening the reporting of observational studies in epidemiology. STROBE provides a checklist for reporting observational studies, including those of medical devices.

SPIRIT⁵⁵ (2013)

Standard Protocol Items: Recommendations for Interventional Trials. "Any conditions relating to the investigators' right to publish or present trial results should be explicitly described as they can interfere with the ethical responsibility of investigators and sponsors to disseminate trial results in an unbiased and timely manner."

AllTrials campaign⁵⁶ (2013)

Supported by 735 organisations. "Despite strong global standards set by the World Health Organisation...in many instances rules are being ignored due to a lack of enforcement."

TIDieR⁵⁷ (2014)

Template for Intervention Description and Replication. Reporting should include the rationale, theory, or goals that underpin an intervention; the expertise and training of those providing the intervention; and whether or not the intervention was tailored or adapted for individual patients.

IDEAL-D⁴⁹ (2016)

Idea, Development, Exploration, Assessment, Long-term study-Devices. Extension of the IDEAL reporting tool for use with trials of medical devices. Includes the recommendation that standards are needed for the reporting of preclinical data.

European Commission DG CONNECT* (2016)

Code of Conduct on privacy for mobile health applications (mHealth apps). Practical recommendations for app developers to provide users with clear information and ensure that data are used in a fair and transparent manner. "The user's consent for the processing of personal data must be free, specific and informed. Explicit consent needs to be obtained for the processing of health data."⁵⁸

CONSORT-NPT⁹⁰ (2017)

Consolidated Standards of Reporting Trials, Non-Pharmacologic Treatment Interventions. "If blinding is not possible in a trial, the updated CONSORT NPT extension recommends reporting this information explicitly and providing a description of any attempts to limit bias, such as collection of data by an independent researcher."

Transparency International with Cochrane Collaboration⁵⁹ (2017)

Clinical Trial Transparency. A guide for policy makers. This report documents how regulatory failings and weak institutional compliance harm patients and undermine decision-making by public health agencies. It proposes legal, regulatory and administrative measures to strengthen transparency.

*DG CONNECT=(Directorate General for Communications Networks, Content and Technology).

medical devices to recommend for their patients, and what information patients need to use their devices safely and appropriately. Although confidentiality is understandable during the regulatory process, it should be abolished once a device has been approved and affixed with a CE mark. Clinically important results from the assessment of a medical device rarely equate with commercially sensitive data.

In 2016, the Council of the EU adopted the European Open Science Agenda, which aims to achieve open access to scientific publications in Europe by 2020.⁶³ This objective should be followed for scientific evidence relating to medical devices. Implementation of transparency should also follow the precedents established by the EMA; access to EU documents containing vital facts about medical devices should be granted on request.

Previous EU guidance on the clinical evidence to be submitted for a new device⁶⁴ did not give notified bodies authority to insist on more evidence from manufacturers if they declined to supply it. As delegated by Article 32.3,¹ new requirements for transparency must therefore be provided by an implementing legislative act to avoid ambiguity, promote uniformity of standards and practice throughout Europe, and support notified

bodies in their interactions with manufacturers. Legal challenges to decisions by EMA confirm this need.⁴⁵

The European Society of Cardiology (ESC) advocated in 2011 that transparency of documents relating to the approval of medical devices is essential.⁶⁶ These more detailed proposals concern full public access to the clinical data used to obtain approval of any medical device, although they are particularly important for implantable cardiovascular devices, in which the risks of device failure can be critical and sometimes fatal. Our recommendations have been developed after careful study of the new legislation and after taking independent legal advice. They present the consensus of expert clinicians and scientists from the major cardiovascular subspecialties.

In our opinion, all the items listed in panel 4 must be publicly available. Clinical data must specify the age and sex of the participants who have received the device, and the cumulative experience (in patient-years) that is being reported, whether for an initial investigation or for follow-up studies. Additionally, we propose the following suggestions.

Regulatory decisions

The Clinical Evaluation Report that is submitted by the manufacturer of a medical device to a notified body,

Panel 4: Information that should be in the public domain for any approved high-risk medical device

Basic information

- Name of manufacturer*, contact details* including website
- Precise name and model of device,* and basic unique device identification code*
- Risk class of device
- Name(s) of patent holder(s) (for disclosure of academic as well as commercial interests)
- Name and contact details of the Notified Body that issued the certificate of conformity
- Notified Body in-house expertise, names of assessors, and names of any external expert advisers who were consulted
- Date of approval, duration of validity of certificate
- Log of iterations for that device* including software upgrades if relevant, with details of supplementary approvals

Clinical evidence

- Intended purpose of device,* approved clinical indications,* target populations*
- Any contraindications* or restrictions for use of the device*
- Details of registration of clinical trial(s) completed and in progress
- Evidence submitted by manufacturer,† with protected intellectual property redacted, with the results of preclinical and clinical evaluation, including as relevant:
 - principles of design, choice of materials
 - biocompatibility studies
 - in-silico simulations (eg, computational fluid dynamics, modelling studies)
 - in-vitro bench testing (eg, durability of materials)
 - in-vivo studies using cells, tissues, or animal models
 - results of first-in-man studies
 - results of clinical observational studies
 - results of randomised clinical trials
 - data on device performance, and on its clinical impact or effectiveness
 - any adverse events*

- Relevant international standards (International Standardisation Organisation [ISO], European Committee for Standardisation [CEN], International Electrotechnical Commission [IEC], European Committee for Electrotechnical Standardisation [CENELEC]), common technical specifications, or professional expert recommendations which the manufacturer used when submitting its evidence,* and/or to which the Notified Body referred when the application for approval was assessed
- The basis for approval (eg, equivalence, pilot phase study, pivotal trial), including:
 - number, age, and sex distribution of participants studied
 - cumulative experience reported (eg, life-years of use)
- If the device has been approved on the basis of equivalence, then the name and manufacturer of the predicate medical device, advice where to find the summary of clinical evidence for that device, and the statistical basis for equivalence
- Report of the assessment by the Notified Body (and if relevant, by the national Competent Authority)
- Summary of advice received by the manufacturer or Notified Body from an expert panel under the new scrutiny procedure, including any dissenting opinions

Postmarket clinical evidence†

- Unanswered questions relating to the use of the device
- Approved programme for postmarket clinical follow-up
- Any requirements for postmarket clinical trials or studies, stipulated by the Notified Body
- Annual summary of postmarket surveillance (all new laboratory and clinical data)
- Any reports of complications or unexpected device failures
- Any field safety notices, alerts, or recalls

*Already specified for public disclosure, in Article 32 of EU 2017/745, which lists minimum contents of the Summary of Safety and Clinical Performance (SSCP). † Article 32(f) refers only to a "summary of clinical evaluation" and "relevant information on post-market clinical follow-up".

and the Clinical Evaluation Assessment Report that is prepared by the notified body to summarise its evaluation of that evidence, should both be publicly available. Access to these documents would supplement the information that will be provided in the summary of safety and clinical performance (SSCP) and in the Instructions for Use (Annex I, Article 23.4).¹ If a high-risk medical device is submitted to the new scrutiny procedure, then the scientific advice of the expert panel will be published (Article 106, paragraph 12).¹ To allow health-care professionals to study all the evidence and understand the regulatory decisions that have been made, the other documents should also be accessible.

Class II devices

Summaries of clinical evidence should be available not only for class IIb and class III medical devices, but also for some class IIa devices. For example, diagnostic

imaging systems that emit ionising radiation are in class IIb, for which an SSCP will be required, whereas those that image radioisotopes or that use other active systems such as ultrasound or magnetic resonance are in class IIa (Annex VIII, classification rule 10).¹ Statutory provision for technical and clinical data to be disclosed through an SSCP for all sophisticated diagnostic imaging systems would match requirements that are specified for in-vitro diagnostic medical devices in Regulation 2017/746, such as reporting diagnostic performance and reference ranges.⁶⁵

Access to standards

Device-specific guidance and standards that are applied during conformity assessment procedures have to be public documents. In Europe, at least 222 standards from the International Standardization Organisation (ISO) are recognised as relevant to medical devices.⁶⁶

These documents and others from the International Electrotechnical Commission (IEC), however, are available only for purchase. The business models of ISO and IEC (and their European counterparts, see panel 4) make this cost unlikely to change, yet this pay wall is a barrier to informed decision making and consent. Ways of overcoming this impediment should be sought.

Postmarket follow-up and registry data

The EU regulatory system has granted rapid access to the market for innovative high-risk medical devices designed to satisfy unmet needs, if the balance between benefit and risk has been considered favourable. The system has relied on postmarket surveillance to identify safety signals, and on follow-up studies to provide further evidence of clinical benefits or risks. Registry data reflects the real-life performance of a device in unselected patients so long as all patients are included in a consecutive series and the collection of data is comprehensive. It is important that any conditions for generating evidence after approval be publicly disclosed.⁴⁹ An open-access database of registries with their funding sources, objectives, and main findings must be available. Each entry should also include a statement about the percent completeness and the number of patients or years of follow-up, to allow calculation of adverse event rates.

Transparency of health technology assessment

Regulatory approval does not guarantee that a device will be available or that its use will be reimbursed; those decisions are usually made by another public body after a health technology assessment (HTA).⁶⁷ HTA agencies across Europe vary substantially in their organisation and in their policies on transparency; only some publish their reports in the public domain. The mission of the EU Network for Health Technology Assessment includes the promotion of “transparency, objectivity, independence of expertise, fairness of procedure and appropriate stakeholder consultations”.⁶⁸ The draft EU regulation on HTA does not propose clear rules for transparency, however, and joint HTA clinical assessments will be mandatory only for a selection of medical devices.⁶⁹ Transparency should extend to the HTA decision making process and the names and potential conflicts of interests of authors and experts involved, including those acting on behalf of manufacturers. Disclosure of information about the appraised health technology should include its clinical and practical effectiveness, cost-effectiveness, and safety. Direct submissions by manufacturers to HTA agencies should be publicly available, and European HTA agencies should develop a common open-access information system where their conclusions are documented.

Evidence for software and apps

Software is also a medical device. At the end of 2017, the number of mobile health apps was estimated to exceed

325 000 and to increase by 200 per day.⁷⁰ Some have a medical function, but only a few have been tested for efficacy and quality, so increasing use raises questions about risks and about the need for validation and clinical evidence.⁷¹ FDA guidance in 2013 and 2015 improved the transparency of descriptions in app stores; if the claimed intended use is for diagnosis, cure, mitigation, treatment or prevention of disease, and not for general wellness, then the app is considered to have a medical device function and to need formal review.⁷² The World Medical Association has recommended that information about health apps must be made publicly available, to allow physicians and patients to be discerning in their use and mindful of potential risks.⁷³ On Dec 7, 2017, the EU Court of Justice ruled that software which collects data from individual patients to monitor drug doses, contraindications, and interactions, is a medical device, even if it does not act directly in or on the human body.⁷⁴ The functions, limitations, data integrity, security, and privacy of mobile health technologies will need to be reviewed by EU notified bodies and that process has to be transparent.

Access to Eudamed

The Eudamed database will eventually include information about all medical devices and so for the first time, it will be possible from official sources in the EU to compile a list of medical devices in any particular category. An open search tool should be available to facilitate public access to this information.

Conclusions—engagement by health-care professionals and patients

We have concentrated on the need for public disclosure of clinical evidence relating to high-risk medical devices, governed by EU Regulation 2017/745, but of course evidence should also be disclosed under the second new Regulation (2017/746) concerning the assessment of in-vitro diagnostic medical devices.⁶⁵ Both regulations will be supported by implementing legislation. A small task force of regulators and invited stakeholders has recommended what information should be included in the summaries of safety and clinical performance and which components of the Eudamed database need to be open to public access. Those recommendations are now under revision. The European Commission has been delegated authority to translate them into further legislation, but it has indicated that it does not consider that to be a priority. Any member of the public or any organisation with an interest in these issues should therefore make representations now to the European Commission. The medical device regulations will take effect from 2020.

If the new provisions fail to satisfy the medical need for individual patients and their physicians to have access to all the evidence for a particular medical device, perhaps because a notified body has accepted the arguments of a manufacturer that the information should remain

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