

# An overview of medical device governance in the UK

Background paper prepared for the HealthWatch Symposium 2019:  
Evidence, Healthcare and Medical Devices & Implants

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## Table of Contents

EXECUTIVE SUMMARY.....	2
SECTION 1: BACKGROUND .....	3
ABOUT THIS PAPER.....	3
CONTEXT.....	3
THIRD PARTY REGULATION VIA NOTIFIED BODIES.....	6
THE NEW MEDICAL DEVICE REGULATION.....	7
SECTION 2: EVIDENCE REQUIREMENTS FOR MEDICAL DEVICES.....	10
EVIDENCE-BASED MEDICINE AND MEDICAL DEVICES.....	10
SECTION 3: REGULATING EVIDENCE ON MEDICAL DEVICES: THE MDR.....	13
NEW EVIDENCE REQUIREMENTS UNDER THE MDR.....	13
GENERATING CLINICAL EVIDENCE.....	14
REPORTING CLINICAL EVIDENCE .....	17
ASSESSING CLINICAL EVIDENCE.....	18
ANNEX 1: POSSIBLE QUESTIONS FOR THE SYMPOSIUM .....	21
ANNEX 2: SUGGESTED FURTHER READING .....	22
ANNEX 3: WHAT INFORMATION SHOULD BE PUBLIC? .....	23
ANNEX 4: RECENT REFORM IDEAS FROM AROUND THE WORLD .....	24
NEW NATIONAL IMPLANT REGISTRY IN GERMANY .....	24
REGULATORY REFORMS IN AUSTRALIA.....	25
REGULATORY REFORMS IN CANADA.....	26
PROPOSED REGULATORY REFORMS IN FRANCE .....	27
REFORM PROPOSALS BY THE UK ROYAL COLLEGE OF SURGEONS .....	28

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## **EXECUTIVE SUMMARY**

This background paper on medical device governance in the UK seeks to inform discussions at the [HealthWatch Symposium 2019](#) on “Evidence, Healthcare and Medical Devices & Implants”.

- **Section 1 provides an overview of the medical device industry and the regulatory landscape**, discusses some criticisms of the current regulatory system in the European Union, and flags aspects of European device regulation that will change as a result of the incoming Medical Device Regulation. Irrespective of the outcomes of the Brexit process, the UK seems likely to remain subject to these regulations, at least in the short term.
- **Section 2 takes a closer look at evidence requirements for medical devices** in general, and the challenges of using clinical trials to produce evidence on device effectiveness and safety in particular.
- **Section 3 takes a deep dive into evidence requirements and transparency of evidence under the Medical Device Regulation.** The section highlights that the regulation is often loosely worded and that many of its details are still being worked out. This may provide opportunities for engagement by HealthWatch and other groups promoting an evidence-based approach to medicine.

**Annex 1** lists questions that symposium participants may wish to explore during the event.

**Annex 2** flags some especially salient publications on the topic.

**Annex 3** lists types of information on medical devices that some experts think should be made public.

**Annex 4** provide examples of recent reform initiatives from a wide range of countries.

## **SECTION 1: BACKGROUND**

### **ABOUT THIS PAPER**

[HealthWatch](#) is a UK-based charity that has been promoting science and integrity in healthcare since 1991, with a particular focus on evidence-based medicine. It is primarily funded from its members' subscriptions, plus some donations from individuals and charitable trusts. HealthWatch does not accept industry funding.

This background paper on medical device governance in the UK seeks to inform discussions at the [HealthWatch Symposium 2019](#) on “Evidence, Healthcare and Medical Devices & Implants”, which will be held on 17 June 2019 in London. The aim of the symposium is to clarify the current issues facing evidence based healthcare in the field of implants and medical devices, and to identify areas where HealthWatch and similar organisations might most productively concentrate their efforts.

The paper focuses on evidence requirements for medical devices in the UK in the context of the recent global [Implant Files](#) investigation and the incoming EU Medical Device Regulation. The latter is scheduled to come into force from May 2020.

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Any remaining errors in this paper are those of the author alone.

### **CONTEXT**

#### **Medical devices and the device industry in the UK**

There are currently [over 500,000](#) different medical devices and in-vitro diagnostic devices on the European (and therefore UK) market, compared to [less than 10,000](#) active pharmaceuticals. At present, [no comprehensive list](#) of devices on the European market exists.

[According to the Office for Life Sciences](#), the medical technology sector in the UK is comprised of over 3,583 companies with a combined turnover of £22 billion and over 120,000 employees, generating around £5 billion in exports every year. The device industry accounts for half of all life science industry employment countrywide, and a third of these jobs are created by small and medium enterprises.

The UK medical device market is the third largest in Europe, behind Germany and France, and the [sixth largest in the world](#).

#### **Government strategy for the device sector**

The government regards devices as an innovative high-tech growth sector with an important role to play in securing the country's future as a manufacturing base. The national [Life Sciences Industrial Strategy](#) envisages strong public sector support for device research and development, and the rapid adoption and uptake of innovative medical devices by the NHS. This includes extending and accelerating NICE's appraisal process, and creating parallel NICE and the MHRA evaluations.

## Regulation of devices in the European Union

The central European player in regulating medical devices is the European Commission, which in turn delegates key regulatory functions to dozens of so-called ‘Notified Bodies’ (more on these below). In contrast to the US Food and Drug Administration, which regulates both drugs and higher-risk devices, the European Medicines Agency ([with minor exceptions](#)) does not play a role.

Calls by patient and medical groups to [centralise the market approval process](#) for medical devices in Europe by setting up a new regulator for devices or creating a dedicated device unit within the European Medicines Agency have been unsuccessful, largely due to strong industry resistance. On a national level, the UK was one of the countries opposing centralisation.

Defenders of the European regulatory system [argue](#) that its performance compares well to that of regulatory regimes in other jurisdictions at lower cost, and imposes less red tape on manufacturers.

## Regulation of devices in the UK

The current regulatory framework for medical devices is based on three European directives, which were transposed into UK law as the [Medical Devices Regulations 2002](#). On a national level, the MHRA is the key regulatory entity, while NICE has influence on which devices are used in the NHS, and how.

## Concerns over weak evidence requirements

Most observers concur that European evidence standards are currently significantly weaker than [those applied in the United States](#).

For example, a [2012 report](#) by the US Food and Drug Administration examining twelve high-risk devices certified in Europe that later turned out to be dangerous or ineffective concluded that the EU had a “lower approval standard” and warned of “serious risks to patients and high cost to the health care system”. According to the report:

*“EU approval is conducted by private companies and based on more limited evidence, often without significant studies in humans, that high-risk devices are safe and that they are mechanically fit to perform the job they are labelled to do. There is no requirement in the EU that a high-risk device provide an actual treatment benefit to patients... the limited testing required in the EU can fail to predict dangerous risks and lack of effectiveness in actual use... In many cases, the dangers of these EU-approved devices were not discovered until the manufacturers had to conduct the clinical studies needed to support US approval of a high-risk device.”*

## Concerns about insufficient data on device harms

The academic literature and media reports have repeatedly highlighted gaps in the current UK systems for detecting, [quantifying](#) and responding to harms caused by medical devices, and a [“shocking” lack of transparency](#) over what data does exist in the UK [and the rest of Europe](#).

### Data gaps and opacity fuel vaginal mesh controversy

The 2017 UK [Mesh Oversight Group Report](#) “found it difficult to gather information on mesh-related adverse incidents other than peer-reviewed publications in the medical

literature which the group feels does not tell the whole story with regard to adverse incidents,” and “agreed there was an incomplete picture of the incidence of complications following mesh surgery due to insufficient reporting and published data.”

According to the Guardian, NHS records suggest that [around one in 15 women](#) fitted with the most common type of mesh support later required surgery to have it extracted due to complications, much higher complication rates than those typically reported in both short-term clinical trials and a 2014 government report. Low rates of reporting of adverse events by clinicians and patients, the inability of Hospital Episode Statistics procedure coding to provide information on removal surgeries, and [patchy reporting of mesh removal operations](#) by individual clinicians may have created a significant data gap.

[According to the Sling the Mesh campaign](#), “There is no information on the MHRA website to search for adverse patient outcomes (unlike USA FDA database) so the public do not know which products have related issues and how many reports are made.” Device vigilance data is [not available in Europe or individual Member States](#) even through Freedom of Information requests due to the primacy placed on commercial confidentiality.

In 2017, UK health agencies found that existing systems were [unable to track the various types](#) of vaginal mesh implants that British patients had received. This lack of traceability – a problem that is [widespread in other jurisdictions too](#) – makes the recall of faulty devices extremely difficult.

In 2018, the Department of Health [announced](#) that it would be investing £1.1m “to develop a comprehensive database for vaginal mesh to improve clinical practice and identify issues.”

## Political economy of device regulation

Medical device regulation has historically [lagged behind drug regulation worldwide](#). The device industry has only been under full regulatory oversight since 1976 in the United States, and since 1990 in Europe.

Advocacy for a tightening of regulatory requirements on the \$400 billion global device market has met with [strong and consistent industry opposition](#). Several factors are at play:

- In addition to the opposition to expensive and burdensome new regulatory requirements common in any sector, there are valid concerns that many of the smaller enterprises producing medical devices might not be able to navigate substantially increased regulatory requirements. (How many small family-owned businesses market medicines?)
- Device regulation continues to be [sparsely funded](#) in Europe, and more effective regulation would likely require the allocation of substantial additional public resources. Currently, most regulatory functions are performed by Notified Bodies, most of which operate without public funding. Thus, while the US Food and Drug Administration’s Center for Devices and Radiological Health (which itself [since 2002 has been collecting user fees](#) from device makers) has around [1,700 full-time equivalent staff](#), the central group in the European Commission that is responsible for coordinating policy on device reportedly has only about 15 members.
- Devices are arguably more difficult to regulate than drugs because they are more numerous, evolve rapidly, and are far more diverse, ranging from simple tongue depressors to high-tech implants.

## THIRD PARTY REGULATION VIA NOTIFIED BODIES

### Gatekeepers to the European device market

Past concerns about device regulation in Europe have often focused on the so-called ‘Notified Bodies’ (NBs) that manage marketing approval for higher-risk<sup>1</sup> medical devices. Instead of having to seek approval from a central regulatory agency, manufacturers can apply to any NB in the European Union, and once they have the necessary certification, their products can be sold anywhere in Europe.

There are currently [around 50 NBs across Europe](#) that are licensed to certify medical devices. (There are [many more NBs overall](#), but only a small minority are permitted to assess medical devices.) NBs within each country are designated and monitored by [EU Member State national authorities](#), based on EU-wide standards. In the case of the UK, [authority for oversight rests with the MHRA](#). There are [four NBs within the UK](#) that are licensed to certify medical devices.

### Role of Notified Bodies

The scope of work of NBs varies according to the risk category of the device examined. [NBs’ role](#) includes design review, production and product quality assurance, and conducting unannounced audits of manufacturers; NBs may subcontract some of these functions. NBs have [no enforcement power](#) beyond issuing, maintaining, suspending, and [withdrawing](#) certificates.

Importantly, certification is not a one-off process, but involves a long-term relationship between manufacturers and NBs including post-marketing interactions, usually spanning a manufacturer’s entire product range. (Media reports have tended to somewhat misleadingly portray manufacturer-NB relationships as a one-off ‘CE rubberstamping’ interaction.)

### Potential conflict of interest

NBs can be state-owned or, more commonly, for-profit private enterprises. NBs are directly paid by device manufacturers for assessing their products. This creates a potential conflict of interest especially in the case of private sector NBs, which compete for business from manufacturers. Thus, manufacturers [can ‘shop around’](#) and may seek to choose to engage the NB perceived to impose the least stringent and time-consuming requirements.

A [series of European Commission assessments of NBs](#) conducted in recent years found that virtually all NBs examined fell short of expected impartiality and independence standards. Some NBs that had identified problems with manufacturers’ technical documentation either “disregarded these issues” or “did not adequately challenge the manufacturers”.

### Concerns about Notified Body performance

In 2014 [an elaborate sting by a Dutch undercover journalist](#) suggested that even a mandarin net may be able to gain NB certification – as a surgical mesh implant. A [2015 report by Dutch authorities](#) found considerable shortcomings in the evidence submitted by breast implant manufacturers. In recent years, the European Union (via national authorities such as the MHRA) has already considerably tightened the rein on NBs, including through [stronger and more stringent audits](#).

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<sup>1</sup> Low-risk devices (such as wheelchairs) [do not require NB certification](#). Instead, these can be self-declared as conforming to the regulation requirements by the manufacturer.

Nevertheless, a [2017 European Commission report](#) found that “some devices had been certified even though they were clearly not in compliance with the essential requirements for safety and performance... e.g. medical devices put on the market without sufficient clinical evidence.”

### **Lack of transparency of assessment processes**

NBs [must inform national authorities](#) about the certificates they issue, modify, withdraw, or suspend for which manufacturers and for what products. National authorities then [upload this data](#) into the EUDAMED database, but there is [no public access to this information](#). Neither the approvals nor the evidence relied on by the Notified Bodies [are publicly available](#).

In general, in the European regulatory sphere for devices, confidentiality requirements have been given priority over [competing](#) transparency imperatives. Crucially, most (if not all) European NBs are [outside the scope of Freedom of Information legislation](#).

### **Lack of transparency of clinical evidence**

The MHRA currently does not independently collect clinical data submitted to NBs. In 2011, UK-based NBs [told a research team](#) that they regarded clinical data supplied to them by manufacturers as “commercially sensitive”. A [2017 study by UK researchers](#) found that:

*“The lack of a publicly accessible registry of licensed invasive devices with details of marketing status and linked evidence prevents accurate assessment of current status for many implantable devices. We were unable to scrutinise the European approval system due to its lack of accessibility.”*

## **THE NEW MEDICAL DEVICE REGULATION**

### **A new framework**

The existing framework will substantially change when the [EU Medical Device Regulation](#) (MDR) comes into force in May 2020. Guidance on clinical evaluation, vigilance, and post-market clinical follow-up have all been integrated into the MDR. Individual Member States are responsible for the implementation of the regulation in their own countries.

### **Brexit and the MDR**

Current UK government consensus<sup>2</sup> appears to be that staying within the European regulatory framework is in the national interest, not least to preserve industry access to the European market for devices. Thus, even in the case of a no-deal Brexit, the government currently plans to adopt national legislation that [mirrors the incoming MDR](#).

The MDR explicitly states that:

*“Except where otherwise provided for in this Regulation, Member States shall not refuse, prohibit or restrict the making available on the market or putting into service within their territory of devices which comply with the requirements of this Regulation.” (Article 24)*

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<sup>2</sup> One reviewer of an early draft of this paper noted that support for alignment with EU rules in the field of medicine is not universal in Westminster. He pointed out that Conservative party politician Michael Gove has [publicly suggested](#) exiting the EU framework for regulating medicines. Presumably, any divergence from the MDR framework would take place over a period of several years, rather than immediately on the date of Brexit.

## Notified Bodies under the MDR

The MDR significantly intensifies the oversight of NBs by national authorities. New and far more stringent rules for NB accreditation are likely to result in [significantly fewer NBs being authorized](#) to approve higher-risk medical devices. All this, plus the MDR requirement to re-certify some old devices and newly certify additional categories of devices, is widely expected to create [substantial NB capacity bottlenecks](#) over the coming years.

Manufacturers can still choose which NB to approach, but individual NBs' decisions will be logged in EUDAMED and hence traceable (Article 53), though not necessarily by the public.

## Unique Device Identifier numbers

Higher-risk devices will be allocated a Unique Device Identifier (UDI) number.<sup>3</sup> EUDAMED aims to provide a data trail of all companies in a device's supply and marketing chains, enabling traceability of each individual device and its components. Patients will receive an implant card including the UDI and the name of the device and its manufacturer (Article 18).

If EUDAMED delivers on this aspiration in practice, it would fill [an important gap](#) in the current regulatory regime, and [facilitate the effective tracing and recall](#) of potentially dangerous devices. This would be a huge positive step forward compared to the status quo.

Parallel efforts to better trace devices through UDIs are also being made in the United States, and there is an ongoing effort to ensure the worldwide interoperability of comparable systems.

## Expanded EUDAMED database

A centrepiece of the MDR is the EUDAMED database, which was originally established in 1998. A substantially expanded version is planned to go live in March 2020, but experience with similar EU projects suggests that its launch could be substantially delayed.

The revamped [EUDAMED will form the core of several interlinked databases](#). The European Commission is responsible for running EUDAMED. Various players, including NBs, will upload information into EUDAMED.

There are seven EUDAMED-linked databases:

1. Economic operators (manufacturers, component suppliers, vendors, etc)
2. Devices
3. Unique Device Identifier (UDI) numbers
4. Marketing certificates by Notified Bodies (issued, suspended, withdrawn etc.)
5. Clinical investigations (clinical trials)
6. Vigilance (incident Reports, Field Safety Corrective Actions, Periodic Safety Update Reports)
7. Market Surveillance

According to Article 33 of the MDR, national regulators, NBs, manufacturers and study sponsors will all enter data into EUDAMED, but the regulation leaves open who will enter what types of data. Also, different stakeholders will have [different levels of access to information](#), but the MDR does not spell

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<sup>3</sup> UDIs must be placed on the labels of high risk (Class III) devices that are MDR certified from May 2021 onwards, and medium risk (Class IIa and IIb) device labels from May 2023 onwards.



out the details. Only the European Commission and national regulators will have access to all information EUDAMED contains.

### Question marks over future compliance

In theory, the MDR [will require](#) uniform performance data reporting to EUDAMED, making it “easier for insurers and health system buyers to compare product performance head-to-head”. However, some EUDAMED contributors may have [strong vested interests](#) in [misreporting](#) or [not generating, collecting and sharing data](#) that reflects badly on medical devices.

In this context, the example of the EU Clinical Trials Regulation provides a cautionary tale. That regulation requires some drug trial results to be reported within 12 months, but [at least half of all trials have failed to post results](#) onto the European trial registry, and no sanctions for non-reporting have been imposed by Member States to date. Due to [weak compliance by both national regulators and trial sponsors](#), that registry is riddled with incomplete, inconsistent, incorrect and out-of-date data.

Article 113 of the MDR<sup>4</sup> states that all Member States must adopt rules on penalties by February 2020, but an [industry analysis](#) notes that the MDR “defines the need for penalties but not against whom, nor does it define the penalty for Member States if they transgress their powers or violate their obligations.”

National regulators across the EU have set up a [taskforce](#) to coordinate and align their approaches to MDR implementation ([roadmap here](#)). It remains to be seen what penalties Member States will adopt, and to what degree they will monitor and enforce compliance in practice.

### Criticisms of the MDR

The MDR has been harshly criticized for [putting the interests of industry ahead of those of patients](#), and for its [loose wording and allegedly weak evidence requirements](#). There are also concerns that the classification system for devices used by the MDR sometimes does not accurately reflect a device’s actual level of risk. While some criticisms of the MDR are well-founded, it is important to acknowledge that the MDR does incorporate significant improvements compared to the present regulatory regime.

It is indisputable that even though the MDR is [four times as long as its predecessor](#), its wording is often vague. However, this presents opportunities as well as threats. Many important details of MDR implementation are still being elaborated by an array of working groups. A reviewer of an early draft of this paper argued that the current process presents many opportunities for medical professionals and other experts to work with regulators and support them in creating a system that promotes and safeguards patients’ interests.

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<sup>4</sup> Article 113: “The Member States shall lay down the rules on penalties applicable for infringement of the provisions of this Regulation and shall take all measures necessary to ensure that they are implemented. The penalties provided for shall be effective, proportionate, and dissuasive. The Member States shall notify the Commission of those rules and of those measures by 25 February 2020 and shall notify it, without delay, of any subsequent amendment affecting them.” In addition, Recital 87 states that: “Member States should take all necessary measures to ensure that the provisions of this Regulation are implemented, including by laying down effective, proportionate and dissuasive penalties for their infringement.”

## **SECTION 2: EVIDENCE REQUIREMENTS FOR MEDICAL DEVICES**

### **EVIDENCE-BASED MEDICINE AND MEDICAL DEVICES**

#### **Different evidence requirements for drugs and devices**

Worldwide, regulators' evidence requirements for issuing marketing licenses for medical devices are [generally weaker than those for licensing drugs](#). Both in the United States and Europe, there are different evidence requirements for different device types, stratified by different risk categories.

The main focus of regulators assessing devices is often on the engineering aspects of a device and on performance against surrogate endpoints, rather than on ultimate patient outcomes, as is (ideally) the case with medicines. This [arguably reflects the fundamentally different nature](#) of the two types of products being regulated.

Devices' [rapid product development and upgrading cycles](#) mean that exploratory trials often lead to minor modifications that make it [hard to determine when to launch a confirmatory trial](#). By the time clinical trial results for a device are in, a new model may already have been developed. (In contrast, pharmaceutical molecules do not evolve over time.) There have been cases in which apparently minor modifications to medical devices resulted in [substantially worse patient outcomes](#).

Patients expected to live for decades longer [may be implanted with devices that have only recently been developed](#), despite the (inevitable) lack of evidence about the real-life long-term durability of these devices.<sup>5</sup>

#### **Common criticisms of device trials**

Clinical trials of medical devices [have been widely criticized for weak methodologies](#). For instance, participant numbers are [sometimes very small](#), use of surrogate endpoints with limited clinical relevance is [very widespread](#), the loss of many patients to follow-up creates bias, a wide range of outcome measures abounds, [conflicts of interest abound](#) and are at times [badly managed](#), and double blinding and control arms are frequently not used.<sup>6</sup>

Another recurrent [criticism of many device trials](#) is that [their follow-up period is too short](#). For example, while the follow-up periods of trials of vaginal mesh implants are often a year or less, many observers believe that mesh complications frequently [only emerge after several years](#), so trial outcome data may significantly misrepresent the true benefit-harm ratio of mesh implants. In addition, industry has at times [failed to complete follow-up studies](#) mandated by regulators.

#### **Structural barriers to larger and better device trials**

Some observers [argue](#) that the way medical device market dynamics operate dis-incentivises investments into costly large-scale clinical trials. Market entry by an innovative new device often leads competitors to rapidly develop 'me-too' copycat products similar to the original. Often, these second movers can then obtain fast-track regulatory approval based on 'substantial

<sup>5</sup> While there are comparable concerns regarding some classes of drugs – consider the ongoing debate about the long-term effects of antidepressants often only tested in short-term trials – it is generally far easier to discontinue a drug regimen than to explant a medical device.

<sup>6</sup> Jeanne Lenzer's highly readable 2018 book on the medical device industry, *The Danger Without Us*, contains an excellent in-depth discussion of the flaws of one medical device trial.

equivalence' to the pioneering device already on the market, obviating the need to conduct expensive clinical trials of their own. This dynamic is compounded by patent law, which reportedly provides weaker protection to devices than to medicines.

Also, small and medium enterprises as well as innovative surgeons often lack the skills to design and the resources to conduct sophisticated larger-scale trials. According to one group of market observers, “the key issue that will remain is: Who pays the costs of clinical research?”

Even critics of the current evidence requirements [acknowledge](#) that extending drug-style evidence requirements to medical devices would sometimes be difficult or even impossible. For example, blinding patients in trials comparing implants to medical management requires sham surgery, and blinding surgeons can be impossible.

### **Barriers to the conduct of randomised controlled trials of devices**

In 2017, a group of experts identified numerous “perceived and real” [barriers to conducting gold-standard medical device trials](#):

- By the time a clinical trial is completed, a new model to replace the original device has already been developed
- Patients and medical professionals often have clear treatment preferences and refuse randomisation
- Double blinding is difficult or impossible
- Sham surgery often poses ethical challenges, and thus restricts the choice of comparator groups
- The experience and expertise of the surgeon may have a larger impact on patient outcomes than the type of device being implanted
- Defining relevant outcomes is complex
- Scientific advice and clear regulatory requirements is lacking

Despite these challenges, some experts [have argued that](#) “the bar of evidence should be higher for devices [than for drugs] because they are implanted and cannot simply be discontinued”.

### **Registries of implantable devices**

Registries are often proposed in order to strengthen the evidence base on devices. They can enable the measurement of long-term patient relevant outcomes and the detection of problems not flagged by pre-market testing and clinical studies. However, existing registries vary considerably in terms of purpose, scale, scope and cost. Therefore, any call to establish a registry needs to be accompanied by a detailed explanation of the kind of registry being proposed.

### **Considerable heterogeneity among existing European device registries**

A 2011 search for national and regional registries of implantable devices in [found a total of 101 registries](#) in European countries. Of these, two thirds were in the fields of cardiac implants (38) and arthroplasty (29). The research team found large variations in registry coverage between countries and implant categories, with a complete lack of registries for some categories. Registries also differed strongly in terms of their aims and structure. Very few were open access, some published aggregated results, while others were completely opaque.

The authors identified the following key registry variables:

- Scope and geographic coverage
- Starting time and duration
- Funding source
- Data users
- Types of information generated (including on cost-effectiveness)
- Transparency

The authors concluded that “there is a lot of potential for improvement,” while also emphasising the potentially “enormous impact” of well-run registries on policy and clinical decision-making, and highlighting the prospect of reducing the economic burden of revision surgery. Registries capable of generating data on cost-effectiveness in particular could add strong value.

In addition to the obvious hurdle of finding sufficient funding to establish and run high quality registries, the authors identified three other common stumbling blocks: additional workload for medical establishments (data entry), resistance by industry players who may fear the consequence of rankings of comparative implant performances, and fears by some physicians of having their work controlled.

### **Health technology assessment agencies as gatekeepers?**

Some observers predict that health technology assessment agencies (HTAs) will emerge as the [new gatekeepers for medical devices](#) whose efficacy and safety is perceived to be uncertain. Agencies like NICE could oppose the reimbursement of such devices, or force manufacturers to provide additional evidence by linking the reimbursement of new medical devices to the conduct of (additional) clinical trials, or to the collection of other types of data.

As is the case with pharmaceuticals, differences in evidence requirements among Europe’s many HTAs are complicating the process of accessing national markets for devices. High evidence standards by HTAs in key European markets (such as the UK) could conceivably drive manufacturers to generate an evidence base that exceeds of minimum EU regulatory requirements.

### **Applying evidence-based medicine principles to medical devices**

A [2017 BMJ article](#) provides a useful blueprint for applying the principles of evidence-based medicine to device regulation, based on the [IDEAL-D framework](#) adapted from surgery. IDEAL-D is essentially a systematic approach to “total product life cycle evaluation,” combining pre- and post-market evidence to develop a strong and reliable evidence base on the benefits and harms of a medical device.

## **SECTION 3: REGULATING EVIDENCE ON MEDICAL DEVICES: THE MDR**

### **NEW EVIDENCE REQUIREMENTS UNDER THE MDR**

#### **How the MDR defines clinical evidence**

Under the MDR, the manufacturer is obliged to compile a summary of safety and clinical performance for higher-risk devices. According to the MDR:

*“‘[C]linical evidence’ means clinical data and clinical evaluation results pertaining to a device of a sufficient amount and quality to allow a qualified assessment of whether the device is safe and achieves the intended clinical benefit(s), when used as intended by the manufacturer.”*  
(Article 2)

#### **Stronger evidence requirements**

The MDR [increases evidence requirements](#) for the certification of many devices. Evidence must cover [both safety and performance](#). (Note that ‘performance’ is not the same as ‘effectiveness’.) The MDR will [require pre-approval clinical studies](#) rather than equivalency statements for many new implants. Cardiovascular devices are likely to form the [single largest group](#) of high-risk medical devices undergoing the new scrutiny procedure.

According to an [analysis by industry](#):

*“Much greater emphasis will be placed on clinical data and clinical evaluations. Equivalence, currently commonly used to justify references to studies done with other devices, will be more rigorously interpreted. This will be a far more challenging way to demonstrate clinical safety or performance for medical devices.”*

Requirements for, and the role and weight of, clinical trial data within the clinical evaluation reports mandated by the MDR are [ambiguous](#) and [somewhat confusing](#). Understandings of what constitutes “sufficient amount and quality” (Article 2) of evidence for any given type of device will likely evolve over time, including through legal challenges.

Manufacturers will have to [keep clinical evidence updated](#) throughout the product lifecycle.

#### **Re-certification of devices already on the market**

All higher-risk medical devices already on the market will need to be re-certified by 2025 (in contrast to [controversial](#) current [US rules](#), there is no ‘grandfathering’ provision), which will in many cases require additional clinical evidence, notably post-market clinical follow-up studies, to be submitted. However, “clinical data relating to a device for which equivalence to the device in question can be demonstrated” (Annex XIV) is acceptable.

#### **Appropriate evidence criteria**

Medical devices are a far more heterogeneous group than medicines. This limits the scope for establishing clear-cut and precise rules applicable to all devices (even within the same risk class) in a regulatory text.

Therefore, expert panels whose members are appointed by the European Commission (more on these below) will draw up “criteria for an appropriate data set for assessment of the conformity of a device, in particular with regard to the clinical data required for clinical evaluation...” (Article 106). In the United States, similar panels currently review [11% of new high-risk devices](#), this share rises to 32% for high-risk devices targeting the circulatory system.

In addition, the European Commission may promulgate supplementary ‘implementing acts’ to ensure that the evidence requirements set out by the MDR are uniformly applied across Europe (Article 81).

### **Device classification under the MDR**

Medical device regulation in Europe follows a risk-based approach. The MDR leaves the existing rule-based classification system for medical devices largely unchanged. There are four categories: I, IIa, IIb and III. With some exceptions, manufacturers can self-certify conformity for low-risk Class I devices such as wheelchairs without involving an NB. All other risk classes require NB certification.

The MDR broadens the scope of device regulation to include contraceptive devices and devices used for aesthetic (as opposed to medical) ends, such as equipment for liposuction. The MDR also assigns some types of devices to a higher risk class. For example, many types of software previously considered Class I now require NB review (some software even falls into Class III), and surgical meshes, spinal disc replacement implants and active implantable devices are all upgraded into the high-risk Class III.

The European Commission, in consultation with Member States, may at a later stage extend the scope of the MDR to additional types of products, or move existing medical devices into a different risk class, by means of ‘delegated acts’. (Article 4)

Manufacturers must decide which class a device will fall into before initiating product development. If the NB responsible later rejects such a classification as incorrect, the issue is referred to the national regulator in the manufacturer’s country for a final decision.

### **Evidence requirements linked to device risk**

Ascending through the risk classes, progressively more stringent rules apply,<sup>7</sup> including in terms of evidence requirements. Manufacturers of Class IIa and IIb devices will be expected to provide more evidence (or a better explanation of why no additional evidence is required) than was previously the case. Unless there is sufficient existing evidence for both safety and performance claims, the MDR requires clinical investigations for all Class III and implantable devices.

## **GENERATING CLINICAL EVIDENCE**

### **Regulation of clinical studies**

As the EU Clinical Trial Regulation only applies to clinical trials of medicines, the MDR sets out a parallel framework for clinical investigations of medical devices. Note that ‘clinical investigation’ as defined by the MDR includes a variety of study types, including but not limited to clinical trials:

*“[C]linical investigation’ means any systematic investigation involving one or more human subjects, undertaken to assess the safety or performance of a device” (Article 2)*

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<sup>7</sup> The detailed rules for each device class are too byzantine to discuss within the scope of this paper. Various Notified Bodies and consulting companies have produced material summarising them, see for example [here](#), [here](#), [here](#), [here](#), [here](#) and [here](#).

Overall, the regulatory framework set out by the MDR is less stringent than that of the EU Clinical Trial Regulation. For example, Recital 64 states that:

*“The rules on clinical investigations should be in line with well-established international guidance in this field, such as the international standard ISO 14155:2011 on good clinical practice for clinical investigations of medical devices for human subjects... In addition, the rules should be in line with the most recent version of the World Medical Association Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects.” [Emphasis added]*

## Players involved

Under the MDR, manufacturers, expert panels, Notified Bodies, national regulatory agencies in member states, and the European Commission all play a role in generating and assessing clinical evidence.

### Interlocking roles on EUDAMED data management

Reportedly, a working group set up by the European Commission recently proposed that only NBs should be able to upload and manage the evidence packages on EUDAMED. Manufacturers in turn should verify that evidence has been uploaded before placing a device on the market.

Conversely, manufacturers have an obligation to keep the packages updated, including by filing periodic safety update reports that include data gathered as a result of the post-market surveillance plan, while NBs shall verify that ‘their’ manufacturers have appropriately updated the information in EUDAMED.

[Past experience](#) suggests that manufacturers may be reluctant to fully report device harms in particular. A participant in the MDR development process [explained](#) the rationale behind EUDAMED public access restrictions as follows: “[T]he authorities feared manufacturers would be less willing to share reports about accidents potentially caused by their devices if that information were made public”. This suggests that national regulators have limited confidence in their ability to fully enforce EUDAMED data management rules.

It is unclear to the author (and may indeed not yet have been determined) whether sufficient information will be made publicly available to allow outsiders to monitor how consistently the numerous manufacturers and NBs involved in contributing data to EUDAMED will comply with the system’s complex rules.

## Design of clinical studies

It is up to the manufacturer to decide in detail which clinical evidence is required to demonstrate device safety and performance:

*“The manufacturer shall specify and justify the level of clinical evidence necessary to demonstrate conformity with the relevant general safety and performance requirements. That level of clinical evidence shall be appropriate in view of the characteristics of the device and its intended purpose.” (Article 61)*



*“Clinical investigations shall be performed on the basis of an appropriate plan of investigation reflecting the latest scientific and technical knowledge and defined in such a way as to confirm or refute the manufacturer's claims regarding the safety, performance and aspects relating to benefit-risk of devices... the clinical investigations shall include an adequate number of observations to guarantee the scientific validity of the conclusions. The rationale for the design and chosen statistical methodology shall be presented... The primary endpoint shall be appropriate to the device and clinically relevant.” (Annex XV, emphasis added)*

Manufacturers can choose to consult one of the expert panels on their clinical investigation plans before initiating any studies (Recital 57). There are parallels to this in drug development: Before launching pivotal Phase III drug trials, pharmaceutical companies routinely confer with regulators to ensure that trial designs meet regulators’ evidence requirements for marketing approval.

### **Approval process for clinical studies**

The MDR requires the study sponsor – the manufacturer or another natural or legal person assuming responsibility for the study (Recital 63) – to apply to the Member State in which the clinical investigation is to be conducted for permission to proceed with the study.

The Member State (i.e. the MHRA in the UK) then assesses the application to ensure that the study design minimises risks to participants, that it “correspond[s] to the state of scientific knowledge”, is “suitable for providing evidence for the safety, performance characteristics or benefit of the device on subjects or patients”, and that it conforms to the requirements for investigations set out by the MDR (Article 70).

The ethics approval process for device studies remains subject to the existing national laws and regulations of individual Member States.

### **Registration of clinical studies**

While current EU rules only require submission for pre-certification device trials, once the MDR comes into force, Member States will also have to be [notified about the conduct of all post-market studies](#).

The registration of device studies has parallels with the registration of clinical trials for medicines. The sponsor submits the application for permission to conduct the study to the relevant Member State through an electronic system that automatically generates a unique single identification number for the study (Article 70), analogous to the trial ID numbers used by existing clinical trial registries. This system should be “interoperable” with the existing EU drug trial registry EudraCT (Article 73).<sup>8</sup>

#### **An accidental new clinical trial registry?**

According to the Declaration of Helsinki (Article 35):

*“Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject.”*

So far, this sentence has been understood as an ethical requirement to register every interventional clinical trial on one of the [WHO primary registries](#) or on Clinicaltrials.gov.

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<sup>8</sup> “[T]he Commission shall ensure that it is interoperable with the EU database for clinical trials on medicinal products... as concerns combined clinical investigations of devices with a clinical trial under that Regulation.” MDR Article 73 (2)



At present, because the European EudraCT registry only accepts drug trials, device trials conducted in the UK and the rest of Europe are scattered across multiple trial registries<sup>9</sup> – [if indeed they are registered at all](#).

The MDR could inadvertently further fragment the evidence base. The MDR does not explicitly require device studies to be registered on a WHO-recognised trial registry. However, it does state that the clinical investigation plan submitted as part of the certification process must include a “[s]tatement of compliance with the recognised ethical principles for medical research involving humans”.<sup>10</sup> Thus, the MDR requires manufacturers (and other study sponsors) to comply with the Declaration of Helsinki.

This raises an intriguing question: Will listing a medical device study on EUDAMED alone be enough to satisfy Helsinki requirements? Can EUDAMED, which contains both public and non-public elements, be considered to be a “publicly accessible database”?

If in future, European device trials are ‘registered’ on EUDAMED but not also on conventional trial registries, they will not be captured and aggregated by the [WHO International Clinical Trials Registry Platform](#).

All of the above could create multiple problems:

- Further fragmentation of the evidence base in medicine
- Incompatible data formats and data gaps
- Need to revise national regulations, funder policies, and institutional policies<sup>11</sup>
- Confusion about trial registration rules

To date, the European Commission, clinical trial registry managers and other stakeholders seem not to have considered the possible implications EUDAMED’s arrival on the scene.<sup>12</sup>

## REPORTING CLINICAL EVIDENCE

### Reporting of clinical study results

Past studies have found [considerable publication bias](#) in the field of medical devices. For example, half of a cohort of 177 studies of new medical devices remained unpublished seven years after their completion, as did half of a cohort of 92 completed post-approval studies that had been mandated by the US Food and Drug Administration. A recent study of a cohort of German device trials found that [27% had not been registered](#) on a public trial registry.

Under the MDR, the study sponsor has to submit the results of a study within one year of the last visit of the last patient, or within three months of a study’s termination. The only exception is if the original study plan presents a scientific reason justifying a longer reporting period (Article 77). This is roughly equivalent to the current EU reporting time frame for drug trials.

The sponsor submits the study report and a lay summary to the Member State in which the trial was conducted through the same electronic system used for study ‘registration’ (Article 77).

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<sup>9</sup> In the case of British trials, the two most frequently used registries for device trials are Clinicaltrials.gov and ISRCTN (the latter is a WHO primary registry). In other European countries, researchers may have different registry preferences.

<sup>10</sup> MDR Annex XV, Chapter II, Article 3.12

<sup>11</sup> For example, the UK’s Health Research Authority [currently states that](#): “For the purpose of clinical trials registration, we recognise any register covered by the World Health Organisation (WHO) list or the International Committee of Medical Journal Editors (ICMJE) list.” EUDAMED is on neither of those lists.

<sup>12</sup> Note that EUDAMED itself is [not new](#). However, public access to (some of) its data is new.

### **No barriers to publication bias in academic device trials**

Many interventional studies of medical devices in the United States are now [legally required](#) to post their tabular summary results onto Clinicaltrials.gov within 12 months of completion. In the UK, there is currently no corresponding regulatory requirement for academic clinical trials of medical devices. (The situation is presumably similar in most or all other EU countries). The MDR [will not change this](#), as it focuses exclusively on studies linked to device certification.

Thus, even if MDR provisions on results reporting are effectively enforced – a big ‘if’ – publication bias will continue to affect much of the clinical evidence base on medical devices being generated in Europe.

While a new transparency strategy covering all clinical trials is currently under development in the UK, the Health Research Authority so far seems to be [resisting calls to impose fines](#) for the non-reporting of clinical trial results.

### **Making clinical study results public**

According to the MDR, the study report and the lay summary become publicly accessible at the latest when the device is registered in EUDAMED, before the device comes on the market. If the device does not proceed to the marketing stage, results are made public within one year of submission. In case of early termination or temporary halt, results become publicly accessible immediately after submission.

The delay of up to one year between submission of device study results by sponsors and public visibility differs from EU disclosure rules for most drug trials, whose results become publicly visible at the time of submission. However, it is broadly analogous to EU disclosure rules for Phase I drug trials, whose results also become public only after a delay due to industry concerns about protecting commercially confidential information from competitors.

## **ASSESSING CLINICAL EVIDENCE**

### **Assessment of evidence by Notified Bodies**

After all evidence has been gathered, the manufacturer compiles the summary of safety and clinical performance, and “together with non-clinical data generated from non-clinical testing methods and other relevant documentation” (Annex XIV) required for the overall conformity assessment process submits this summary to its chosen NB. The MDR explicitly states that “Both favourable and unfavourable data considered in the clinical evaluation shall be included in the technical documentation.” (Annex XIV)

To ensure that the evidence review and validation process used by NBs is sound, national regulatory agencies (in the case of the UK, the MHRA) periodically inspect a sample of validations performed by the NBs within their own country (Article 45).

### **Assessment of evidence by expert panels**

For the certification of all Class III implantable devices and some Class IIb devices, additional rules apply. (Annex IX: Article 5) For these devices, after receiving the evidence package from the

manufacturer, the NB is obliged to forward it to the European Commission, which in turn sends it on to the relevant expert panel for further scrutiny.<sup>13</sup>

After an initial review, the panel decides “whether to provide a scientific opinion on the clinical evaluation assessment report” of the NB and the underlying evidence. If the panel sees no reason to provide an independent opinion, or fails to provide an opinion within 60 days, the NB can proceed with certifying the device.

### **Roles and powers of expert panels**

According to the MDR, if an expert panel decides to provide an opinion on a medical device:

*“The notified body shall give due consideration to the views expressed in the scientific opinion of the expert panel. Where the expert panel finds that the level of clinical evidence is not sufficient or otherwise gives rise to serious concerns about the benefit-risk determination, the consistency of that evidence with the intended purpose, including the medical indication(s), and with the PMCF [Post-Market Clinical Follow-up] plan, the notified body shall, if necessary, advise the manufacturer to restrict the intended purpose of the device to certain groups of patients or certain medical indications and/or to impose a limit on the duration of validity of the certificate, to undertake specific PMCF studies, to adapt the instructions for use or the summary of safety and performance, or to impose other restrictions in its conformity assessment report, as appropriate. The notified body shall provide a full justification where it has not followed the advice of the expert panel in its conformity assessment report and the Commission shall without prejudice to Article 109 make both the scientific opinion of the expert panel and the written justification provided by the notified body publicly available via Eudamed.” (Annex IX: Article 5.1. (g))*

The text of the MDR suggests that the NB, and not the expert panel, will have the final word on certification. In addition, there does not appear to be a pathway from a negative expert panel assessment to an outright refusal of certification. (The BioMed Alliance [has also noted](#) that it is unclear how difference of opinion between panels and NBs will be resolved.)

On the positive side, if the NB disagrees with the expert panel’s scientific opinion, the arguments of both sides will be made public. The author is unclear whether and when scientific opinions that were accepted by NBs will also become publicly available, or even whether this issue has been decided upon yet.

### **Expert panels: access to information and resources are key**

The BioMed Alliance, an umbrella organisation of 29 scientific and professional medical associations across Europe, in 2018 published a [detailed opinion on the new expert panel system](#):

“Expert panels must have the fullest information possible on the safety, performance and effectiveness data of the device... In practice, unless the expert panel can devote the same amount of time, personnel, experience and expertise to the evaluation of a new device that a competent and scrupulous Notified Body does, they will not be able to provide worthwhile

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<sup>13</sup> Article 106 of the MDR sets out the basic functions and responsibilities of these expert panels, whose members are appointed by the European Commission. Reportedly, the detailed rules that will govern the operations of these expert panels – including conflict of interest rules - have already been drafted, but they have not yet been formally approved.

scientific advice. Rigorous scientific evaluation of a potentially dangerous product is much more important than a rapid decision...”

“An expert panel may be asked to adjudicate on adverse events and serious incidents on the basis of few cases or relatively limited experience of a new device. It should therefore have authority to recommend to the notified body that it should require the manufacturer to collect additional clinical evidence...”

“It will be important to conduct pilot exercises to test how they [the expert panels] work, and then to adapt and develop the structures as experience is accumulated... For these new structures to be successful, it is essential that the European Commission invests adequate resources.”

### Concerns about transparency of evidence

Recital<sup>14</sup> 43 of the MDR states that:

*“Transparency and adequate access to information, appropriately presented for the intended user, are essential in the public interest, to protect public health, to empower patients and healthcare professionals and to enable them to make informed decisions, to provide a sound basis for regulatory decision-making and to build confidence in the regulatory system.”*

However, the MDR contains [competing](#) commercial confidentiality and transparency stipulations, and the its transparency provisions are vague and full of loopholes (see this [excellent analysis by Carl Heneghan](#) for details). Thus, it is still unclear how the balance between will be struck in practice.

For example, the public may not be able to access information on device studies that are listed in EUDAMED, but for which results have not been submitted. In that case, only very few stakeholders, such as national regulators, would be able to determine what studies have been initiated, and which of those studies have failed to report results, opening the door to publication bias and evidence distortion.

(While this paper focuses on clinical evidence, a reviewer of an early draft commented that pre-clinical testing and pre-clinical modelling was also very important, and that this research too should be made publicly available.)

To give another example, the European Commission has already indicated that the injury and malfunction reports contained in EUDAMED [are likely to remain confidential \(as they are today\)](#).

The BMJ [recently called](#) for EUDAMED to be made fully transparent:

*“[A]ll data, including clinical studies and investigations, should be available to everyone, ending differential rights of access for regulators and the public.”*

Reportedly, the question of what information exactly should be made public is currently being reviewed again by the European Commission.

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<sup>14</sup> The Recitals section of the MDR states general principles. While not directly ‘actionable’, these can inform and sway future rulings by European courts or the European Ombudsman. In the past, similar Recital passages in other EU regulations have influenced decisions that led to improvements in clinical trial transparency.

## **ANNEX 1: POSSIBLE QUESTIONS FOR THE SYMPOSIUM**

HealthWatch promotes science and integrity in healthcare. The aim of the symposium is to clarify the current issues facing evidence based healthcare in the field of implants and medical devices, and to identify areas where HealthWatch and similar organisations might most productively concentrate their efforts.

Possible questions to consider:

1. Is it worthwhile trying to influence the MDR rules while they are still being written, even at this late stage? Or is it better for HealthWatch to wait until after May 2020 and then monitor how the rules are applied in practice?
2. Once the MDR is in force and EUDAMED is up and running, which aspects of implementation should HealthWatch and similar groups monitor most closely?
3. Can we realistically expect the UK to unilaterally impose more stringent evidence, safety and/or transparency requirements than the European Union does? If so, what should these requirements be? Who (MHRA? NICE?) could apply them, and how? In the long term, should the UK get out of the European regulatory framework for medical devices altogether?
4. Are there important gaps in the current implant registry landscape in the UK? If so, which gaps are most important? Which politically and fiscally feasible options are there for filling these gaps on a national level?
5. Should HealthWatch be worried about EUDAMED potentially undermining the use of established clinical trial registries? Is this an issue worth engaging on?

## **ANNEX 2: SUGGESTED FURTHER READING**

**Fraser et al. 2018. The need for transparency of clinical evidence for medical devices in Europe**

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(18\)31270-4/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)31270-4/fulltext)

An excellent discussion of transparency of clinical evidence in the context of the MDR, explaining key MDR provisions and flagging key areas of concern.

**Heneghan et al. 2017. Transvaginal mesh failure: lessons for regulation of implantable devices**

<https://www.bmj.com/content/359/bmj.j5515>

Useful blueprint for applying the principles of evidence-based medicine to device regulation, based on the IDEAL-D framework.

**ICIJ. 2018-2019. The Implant Files**

<https://www.icij.org/investigations/implant-files/>

Reporting on medical devices by the International Consortium of Investigative Journalists that sparked calls for reform in several countries. Highly critical of the industry and regulators. Multiple articles.

**Lenzer. 2018. The Danger Within Us**

<https://jeannelenzer.com/the-danger-within>

Book on medical device industry misdeeds and regulatory shortcomings in the United States by a former BMJ journalist. Highly readable and informative, but does not discuss European regulations.

**Niederlander et al. 2012. Registries of implantable devices in Europe**

<https://www.ncbi.nlm.nih.gov/pubmed/24075007>

Survey of 101 implant registries in Europe, combined with a discussion of different registry models and their respective advantages and drawbacks.



## ANNEX 3: WHAT INFORMATION SHOULD BE PUBLIC?

The table below may provide a useful point of reference for symposium discussions.

Please note that HealthWatch does not (yet) have a position regarding any of the items listed below.

Panel 4: Information that should be in the public domain for any approved high-risk medical device	
<b>Basic information</b> <ul style="list-style-type: none"> <li>Name of manufacturer*, contact details* including website</li> <li>Precise name and model of device,* and basic unique device identification code*</li> <li>Risk class of device</li> <li>Name(s) of patent holder(s) (for disclosure of academic as well as commercial interests)</li> <li>Name and contact details of the Notified Body that issued the certificate of conformity</li> <li>Notified Body in-house expertise, names of assessors, and names of any external expert advisers who were consulted</li> <li>Date of approval, duration of validity of certificate</li> <li>Log of iterations for that device* including software upgrades if relevant, with details of supplementary approvals</li> </ul>	<ul style="list-style-type: none"> <li>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</li> <li>The basis for approval (eg, equivalence, pilot phase study, pivotal trial), including: <ul style="list-style-type: none"> <li>number, age, and sex distribution of participants studied</li> <li>cumulative experience reported (eg, life-years of use)</li> </ul> </li> <li>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</li> <li>Report of the assessment by the Notified Body (and if relevant, by the national Competent Authority)</li> <li>Summary of advice received by the manufacturer or Notified Body from an expert panel under the new scrutiny procedure, including any dissenting opinions</li> </ul>
<b>Clinical evidence</b> <ul style="list-style-type: none"> <li>Intended purpose of device,* approved clinical indications,* target populations*</li> <li>Any contraindications* or restrictions for use of the device*</li> <li>Details of registration of clinical trial(s) completed and in progress</li> <li>Evidence submitted by manufacturer,† with protected intellectual property redacted, with the results of preclinical and clinical evaluation, including as relevant: <ul style="list-style-type: none"> <li>principles of design, choice of materials</li> <li>biocompatibility studies</li> <li>in-silico simulations (eg, computational fluid dynamics, modelling studies)</li> <li>in-vitro bench testing (eg, durability of materials)</li> <li>in-vivo studies using cells, tissues, or animal models</li> <li>results of first-in-man studies</li> <li>results of clinical observational studies</li> <li>results of randomised clinical trials</li> <li>data on device performance, and on its clinical impact or effectiveness</li> <li>any adverse events*</li> </ul> </li> </ul>	<b>Postmarket clinical evidence†</b> <ul style="list-style-type: none"> <li>Unanswered questions relating to the use of the device</li> <li>Approved programme for postmarket clinical follow-up</li> <li>Any requirements for postmarket clinical trials or studies, stipulated by the Notified Body</li> <li>Annual summary of postmarket surveillance (all new laboratory and clinical data)</li> <li>Any reports of complications or unexpected device failures</li> <li>Any field safety notices, alerts, or recalls</li> </ul>

\*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".

Source: Alan Fraser et al. 2018. ["The need for transparency of clinical evidence for medical devices in Europe"](#)

## **ANNEX 4: RECENT REFORM IDEAS FROM AROUND THE WORLD**

The 2018-2019 Implant Files investigations documented weaknesses in current medical device regulations. In response, various stakeholders announced or proposed measures to improve the system. The section below flags some measures that may be relevant to strengthening device regulation in the UK.

### **NEW NATIONAL IMPLANT REGISTRY IN GERMANY**

The German government in February 2019 presented plans to create a wide-ranging national implant registry.

According to the [draft law \(summary here\)](#), the registry will document who received which implant, when and where. The federal government will fund the initial setup of the registry. Its running operations will be covered by user fees. The law is expected to come into force in January 2020. Many details of how the registry will be run have yet to be determined, including which types of implants will be included.

The draft law requires all medical institutions and insurers, both public and private, to report all implants and explants performed, with fines for non-compliance. Reporting costs incurred by medical institutions will be reimbursed. Reporting requirements will come into force as and when relevant elements of the registry have been developed. This process is expected to take [three to five years](#), with reporting for the first implant types expected to start in mid-2021.

Device manufacturers will be required to register their devices in the national registry. Implantation of any device not covered by the registry will become illegal. Data from existing registries will be migrated into the new registry. A process of replacing patient names with pseudonyms will seek to ensure patient confidentiality.

The proposal was broadly welcomed by a [wide range of stakeholders](#). The German EBM group Deutsches Netzwerk Evidenzbasierte Medizin [strongly welcomed](#) plans to make reporting mandatory. At the same time, it voiced concerns that the proposed decision-making process for revoking reimbursement coverage of particular devices based on registry data (which would allow the Ministry of Health to overturn earlier HTA decisions) left the system vulnerable to political and commercial influence (see also [this statement](#)).

The German EBM group also made the following suggestions:

- Adopt an evidence-based methodology for which implants to include (as yet undetermined)
- Capture studies that use the registry's data, including observational studies, in the registry
- Craft the design and data access rules of the registry to enable extending the follow-up periods of clinical trials (citing [Hemkens et al 2016](#) and [Hemkens 2018](#))

A patient group [pointed out](#) that under the draft law, only government institutions – but not doctors or patients – would have access to registry data. It considered this unacceptable.



## REGULATORY REFORMS IN AUSTRALIA

Australia's medical device regulator in April 2019 published the [outlines of a plan](#) to improve regulation.

The plan will undergo public consultation and further elaboration over the course of the year, and any final plan will require parliamentary approval. [Critics charge](#) that the plan, while impressive in some ways, lacks detail, will take years to put in place, and will require "significant legislative change." (Currently, Australia broadly accepts devices CE-marked in the EU, but some high risk devices are additionally assessed or subjected to a detailed audit by the national regulator, in addition to the reviews already done in Europe.)

- **Clinical evidence.** Require greater levels and scrutiny of clinical evidence for certain groups of devices. These devices include spinal implants, devices that make diagnoses, diabetes management devices, medical devices used for IVF, and companion diagnostics (tests used to guide the choice of medicines for particular cancers or rare diseases). Make clinical evidence public.
- **Adverse events.** Require more timely and improved reporting of adverse events by industry. Possibly make it mandatory for healthcare facilities to report adverse events and safety problems. Develop simpler ways for consumers to report adverse events, including through smartphone apps, and strengthen public awareness of these mechanisms. Enhance IT systems and analysis capability for adverse events. Confirm with other regulators whether they have also had significant reports of adverse events with particular products.
- **Patient empowerment.** Establish expert working groups with strong patient representation to provide advice and feedback on devices of concern (e.g. surgical mesh). Publication of consumer-friendly information on each new higher-risk device. Require manufacturers to provide consumer information leaflets and implant cards for implanted medical devices.
- **Tracing and recalls.** Unique Device Identifier system. Enhanced powers for recalls and other powers relating to cancelled devices.
- **Regulatory transparency.** More information on how regulatory decisions are reached for individual higher risk devices, including publishing clinical evidence, searchable incident reports, manufacturers' inspection reports, and regulatory actions on individual devices.

## REGULATORY REFORMS IN CANADA

Health Canada presented an [action plan](#) for improving device regulation in December 2018. Many of the changes will be implemented before the end of 2019.

- **Evidence requirements.** Review evidence requirements related to higher-risk medical devices, with a view to strengthening the evidence requirements for devices based on previously authorized versions. Expand the use of real world evidence to monitor the safety and effectiveness of products already on the market (RWE framework to be published in June 2019).
- **Transparency of evidence.** Proactively make public clinical information on medical devices, and launch a searchable public web portal. New regulations to be published in June 2019. In addition, broaden the scope of current transparency rules for device appraisals to also cover Class III devices. Summaries of these licensing application decisions will be published online.
- **Incident reporting.** Reporting medical device incidents will become mandatory for Canadian hospitals. (Manufacturers and importers are already required to submit medical device incident reports.) Improve voluntary reporting from other healthcare facilities by extending the existing Sentinel Network, and by providing training on incident reporting. “If reporting frequency does not sufficiently increase with education, additional regulations for mandatory reporting from healthcare sites besides hospitals will be considered.”
- **Transparency of incident reporting.** Public database containing de-personalized medical device incident reports, complaints and recalls in a user-friendly, searchable, online format. (Currently such reports are only available through FOI requests.) Facilitate public access to Health Canada’s medical device inspection database, including individual inspections and subsequent regulatory actions. Implementation by end of 2019.
- **Global safety alerts.** Manufacturers will be required to inform Health Canada within 72 hours if selected foreign regulatory agencies issue warnings about serious risks related to their medical device. Manufacturers will also be required to submit information regarding label changes or license suspensions. Vanessa’s Law, an older medical transparency law currently being implemented, will give Health Canada the power to compel manufacturers to reassess their product in light of such new information.
- **Patient involvement.** Forming a new expert advisory committee on women’s health issues for drugs and medical devices, in collaboration with the Canadian Institutes of Health Research, with a focus on patient participation and perspectives.

## PROPOSED REGULATORY REFORMS IN FRANCE

A French parliamentary commission of inquiry in March 2019 [called for sweeping reforms](#) of medical devices regulation in France and across Europe.

The commission's 36 recommendations, which include transferring responsibility for assessing high-risk devices to a new department within the European Medicines Agency, carry no legal weight. Some of the recommendations set out in the [commission's report](#) are summarised below.

- **Penalties.** Increase penalties for companies that fail to provide various types of information or data in violation of existing laws.
- **Incident reporting.** Change national legislation to make additional types of incidents subject to mandatory reporting.
- **Transparency.** Create a “citizens’ observatory” to oversee the rollout of planned new transparency measures.
- **Analysis of explants.** Mandate the recording of all explants, and the preservation of the explanted device itself for further analysis. Set up a central, publicly managed laboratory to analyse all explanted devices. (Note: [According to ICIJ reporting](#), medical devices suspected of being faulty are currently usually sent straight back to the manufacturer for analysis; hospitals sometimes fail to do this and instead discard the explant.)

In a separate development, France’s National Agency for Safety of Medicines and Health Products in April 2019 [banned](#) the placing on the market, distribution, and use of certain makes of textured breast implants due to the “rare but serious danger” they posed ([letter here](#)).

## REFORM PROPOSALS BY THE UK ROYAL COLLEGE OF SURGEONS

The Royal College of Surgeons recently released a lengthy report titled “[Future of Surgery](#)”. The document contains some recommendations salient to device regulation in the UK.

Taking into account that patient outcomes post-implantation depend on surgical approaches as well as the performance of the implanted device itself, the report states that:

*“The present system where individual hospitals oversee and collect data on innovations, without sharing information, is neither safe nor effective. It prevents national evaluation and the collection of evidence to support wider uptake of devices that benefit patients... [T]here remains a need for a recognised and established evidence-based mechanism to evaluate innovations in surgery – both devices and procedures – and assess their long-term effects...”*

The Royal College of Surgeons’ relevant recommendations are reproduced verbatim below.

- **National device registry.** A UK-wide registry should be established to track new devices. Implantable devices should have long-term monitoring in a register akin to the breast implant registry.
- **Central registration.** New procedures and devices should be centrally registered. This would allow their introduction in a controlled fashion and at a scale that is appropriate for evaluation. For example, a low-risk intervention (such as a new skin preparation for surgery) could be released through 20 hospitals for prospective evaluation, but a new biodegradable mesh could be released only at 3 designated units for detailed early evaluation. This would lead to a far more co-ordinated approach following a nationally agreed pathway.
- **Individual patient tracking.** For devices used in the operating theatre, there are systems already in place that can monitor a specific item using a barcode. Such systems are also used to track patients through theatre. Device codes linked to each patient could, therefore, be introduced into routine practice without establishing new processes.
- **Longitudinal monitoring:** It is crucial for implantable devices to undergo long-term monitoring... Such oversight... would allow long-term safety to be established, and, if adverse effects were identified, patients could be tracked and contacted for review. Achieving this would require a national collaboration, with a searchable database and regular outcome publication. Complete submission of data would be an integral part of the pathway for innovation.