Transparency – left to its own devices until now

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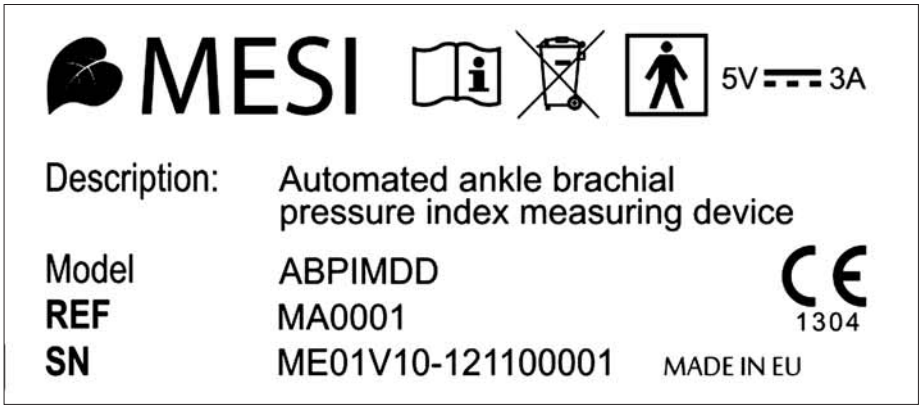
Abstract
Transparency has been an objective in the pharma world in recent years, culminating in the recent decision by the EMA to release full clinical study reports into the public domain. In spite of the publicity surrounding transparency and data sharing in pharma, the world of medical devices has largely flown under the transparency radar, but change is on the way. The final text of the long-awaited Medical Device Regulation was published in late February, and jumped the final hurdle of adoption by the European Parliament in April. This overhaul was prompted by scandals surrounding silicone gel breast implants and metal-on-metal hip replacements in the early 2010s that highlighted the lack of oversight and transparency. So why is this important and what are the implications for transparency?

Medical device approval in Europe – a fragmented process
Unlike approval of medicinal products in the US and Europe and medical devices in the US, approval of medical devices in Europe is not centrally regulated. In Europe, devices are generally assessed by one of over 50 privately owned "notified bodies" in different member states. If the notified body judges the device to conform with the relevant EU directives, a Conformité Européenne (CE) mark is issued and the device can be marketed in any EU country (Figures 1 and 2).[1,2]

Notified bodies are designated by national competent authorities such as the MHRA (Medicines and Healthcare Products Regulatory Agency) in the UK (https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency). Until 2010, data on medical device approvals were held at a national level even though CE-marked devices can be marketed throughout the EU. This means that a device approved by a notified body and the competent authority in, say Portugal, could be marketed in any EU member state without that state's competent authority having automatic, easy access to regulatory information about the product.

Eudamed – the early years
The European Database for Medical Devices (Eudamed; http://ec.europa.eu/idabc/en/document/2256/5637.html) is a centralised



Source: medimedical.com

Figure 1. Example of a CE mark

web-based repository that was the first to address the lack of cross-talk between notified bodies and different member states throughout the EU. Eudamed started life in 1997 as a European-funded project managed by the DDMI (German Institute of Medical Documentation and Information; https://www.dimdi.de). The European Commission (EC) then took over Eudamed, updating it in 2009 and mandating in 2010 that it be used by all competent authorities.[3] Today, Eudamed serves as a centralised repository where national competent authorities submit information about manufacturers, certificates, clinical investigations, and vigilance/monitoring to the EC.[4] A 2012 survey carried out by the EC reported that competent authorities mostly used Eudamed to monitor the activity of notified bodies. However, most member states were not using Eudamed for market surveillance or clinical investigation decisions, arguing that the datasets were insufficient.[5]

Today, little information is publicly available about medical device CE marks received, denied, and withdrawn, whereas this information is readily available for medicinal products. For example, according to the EMA 2015 annual report, 93 medicines were recommended for marketing authorisation, including 39 new active medicines.[6] Comparable information simply isn't publicly available on a pan-European level for medical devices.

Figure 2. The far-reaching role of Eudamed under the new medical device regulation (MDR)

The rise of registries

Since the advent of Eudamed, clinical trial registries have emerged as a key tool for facilitating transparency in clinical trials. In the US, as with medicinal products, prospective controlled clinical studies to test health outcomes of medical devices must be registered on Clinicaltrials.gov. Pre-registration of trial protocols on public registries is designed to reduce the number of trials with unreported results and to prevent selective reporting of outcomes.

European trial registries have lagged behind Clinicaltrials.gov in encouraging sponsors to post results of registered clinical trials. Since 2014, sponsors of drug trials with at least one European site must upload study results to EudraCT (https://eudract.ema.europa.eu/), which then automatically populates the publicly accessible EudraCT Clinical Trials Register. Some sponsors voluntarily register trials of medical devices in the EudraCT registry, even if though they are not included in its mandate.

The reincarnation of Eudamed

This gap in registration of medical device trials has just been plugged by the new Medical Device

Medical device transparency on the up

Transparency of medical devices is moving forward.

Via the new Eudamed described in the MDR, the public will be able to access:

- Lists of devices on the market, the relevant economic operators and certificates
- Ongoing recalls and other field safety corrective actions
- A list of devices withdrawn from the market, or restricted
- A database of clinical investigations registered
- Clinical investigation reports and lay summaries of these reports

Regulation (MDR),[7] and big changes are planned for Eudamed. The repository will be completely overhauled, transforming it into a public-facing searchable database, with different levels of access for competent authorities, notified bodies, manufacturers, and the public. More information will be collected, including results of clinical investigations (Article 77.5 of MDR, see sidebar) and post-marketing vigilance data. According to a spokesperson from the Irish competent authority, the Health Products Regulatory Authority, "The sponsor of a clinical investigation will be required by the new MDR to upload the final report of their clinical investigation and a summary of the clinical investigation report (that is readily understandable to the public) to the European database Eudamed. The summary report will be available to the public."

The International Committee of Medical Journal Editors requires all clinical trials – for drugs and devices alike – to be pre-registered on clinicaltrials.gov or other registries before submitting the results to a peer-reviewed journal.

From posting to peer review

Currently, the results of medical device clinical investigations are not always published. However, medical device manufacturers rely on the scientific literature to prepare the clinical evaluation report when applying for the CE mark. According to the spokesperson from the Health Products Regulatory Authority, "The new MDR places an increased emphasis on data for peer reviewed journals when it is used as part of a manufacturer's literature review of similar devices." This is particularly true when a manufacturer wants to demonstrate compliance based on equivalence with another device.

Ronald Boumans, Senior Regulatory Consultant with Emergo Group, points out that fewer clinical investigations are needed for approval of a medical device than for a new drug. "Many of these investigations are published in articles," says Boumans, but he warns against directly comparing publication rates for devices and drugs. "The clearest way to describe it is to consider them as different universes," he says. "On average more new medical devices enter the European market in a single day, than new medicinal substances in a year. The sheer numbers require a different approach."

Despite the different paths to approval for drugs and devices, the International Committee of Medical Journal Editors requires all clinical trials – for drugs and devices alike – to be pre-registered on Clinicaltrials.gov or other registries before submitting the results to a peer-reviewed journal.[8] Their proposals to share the patient-level data underpinning the article will further encourage transparency of clinical trial data.[9]

Boumans adds that there is a gap in the MDR regarding data from clinical investigations on medical devices. If the study is done outside Europe, data do not have to be entered into Eudamed and the study results do not have to be made public, although the manufacturer can still rely on the data to demonstrate compliance. This could become more common as European hospitals are expected to be flooded with requests for medical device studies.

The countdown to implementation of the MDR

The final adoption of the MDR by the European Parliament in April has triggered a 3-year countdown to its implementation. Eudamed will then be under pressure to complete, test, and deploy its plans to improve its transparency within this time frame. The clock will also be ticking for medical writers to expand their knowledge and capabilities in the medical device arena to help in the push towards a more transparent system by providing clear, well written documents for the general public. ■

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