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The ORACLE is a free newsletter of recent medical device regulatory & computer information that is of interest to designers, and device manufactures.

Delphi Consulting Group (DCG), provides medical device regulatory (FDA) release to market via the 510(k) and PMA pathways. DCG is Internet based to boost efficiency and reduce costs

How ethylene oxide became a public safety concern: A time line

Maia Anderson -

In recent months, several medical device sterilization plants have been forced to shut down among rising concerns that ethylene oxide, a chemical used to sterilize more than half of the country's medical devices, can cause cancer.

The U.S. Environmental Protection Agency and some state policymakers have been pushing for regulations to reduce emissions of ethylene oxide.

But the FDA has warned that shutting down plants will cause shortages of critical medical devices, such as feeding tubes used in neonatal intensive care units, catheters and shunts, since there aren't any other known, reliable ways for medical devices to be sterilized.

A timeline of plant closures, FDA warnings and policy changes reported since last year by *Becker's Hospital Review*:

Feb. 15: Illinois EPA shuts down sterilization operations at Sterigenics plant
The Illinois EPA shuts down sterilization operations at Sterigenics' plant in Willowbrook, Ill., after determining it was releasing excessive amounts of ethylene oxide.

March 27: FDA takes steps to prevent device shortages after sterilization plant shuts down
The FDA sends out a notice that it is actively working to prevent medical device shortages after sterilization operations were shut down at Sterigenics' Willowbrook plant.

April 15: Medical device deliveries stalled after sterilization plant closes
The FDA says that several medical devices are in short supply, despite its efforts to prevent shortages.

Sept. 6: Another Sterigenics plant shuts down
A Sterigenics plant in Atlanta temporarily shuts down after signing a consent order with the Georgia EPA to reduce ethylene oxide emissions.

Sept. 10: Judge approves reopening of Sterigenics' Willowbrook plant
An Illinois judge signs a consent agreement to allow Sterigenics to reopen its sterilization plant in Willowbrook on the condition that Sterigenics installs additional emission control systems that allow the plant to meet the state's new standards.

Sept. 27: EPA says it is considering putting new regulations on ethylene oxide
The U.S. Environmental Protection Agency says it is considering creating new regulations for ethylene oxide emissions. The medical device industry pushes back, arguing that restricting ethylene oxide will harm patients.

Sept. 30: Sterigenics won't reopen Illinois plant
Sterigenics says it won't reopen its Willowbrook plant because it can't reach an agreement to renew the facility's lease. Sterigenics also cites an "unstable legislative and regulatory landscape in Illinois" as a reason it won't reopen the plant.

Oct. 25: Georgia Gov. tries to close sterilization plant
Georgia Gov. Brian Kemp tries to shut down the Becton Dickinson sterilization plant in Covington, Ga., arguing it emits too much ethylene oxide. But AdvaMed, which represents 97 percent of the country's medical devicemakers,

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claims medical procedures are in jeopardy if the plant closes.
Oct. 28: FDA warns of critical medical device shortages
The FDA sends out a warning that the two Sterigenics plant closures and the possibility of the Becton Dickinson plant closing could mean hospitals will soon face shortages of critical medical devices.
Oct. 30: Proposed Illinois bill threatens to close Medline sterilization facility
Illinois lawmakers propose a bill that would close a Medline sterilization facility in Waukegan, Ill., threatening further device shortages.
Nov. 6: FDA panel searching for alternative medical device sterilization techniques
The FDA holds a two-day meeting with the General Hospital and Personal Use Devices Panel to develop strategies to reduce reliance on ethylene oxide to sterilize medical devices.
Nov. 25: FDA touts efforts to cut devicemaker reliance on ethylene oxide
The FDA says it has picked proposals from 12 companies to cut down on ethylene oxide reliance and will work with the companies to implement them.
Dec. 4: Viant to shut down sterilization operations at Michigan facility
Viant Medical signs a consent order with the state of Michigan to end its sterilization operations in Grand Rapids by the end of the year.
Dec. 13: Elevated levels of carcinogen found in neighbors of Medline sterilization plant
Researchers at the University of Illinois at Chicago say they found that people who live close to Medline's sterilization plant in Waukegan have higher levels of ethylene oxide in their blood.
Dec. 13: 22 more lawsuits are filed against Sterigenics over ethylene oxide concerns
Almost two dozen more lawsuits are filed against Sterigenics, bringing the total number to 73. The new lawsuits accuse the company of causing leukemia, lymphoma, breast cancer, miscarriages and other medical conditions.
Jan. 10: Georgia device sterilizer fined $3K per day over ethylene oxide emissions
Sterilization Services of Georgia is fined $3,000 per day for failing to install new filters to reduce ethylene oxide emissions by its deadline.
Jan. 17: EPA backs down on ethylene oxide queries after FDA marks turf
The U.S. Environmental Protection Agency backs down on its request to find out more about how medical sterilization facilities use ethylene oxide after the FDA claims jurisdiction in the matter.
Jan. 22: Medline halts sterilization at Illinois facility over ethylene oxide concerns
Medline says it hasn't been sterilizing medical equipment at its Waukegan facility since mid-December because it didn't meet new state standards for ethylene oxide emission.
More articles on supply chain:
Cardinal Health recalls 9 million surgical gowns
Devicemaker broke $2.1B contract to provide VA hospitals with critical medical supplies, lawsuit alleges

US Issues Cyber security Warnings Over Flawed Medical Devices

Sarah Coble News Writer

Warnings have been issued in the United States after cybersecurity flaws were detected in medical monitoring devices manufactured by GE Healthcare Systems (GEHC).

Safety notices were published yesterday by both the US Food and Drug Administration (FDA) and the US Department of Homeland Security's Industrial Control Systems—Cyber Emergency Response Team (ICS-CERT) regarding vulnerabilities in certain clinical information central stations and telemetry servers.

Exploitable flaws in the ApexPro and CARESCAPE telemetry servers, in version 1 of the CARESCAPE Central Station, and in CIC Pro Clinical Information Center Central Station version 1 were discovered by CyberMDX. The flawed devices are used mostly in health care facilities for displaying information regarding the physiologic parameters of a patient, such as heartbeat and blood pressure. They are also used to monitor the status of a patient from a central location in a facility, such as a nurse's workstation.
The FDA said the vulnerabilities "may allow an attacker to remotely take control of the medical device and to silence alarms, generate false alarms and interfere with alarms of patient monitors connected to these devices."
ICS-CERT said that an attacker could use the flaws to obtain protected health information (PHI) data and to make the device unusable.

In a statement published yesterday, GEHC said: "In the instructions provided with the devices, GEHC requires that the MC and IX networks are properly configured and isolated from other hospital networks. If those instructions are not followed, a vulnerable situation can exist where an attacker could gain access to the MC and IX networks via the hospital network."
GEHC has published instructions for risk mitigation along with instructions on where to find software updates or patches when they become available.

The FDA said yesterday that it was "not aware of any adverse events related to this vulnerability," while also saying that such incidents may be extremely hard to detect.

"These vulnerabilities might allow an attack to happen undetected and without user interaction. Because an attack may be interpreted by the affected device as normal network communications, it may remain invisible to existing security measures," said the FDA.

In a statement published yesterday, GE Healthcare said: "There have been no reported incidences of a cyber-

attack in a clinical use or any reported injuries associated with any of these vulnerabilities."

In July 2019, ICS-CERT issued a warning after vulnerabilities were detected in GE anesthesia and respiratory devices, GE Aestiva and GE Aespire (models 7100 and 7900).

How will EU MDR affect the CE marking process for medical devices?

Sophie Laurenson
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All medical devices to be placed on the EU market need to get a CE mark. The latest EU Medical Device Regulations (EU MDR) have significantly impacted the compliance process. Sophie Laurenson, medical device consultant at Kolabtree, an online platform for scientists, outlines the major changes in EU MDR and the consequences of these changes.

In recent years, several high-profile incidents have highlighted the weaknesses in the Medical Device Directives (MDD) active in the European Union (EU). The Medical Device Regulation (MDR) was introduced to address these weaknesses and improve the performance and safety of medical devices in Europe. The new regulations (fully titled Regulation (EU) 2017/745 of the European Parliament and of the council of 5th April 2017 on medical devices) were approved by the European Parliament on the 5th April 2017 and published in the Official Journal of the European Union on 5th May 2017. The MDR represents a significant shift in approach to regulating medical devices, in response to changes in the scientific and technical landscape shaping the medical device industry. The implementation of the regulation is staged over a three-year transition period to enable manufacturers to adjust. To ensure market access within the EU, all medical device products must achieve a CE mark under the new regulation 2017/745. This obligation affects existing on-market products as well as products that are currently in development.

The changes introduced in the MDR affect many aspects of the CE-marking process including device classification, technical file documentation, post-market activities as well as business partners of device manufacturers.

Reclassification

Medical device classification stratifies products according to risk and specifies the conformity assessment routes required for CE marking. While the overall classification scheme from class I to class III has been retained in the MDR regulation, some products have been reclassified. The MDR classification rules are outlined in Annex VIII. In particular, the requirements for some digital and software products have been delineated in classification rule 11.

Reformed obligations also apply to reusable class 1 devices, cosmetic implants and products without an intentional medical function (described in MDR Annex XVI). Manufacturers will need to accurately classify their products and determine whether new conformity assessment routes are required. This represents a challenge in cases where devices are reclassified in a higher risk profile group, requiring clinical and technical data that may not be readily available.

The MDR regulation affects both manufacturers and their business partners, including economic operators within the product supply chain. This includes product importers and distributors, which are explicitly regulated under MDR Article 25 (in addition to Articles 13 and 14). There are also more prescriptive requirements placed on EU Authorised Representatives (EUAR) as described in MDR Article 11. EUAR partners must be registered, have appropriate regulatory systems, personnel and liability insurance in place. MDR Article 15 describes the requirement for a Person Responsible for Regulatory Compliance (PRRC) to be appointed for manufacturers and EUAR organisations. This individual must have either appropriate academic qualifications in a relevant scientific discipline and at least one year of professional experience; or alternatively, four years of professional experience. Micro and small enterprises are excluded from requiring a permanent PRRC position but must have a suitable candidate continuously at their disposal.

Technical documentation

The technical file (or design dossier) is an important component of medical device regulation. This documentation should include a comprehensive description of the device and demonstrate regulatory compliance. A technical file contains detailed information on the function, design, intended use, clinical evaluation and claims surrounding a medical device. The MDR specifies a significant revision of the current approach to technical file generation. To harmonise the technical documentation required by global regulators, requirements have been based on the cur-

rent GHTF (Global Harmonisation Task Force) STED guidance document.

Essential Requirements (ERs) in the MDD have been replaced by safety and performance requirements (MDR Annex I). Manufacturers will need to identify the applicable requirements and ensure compliance through technical and clinical data and risk management. For devices that are in conformity with relevant harmonised standards, the presumption of conformity remains (outlined in MDR Article 8). However, in instances where harmonised standards do not exist or are insufficient, the European Commission may define common specifications.

Clinical Evaluation Reports (CERs)

CERs document the clinical data pertaining to a medical device. Recent revisions to the MDD placed greater emphasis on clinical investigations in the CER. The MDR is more explicit regarding the need for clinical evidence and evaluation (MDR Annex XIV, Part A). The criteria for establishing equivalence will become more stringent and the use of scientific literature in clinical evaluations will become strictly regulated. This may require manufacturers to alter their CER processes and obtain additional data from clinical investigations.

It is also anticipated that there will be enhanced scrutiny of CERs by Notified Bodies (NBs). Manufacturers should review the CERs in their legacy and development portfolios and ensure that they conform to new specifications. This is particularly important in cases where the initial CE marking was supported with limited clinical data and post-market surveillance activities have generated additional data. For devices with high risk profiles (such as class III or implantable devices), a summary of safety and clinical performance must be compiled and deposited on the European Data Bank on Medical Devices (EUDAMED) database (see below) (MDR Article 32).

Post Market Surveillance (PMS) and vigilance

Requirements for PMS and vigilance activities are expected to change significantly under the new MDR. Device manufacturers are required to collect Post Market Clinical Follow up (PMCF) data to assess potential safety risks. This process continues throughout the lifecycle of a product and contributes to continuous clinical evaluation (MDR Annex XIV, Part B). Periodic Safety Update Reports (PSUR) will be required, although the frequency is dependent on device type (MDR Article 86). Electronic vigilance reporting will be introduced (MDR Article 92) and reporting timeframes are reduced for serious incidents (MDR Article 87).

Traceability and transparency

Transparency is one of the key areas that the MDR is seeking to improve: "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''. MDR Article 33 contains a provision for EUDAMED containing data provided by manufacturers on registered devices and economic operators, clinical investigations and post-market activities. NBs will also provide information and certificates on this system. In some instances, this data will be available to the public. The EUDAMED system is an ongoing project, managed by the European Commission and manufacturers should closely follow the development of the project to ensure compliance.

Unique Device Identification (UDI) System

The MDR mandates the identification and traceability of all devices marketed within the EU through UDI System (MDR Articles 27 – 29 and MDR Annex VI). The UDI system is recommended based on international guidance and aims to improve post-market safety related activities. Under these regulations, each device must be assigned a UDI and the data stored in the EUDAMED database. UDIs will be provided by an approved supplier, prior to the launch of the product, and the UDI carrier must be specified on the device or its packaging. The exact specifications of the proposed EU UDI system have yet to be confirmed, but it is expected to mirror the newly established U.S.A system. Consequently, these requirements will not be mandatory at the end of the transition period but will come into force in early 2021 for devices with high risk profiles. Devices with lower risk profiles will be gradually phased in over subsequent years.

Labeling

The MDR regulations also stipulate some changes surrounding product labeling and precautionary statements for products. In addition to data located on packaging, relevant information should also be made available and regularly updated on the manufacturer's website. These requirements apply to specific details for labels and for sterile packages (MDR Annex I), inclusion of information for vulnerable patient groups, precautionary measures and information on hazardous substances.

Single use devices and their reprocessing

The reprocessing of single-use devices will only be permitted in settings where permitted by national law, with overarching requirements specified in MDR Article 17. Under these regulations, any entity which reprocesses a single-use device is considered a manufacturer and must ensure an equivalent level of safety and performance compared to the initial single-use device. Affected organizations should check that reprocessing is permitted in their national law and ensure that the resulting obligations are met. This may involve implementing processes, training personnel and mobilizing resources which were previously unnecessary.

Conclusions

The MDR is expected to result in significant changes in the CE-marking process for medical devices in Europe. The changes are extensive and may require organizations to take a comprehensive and structured approach to preparing for the full implementation of the MDR. Many of the changes affect several functions within a manufacturer organization as well as their business partners and NBs. Some changes broadly affect organizations, such as more detailed requirements for Quality Management Systems (QMS) (MDR Annex IX) or the requirement for insurance providing sufficient financial coverage for any potential liability. Coordination between stakeholders within and between organizations will help to smooth the transition between regulatory phases.

From the totally useless file

Did the folks at Google create the name "GOOGLE" out of thin air? In their minds – no, they long have held a special significance with numbers. When the internet company was founded in 1998, it based its name on the mathematical term "googol," which refers to the numeral 1 followed by 100 zeros.

When the company filed to go public in 2004, it said it planned to raise $2,718,281,828, which was the sum of multiplying $1 billion with the mathematical constant "e." The Oracle wonders why they did not have so-called fun with "base 12." Then maybe Google was created out of thin air, or nonsense.

Recognized Consensus Standards

The U.S. Food and Drug Administration (FDA), updated its Recognized Consensus Standards database. New or revised recognized standards were added and standards that re no longer recognized were deleted.

According to the FDA Guidance Appropriate use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices the FDA may determine which new or revised standards are appropriate for meeting requirements under the Food, Drug, and Cosmetic Act for medical devices, and may issue recognition numbers and provide supplemental information in the standards database in advance of a Federal Register Notice.

View the updated Database.

See you next month.