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# U.S. federal safety standards, guidelines and regulations for MRI systems: An overview

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**T**he Division of Radiological Health within the U.S. Food and Drug Administration's (FDA's) Center for Devices and Radiological Health (CDRH) is responsible for ensuring the safety and effectiveness of medical devices and the safety of radiation-emitting electronic products.

The FDA regulates firms that manufacture, repackage, re-label, and/or import these products, including magnetic resonance imaging (MRI) equipment, sold in the United States. Other federal and state agencies regulate the use of MRI devices through personnel qualifications, institutional quality assurance programs and facility accreditation.

Investigators conducting clinical research involving MRI equipment are subject to Investigational Device Exemption (IDE) regulations. These regulations require that investigators consider the level of risk involved in their study and whether they are required to obtain an IDE from FDA in addition to Institutional Review Board (IRB) approval. This article provides an overview of the federal safety standards, guidelines, and regulations for MRI systems in the United States and the role of the FDA in ensuring the safety and effectiveness of these nonionizing-radiation-emitting medical devices.

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## Laws, regulations and guidance

The FDA's Center for Devices and Radiological Health (CDRH) promotes and protects public health by ensuring the safety and effectiveness of medical devices<sup>1</sup> and the safety of radiation-emitting electronic products.<sup>2</sup> FDA's authority comes from the Food, Drug, and Cosmetic Act<sup>3</sup> as amended,<sup>4</sup> and the Electronic Product Radiation Control Act.<sup>5</sup> MRI systems are both medical devices and radiation-emitting electronic products.

## FDA's risk-based approach to medical device regulation

FDA takes a risk-based approach to medical device regulation, and medical devices are placed in one of three device classes based on the level of control necessary to provide a reasonable assurance of the safety and effectiveness of the device.

Class I devices, such as toothbrushes, tongue depressors, and hospital beds, are the lowest-risk devices and are subject only to general controls, such as good manufacturing practices. Though premarket notification (ie, 510(k) clearance) is a general control, most Class I devices are exempt from premarket notification and are not reviewed by FDA before they can be legally marketed.

Class II devices are those for which general controls alone are insufficient to guarantee a reasonable assurance of safety and effectiveness. Devices as

diverse as hemodialysis machines, imaging equipment, implantable stents, and ventilators are Class II devices, as are MRI systems. Class II devices may have special controls, such as performance standards, special labelling requirements, and/or premarket data requirements in addition to general controls. A few Class II devices are exempt from premarket notification, but the vast majority of Class II devices require FDA clearance before they may be introduced into interstate commerce. Through the premarket notification process, the manufacturer of a Class II device must demonstrate that the device it intends to market is substantially equivalent to a device that is legally marketed. The 510(k) premarket notification process is discussed in greater detail below.

Finally, Class III devices are the highest risk devices. These are devices that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury.<sup>6</sup> Devices such as cardiac pacemakers or a novel type of breast imager are Class III devices. In addition to general controls, Class III devices usually require premarket approval. Through the premarket approval process, the manufacturer of a Class III device must demonstrate that the device they intend to market is safe and effective for its intended use.

## General controls

General controls apply to all medical devices, regardless of classification, unless they are exempted by regulations. (If a device is exempted from one of the general controls, the exemption is stated in the classification regulation for that device). General controls include provisions related to adulteration (Section 501); misbranding (Section 502); device registration and listing and premarket notification (Section 510); banned devices (Section 516); notification, including repair, replacement, or refund (Section 518); records and reports (Section 519); restricted devices; and good manufacturing practices (Section 520).<sup>7</sup> MRI systems are not exempt from any general controls. Some key general controls are discussed in greater detail below.

## Device registration and listing

Owners or operators of places of business (also called establishments or facilities) that are involved in the production and distribution of medical devices (including MRI systems) intended for use in the United States are required to register annually with FDA. This process is known as establishment registration. Most establishments required to register with FDA are also required to list the devices made there and the activities performed on those devices.<sup>8</sup> Registration and listing provide FDA with the location of medical device establishments and the devices manufactured at those establishments. Firms registered and listed with FDA are regularly inspected, and knowledge of device manufacturing locations is essential in the event that a device is recalled. Registration and listing are conducted electronically,<sup>9</sup> and a publicly-searchable registration and listing database is available on FDA's website.<sup>10</sup>

## Premarket notification

Section 510(k) of the Act requires device manufacturers who must register to notify FDA of their intent to market a medical device at least 90 days in advance. This Premarket Notification means that manufacturers must obtain

explicit approval to market the device before it can be introduced into interstate commerce. The typical pathway to market for a Class III device is the Premarket Application (PMA), while the typical pathway to market for a Class II device is the Premarket Notification, or 510(k).

MRI systems are Class II devices subject to premarket notification, or 510(k). The 510(k) premarket notification pathway is based on "substantial equivalence." To gain market access via this pathway, a manufacturer demonstrates that the new device they intend to market is substantially equivalent to a device already on the market, called a predicate device. Manufacturers must submit a 510(k) premarket notification before introducing a new device into commercial distribution for the first time or when they are making certain significant changes to a currently marketed device.<sup>11</sup>

The new device is substantially equivalent if it has the same intended use and the same technological characteristics as the predicate device, or if it has the same intended use, has different technological characteristics that do not raise different questions of safety and effectiveness, and is as safe and effective as the predicate device.<sup>12</sup>

When demonstrating that a new MRI system is substantially equivalent to a predicate device, a manufacturer addresses aspects of the system's safety—such as static field strength, acoustic output, gradient-induced electric fields, gradient-induced heating, RF energy deposition (SAR), heating of surface coils, biocompatibility of patient-contacting parts, general safety and electromagnetic compatibility—and effectiveness—such as diagnostic image quality, signal-to-noise ratio, geometric distortion, image uniformity, slice thickness, spatial resolution, and image contrast.

FDA has a guidance document that provides a detailed description of the information that should be included in a premarket notification for an MRI system. This guidance document,

"*Guidance for Industry: Guidance for the Submission of Premarket Notifications for Magnetic Resonance Diagnostic Devices*," is available on FDA's website at no cost.<sup>13</sup> However, it is important to note that guidance documents are not legally binding, and a manufacturer may pursue other approaches to demonstrating substantial equivalence.

## Recall

Manufacturers of MRI systems are responsible for removing or correcting products that are in violation of the Act. Title 21 of the Code of Federal Regulations (CFR) Parts 7.41 through 7.59 describe how responsible firms can effectively discharge their recall responsibilities, as the majority of medical device recalls are conducted voluntarily by the device manufacturer. In rare instances where the manufacturer or importer fails to voluntarily recall a device that is a risk to health, FDA may exercise its Medical Device Recall Authority under 21 CFR 810 and issue a recall order to the manufacturer.

Manufacturers and importers are required to report a correction or removal of a product to FDA if the correction or removal was initiated to reduce a risk to health posed by the device or to remedy a violation of the Act caused by the device which may present a risk to health. Only the person that initiates the correction or removal is required to report. The report must be submitted to FDA within 10 working days from the time the firm initiates the recall. If there is not a "risk to health" involved, a report to FDA is not required, but the manufacturer or importer must keep a record of the recall. FDA maintains a publicly-searchable medical device recall database.<sup>14</sup>

## Adverse event reporting

MedWatch is the FDA's nationwide adverse event reporting system that serves to monitor medical device performance after a device is introduced into interstate commerce. Manufacturers, consumers, and user facilities (such as hospitals) all report under MedWatch.

FDA also has an alternate hospital-based reporting mechanism known as the Medical Product Safety Network, or MedSun, which is a group of hospitals who report to FDA.

The database that stores reported events is known as the Manufacturer and User Device Experience (MAUDE) database, and FDA makes a publicly-releasable version of most MAUDE reports available on its website<sup>15</sup>. Reporting requirements for device manufacturers and user facilities are outlined in 21 CFR 803 (Medical Device Reporting). In accordance with 21 CFR 803.50(a), medical device manufacturers must submit an adverse event report to FDA within 30 calendar days of becoming aware that the device they market:

1. May have caused or contributed to a death or serious injury; or
2. Has malfunctioned and this device or a similar device that the manufacturer also markets would be likely to cause or contribute to a death or serious injury, if the malfunction were to recur.

In accordance with 21 CFR 803.30(a), user facilities must submit an adverse event report to FDA and the manufacturer within 10 working days of becoming aware that:

1. A device has or may have caused or contributed to the death of a patient at the facility
2. A device has or may have caused or contributed to a serious injury to a patient at the facility.

An alternative method of reporting to FDA for User Facilities is the Medical Product Safety Network, or MedSun.<sup>16</sup> MedSun fosters two-way communication between FDA and the clinical community, and allows FDA to work collaboratively with the clinical community to identify, understand, and solve problems with the use of medical devices. Like all user facilities, MedSun hospitals are subject to the mandatory reporting requirements in 21 CFR 803, but MedSun hospitals also report potential for harm events such as near misses to FDA. The goal of MedSun is to foster communication between the clinical community

and FDA and to resolve problems or potential problems with a device before those problems lead to serious patient injuries. MedSun hospitals agree to participate in FDA surveys, site visits, and other safety initiatives. In return, FDA fosters an open culture of safety with MedSun hospitals, providing feedback on the adverse event information reported by the hospital and hosting educational webinars. The MedSun hospital network currently includes approximately 250 hospitals throughout the US. There is great interest in the program and a waiting list for enrollment.

FDA also accepts voluntary reports from anyone who wishes to alert the FDA to a problem with a medical device, and FDA receives a handful of adverse events from patients and consumers each year.

***Good manufacturing practices***

The Quality System Regulations (21 CFR Part 820) contain requirements for the design, manufacture, packaging, labeling, storage, installation, and servicing of all finished medical devices intended for human use.<sup>17</sup> Manufacturers of finished medical devices who intend to commercially distribute their products within the United States must establish and follow a quality system to help ensure that their products consistently meet requirements and specifications. The quality system regulations include requirements related to the methods used in the facilities and controls used for: designing, purchasing, manufacturing, packaging, labeling, storing, installing and servicing of medical devices. Manufacturing facilities undergo FDA inspections to ensure compliance with the quality system regulations.

**Radiation-emitting electronic product regulations**

In addition to being Class II medical devices, MRI systems are also radiation-emitting electronic products. Manufacturers and importers of MRI systems are subject to the radiological health requirements in Title 21, Subchapter J, Parts

1000 through 1050 of the Code of Federal Regulations. All radiation-emitting electronic products are subject to these regulations and include applicability of general and specific performance standards (21 CFR 1010-1050) and other general requirements for reporting and recordkeeping (1002), notification and corrective actions for defective or non-compliant electronic products (1003, 1004), and importation (1005). However, because MRI systems do not have a specific performance standard, manufacturers of MRI systems are only required to comply with the general requirements.

For devices such as MRI systems that are both radiation-emitting electronic products and medical devices, there is some overlap between the Electronic Product Radiation Control (EPRC) and medical devices requirements. For such products, regulatory actions are usually managed using one set of requirements. For example, a device recall is tracked as either a medical device (21 CFR 806) voluntary recall or as a mandatory EPRC notification of defect or failure to comply (21 CFR 1003), accompanied with an approved corrective action plan (21 CFR 1004), but not both. The EPRC regulations specifically state that if a manufacturer is required to submit an accidental radiation occurrence as well as a medical device adverse event report, the medical device reporting requirements under 21 CFR 803 shall take precedent [21 CFR 1002.20(c)]. Therefore, in practice, the EPRC requirements do not impose an additional regulatory burden on manufacturers of MRI systems.

**Investigational devices**

In addition to the above requirements for the manufacturers, distributors and importers of MRI systems, FDA has an interest in ensuring that MRI devices in investigational studies are used safely, although the role of FDA within this sphere is quite different. FDA supervises significant-risk research studies, and significant-risk study protocols require FDA approval via an IDE before the study can proceed<sup>18</sup>. The local IRB

is responsible for supervising non-significant risk research studies.

It is the responsibility of an investigator or the local IRB to make an initial risk determination. FDA becomes involved in this process when an IRB or an investigator determines that a study is significant risk. In accordance with [21 CFR 812.3(m)], a significant risk (SR) device is one that:

1. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
2. Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
3. Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
4. Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

A study involving a significant risk device is always a significant risk study, but a study involving only non-significant risk devices can also be a significant risk study,<sup>19</sup> depending on how the devices are used. For example, nonsignificant risk imaging used to select patients for investigational therapy could be a significant risk study. This is why the entire study protocol is evaluated when making a risk determination. A nonsignificant risk study is one that does not meet the definition of significant risk.

To provide additional guidance to investigators of MR diagnostic devices, FDA has published a guidance document, *Criteria for Significant Risk Investigations of Magnetic Resonance Diagnostic Devices*<sup>20</sup> (2003), which

identifies the operating conditions for MRI systems that FDA considers significant risk. An MRI system that exceeds any of these operating conditions would be considered significant risk and require FDA oversight via an IDE:

Main static magnetic field over 8 tesla for adults, children, and infants >1 month of age; main static magnetic field over 4T for infants less than 1 month of age, or

- Specific absorption rate (SAR) greater than 4 W/kg whole body for 15 minutes, 3 W/kg averaged over the head for 10 minutes, or
- dB/dt sufficient to produce severe discomfort or painful stimulation, or
- Peak acoustic noise over 140 dB or
- A-weighted root mean square sound pressure level greater than 99dBA with hearing protection in place.

If a study protocol does not exceed any of these operating conditions, FDA would likely consider the MRI portion of that study to have a nonsignificant risk and under the jurisdiction of the local IRB. In general, both hardware and software development at 1.5T and 3T is considered to have a non-significant risk provided the operating conditions specified above are not exceeded. Additionally, investigations conducted using commercially-available MRI systems used in accordance with their cleared indications for use do not require an IDE.

## Conclusion

Multiple safety standards, guidelines, and regulations exist to ensure the safety and effectiveness of magnetic resonance imaging systems in the United States. The US Food and Drug Administration regulates firms that manufacture, repack, re-label, and/or import these non-ionizing, radiation-emitting medical devices sold in the United States. Other federal and state

agencies regulate the use of magnetic resonance imaging devices through personnel qualifications, institutional quality assurance programs and facility accreditation.

## REFERENCES

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