Guidance for Industry

Guidance for the Submission Of Premarket Notifications for Magnetic Resonance Diagnostic Devices

Document issued on: November 14, 1998

This document supersedes the Guidance for the Content and Review Of a Magnetic Resonance Diagnostic Device 510(k) Application Dated 8/2/88.

U.S. Department Of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Radiological Devices Branch
Division of Reproductive, Abdominal, Ear, Nose and Throat, and Radiological Devices
Office of Device Evaluation

Preface

Public Comment

Comments and suggestions may be submitted at any time for Agency consideration to Loren A. Zaremba, Ph.D. HFZ-470, Computed Imaging Devices Branch, Office of Device Evaluation, FDA, 9200 Corporate Boulevard, Rockville, MD 20850. Comments may not be acted upon by the Agency until the document is next revised or updated. For questions regarding the use or interpretation of this guidance contact Loren A. Zaremba, Ph.D. at (301) 594-1212 ext. 137 or by electronic mail at lzz@cdrh.fda.gov.

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I. Purpose

The purpose of this document is to provide a detailed description of the information which should be included in a premarket (510(k)) notification for a magnetic resonance diagnostic device (MRDD) submitted to the Center for Devices and Radiological Health (CDRH). This information is an elaboration of the general requirements contained in 21 CFR 807.87.

MRDDs were reclassified by FDA from Class III to Class II effective July 28, 1988. Shortly thereafter, on August 2, 1988, the Guidance for Content and Review of a Magnetic Resonance Diagnostic Device 510(k) Application (the original MRDD Guidance) was issued. Since that time MRDDs have undergone considerable technological changes. Several regulatory decisions have been issued by the agency relating to dB/dt, software, biocompatibility and significant risk criteria. Standards have been developed by the National Electrical Manufacturers Association (NEMA) for the measurement of performance and safety parameters. Also, an international standard, IEC 60601-2-33 has been developed which addresses many of the safety issues associated with MRDDs.

A number of legislative changes relating to the authority of the agency have also occurred. These changes have resulted in the adoption of new regulations and administrative procedures by CDRH which affect the 510(k) process. The Safe Medical Devices Act of 1990 (SMDA) has resulted in new Good Manufacturing Practice (GMP) regulations requiring pre-production design controls, and several administrative requirements (Truthful and Accurate statements, Summaries of Safety and Effectiveness, and Statements of Indications for Use) have been added. The Food and Drug Administration Modernization Act (FDAMA) of 1997 and a re-engineering effort have resulted in the development of a new 510(k) paradigm which incorporates alternative approaches to demonstrating substantial equivalence in premarket notifications. These approaches are intended to facilitate the marketing clearance of devices, such as MRDDs, for which recognized standards exist, and for cases in which the new device is a modification of a previously cleared product.

This updated guidance reflects the regulatory decisions issued by the agency since reclassification, the standards which have been developed for MRDDs, legislative changes, as well as the new administrative procedures adopted by the Center for the demonstration of substantial equivalence.

II. Scope

This document is applicable to MRDDs as defined in 21 CFR 892.1000:

“A magnetic resonance diagnostic device is intended for general diagnostic use to present images which reflect the spatial distribution and/or magnetic resonance spectra which reflect frequency and distribution of nuclei exhibiting nuclear magnetic resonance. Other physical parameters derived from the images and/or spectra may also be produced. The

device includes hydrogen-1 (proton) imaging, sodium-23 imaging, hydrogen-1 spectroscopy, phosphorus-31 spectroscopy, and chemical shift imaging (preserving simultaneous frequency and spatial information)".

MRDDs are currently in Class II and require premarket notification and an agency determination of substantial equivalence prior to marketing. Three product codes are currently used to identify these devices:

LNH - Magnetic Resonance Imaging System
LNI - Magnetic Resonance Spectroscopy System
MOS - Magnetic Resonance Specialty Coil

The principal components of current MRDDs include the main magnet, shim and gradient systems, RF transmitter and receiver, transmit and receive coils, power supplies, computer and software. This guidance is applicable to premarket notifications for new magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) systems, new components, and modifications to systems and components which have a significant influence on safety or effectiveness.

III. Background

A. Supplementary Decisions and Guidance

1. MRI Guidance Update for dB/dt

On April 21, 1995 CDRH released a draft for public comment which contained revisions to the original MRDD Guidance relating to operation at dB/dt levels beyond the levels of concern listed in that document. A public meeting of the Radiological Devices Panel was held on September 11, 1995 to discuss the proposed revisions, and a final version was issued on October 11, 1995.

The original MRDD Guidance had established a level of concern for dB/dt at 20 T/sec for pulse duration over 120 microseconds. As an alternative, a manufacturer could demonstrate that the rate of change of the gradient field was not sufficient to cause peripheral nerve stimulation by an adequate margin of safety. The development of echo planar and similar fast imaging techniques, and the clinical benefits which they provide, caused a re-evaluation of this policy. Evidence was presented that although peripheral nerve stimulation could potentially startle a patient and cause motion which could interfere with image acquisition, the sensation is not harmful. However, painful stimulation should be avoided.

The Guidance Update for dB/dt recommended that manufacturers of equipment which exceeds 20 T/sec conduct volunteer studies to determine if peripheral nerve stimulation is possible with their device. If so, the device should incorporate a warning to the operator below the level at which stimulation begins to occur. Acknowledgment of the warning by the operator should then be necessary to proceed with the scan. Instructions for use

should advise the operator to inform the patient when nerve stimulation is possible, and describe the nature of the sensation to the patient. Equipment intended for routine clinical use should be limited so that painful stimulation is not induced.

2. Biocompatibility of Materials

On February 15, 1996 CDRH responded to a request by the NEMA MR Technical Committee that biocompatibility studies not be required in 510(k) submissions for external RF coil assemblies (e.g. surface coils) used with MRI systems. In this response the agency stated that biocompatibility data need not be provided for external RF coil assemblies and other MRI components which are not intended to contact the body. Such data also need not be provided for devices that contact the skin, if the materials used for patient contact in final finished form have a history of safe use. In such cases the manufacturer should document the use of the material in a legally marketed predicate. However, biocompatibility data will be required for MRI devices which incorporate a non-routinely used material, and for devices which are intended for invasive use (e.g. endocavitary coils). The type of data required in such cases will depend upon the nature of the contact, as described in ISO-10933, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing". In cases were biocompatibility data are required they may be incorporated by reference.

3. Software Level of Concern

On August 17, 1997 CDRH responded to a request from the NEMA Magnetic Resonance Section that MRI software be reclassified from Moderate to Minor Level of Concern. In this response the agency distinguished between software that is used for scan control, image reconstruction and image processing. Software used for image reconstruction and processing will generally be considered to be Minor Level of Concern. However, software which performs scan control functions (e.g. regulation of the output of the RF and gradient subsystems and estimation of SAR and dB/dt) will be considered as Moderate Level of Concern for those systems which are capable of reaching the First and Second Level Controlled Operating Modes as described in IEC 60601-2-33. Premarket notifications for Moderate Level of Concern software should contain a detailed description of the algorithms used, and a summary of the verification and validation testing.

4. Significant Risk Criteria

On September 29, 1997 CDRH formally issued a "Guidance for Magnetic Resonance Diagnostic Devices - Criteria for Significant Risk Investigations". This document defined the operating conditions above which patient studies would be considered significant risk investigations, and require approval of an investigational device exemption (IDE). These conditions are:

a. Main static magnetic field over 4 tesla, or

b. Specific absorption rate (SAR) greater than 4 W/kg whole body for 15 minutes, 3 W/kg averaged over the head for 10 minutes, 8 W/kg in any gram of tissue in the head or torso for 15 minutes, or 12 W/kg in any gram of tissue in the extremities for 15 minutes, or
c. dB/dt sufficient to produce severe discomfort or painful stimulation, or
d. Peak acoustic noise over 140 dB.

These criteria apply only to device operating conditions. Other aspects of the study may involve significant risks, and the study may therefore require IDE approval by CDRH.

The original MRDD Guidance stated a level of concern for static magnetic field strength of 2T. Above 2T a manufacturer was to provide evidence of safety. Clause 6.8.2(jj) of IEC 60601-2-33 states that examination of the whole body above 2T, or locally set limit, should be performed under an approved investigational human studies protocol, and vital body functions should be monitored. However, this requirement was published in July 1995. Since that time a number of research sites have been in operation at field strengths up to 4T with no reported occurrence of adverse events. Consequently, operation at up to 4T is not considered significant risk.

The original MRDD Guidance stated a level of concern related to whole body RF heating of 0.4 W/kg, or exposure sufficient to produce a core temperature increase of 1 degree C. The value of 0.4 W/kg was very conservative, and it was later found that operation at up to 4 W/kg was possible without incurring a core temperature rise of 1 degree C. As a result, MRDDs have been cleared for market operating at up to 4 W/kg since reclassification. An SAR of 4 W/kg corresponds to the upper limit to the first level controlled mode in IEC 60601-2-33. Operation above this level requires an approved human studies protocol under the IEC standard.

The criterion that dB/dt not be sufficient to produce painful stimulation is based on the MRI Guidance Update for dB/dt. The acoustic noise criterion is based on IEC 60601-2-33, which places an upper limit of 140 dB (peak) on all MRDDs.

B. The New 510(k) Paradigm

On March 20, 1998 CDRH issued a document entitled "The New 510(k) Paradigm - Alternative Approaches to Demonstrating Substantial Equivalence in Premarket Notifications." This document is available on the CDRH web site (http://www.fda.gov/cdrh/ode/parad510.html). In addition to the traditional 510(k), this document describes two alternatives, the "Special 510(k): Device Modification" and the "Abbreviated 510(k)".

1. Special 510(k)

The Special 510(k) is based on the requirement that manufacturers establish design controls in accordance with the SMDA and 21 CFR 820.30. A manufacturer uses the FDA guidance document entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" to decide if a device modification could be implemented without submission of a new 510(k). If a new 510(k) is needed, and if the modification does not affect the intended use of the device or the basic fundamental scientific technology, conformance with design controls may form the basis for clearing the application. Under this option, a manufacturer who is intending to modify a legally marketed Class II device would conduct the necessary verification and validation activities to demonstrate that the design output of the modified device meets the design requirements. Once the company has ensured the satisfactory completion of this process through a design review, a Special 510(k) may be submitted. While the basic content requirements for the submission are the same, this type of submission should also reference the cleared 510(k) and contain a "Declaration of Conformity" with design control requirements. In the Special 510(k) the manufacturer has the option of using a third party to assess conformance with design controls (refer to the paradigm document for details). Special 510(k)s are to be processed by the Office of Device Evaluation within 30 days of receipt by the Document Mail Center.

2. Abbreviated 510(k)s

The Abbreviated 510(k) is based on the use of conformance to voluntary standards in place of data review as the means by which the safety and effectiveness of Class II devices can be assured. Manufacturers may submit an Abbreviated 510(k) when FDA has recognized an individual or several voluntary standards that cover aspects of the new device. In addition to the required elements of a 510(k) as described in 21 CFR 808.87, Abbreviated 510(k) submissions should include information that describes how conformance to one or several voluntary standards, recognized by CDRH, have been used to address risks associated with the device, and a "Declaration of Conformity" to those standards. The "Declaration of Conformity" should provide the information listed in the paradigm. A third party may be used to assess conformance with these standards (refer to the paradigm document for details). The review of abbreviated 510(k)s is intended to be more efficient since they are not required to contain the experimental data from which conformance is determined.

C. Standards for Magnetic Resonance Devices

The Food and Drug Administration Modernization Act of 1997 authorizes CDRH to recognize consensus standards established by national and international standards development organizations that may be used to satisfy identified portions of device review requirements. On February 19, 1998 CDRH issued a "Guidance on the Recognition and Use of Consensus Standards" which is intended to provide information relating to the recognition and use of national and international consensus standards. It is available on the

CDRH web site (http://www.fda.gov/cdrh/modact/k982.html), and describes how the agency will use information on conformance with recognized standards to satisfy premarket review requirements. It also describes the content of a declaration of conformity. In the case of 510(k)s, information on conformance with recognized standards may help establish the substantial equivalence of a new device to a legally marketed predicate in the areas covered by the standards. If a premarket notification contains declarations of conformity, this will in most cases eliminate the need to review the actual test data for those aspects of the device addressed by the standards. However, the results of testing are expected when the standard specifies a test method without the associated performance limits, as in the case of the NEMA standards discussed below.

1. NEMA Standards

The NEMA standards MS 1 through 8 are recognized by FDA and thus may be used in Abbreviated 510(k)s for magnetic resonance diagnostic devices. They provide standardized methods for measuring performance and safety parameters for MRDDs. To the extent possible, these methods should be utilized in Traditional as well as Abbreviated 510(k)s. The following specific standards have been published by NEMA:

MS 1 - Determination of Signal-to-Noise Ratio (SNR) in Diagnostic Magnetic Resonance Images

MS 2 - Determination of Two-dimensional Geometric Distortion in Diagnostic Magnetic Resonance Images

MS 3 - Determination of Image Uniformity in Diagnostic Magnetic Resonance Images

MS 4 - Acoustic Noise Measurement Procedure for Diagnostic Magnetic Resonance Imaging Devices

MS 5 - Determination of Slice Thickness in Diagnostic Magnetic Resonance Imaging

MS 6 - Characterization of Special Purpose Coils for Diagnostic Magnetic Resonance Images

MS 7 - Measurement Procedure for Time-Varying Gradient Fields (dB/dt) for Magnetic Resonance Imaging Systems

MS 8 - Characterization of the Specific Absorption Rate for Magnetic Resonance Imaging Systems

A detailed discussion of the use of these standards in obtaining laboratory data to support a 510(k) for an MRDD is provided in section IV.D below. It is important to recognize that the NEMA standards only prescribe standard measurement methods. They do not specify acceptable levels of performance or safety. Acceptable levels of performance are determined by FDA on a case-by-case basis, depending upon intended use, and the

substantial equivalence criterion. Levels of safety parameters are addressed by the IEC standard discussed below.

2. IEC 60601-2-33

IEC 60601-2-33 is the international standard for the safety of magnetic resonance equipment intended for medical diagnosis. CDRH representatives participated in the development of this standard. It was released in July 1995 and addresses most of the important safety issues associated with MR, such as instructions for use and safe operating levels. The NEMA standards for measuring acoustic noise, dB/dt and SAR have been incorporated into the IEC standard. However, the IEC standard does not address performance issues, such as SNR, image uniformity, geometric distortion and slice thickness.

An important aspect of the IEC standard is the establishment of three operating modes for MR systems, the normal operating mode, first level controlled mode and second level controlled mode. The normal operating mode is considered safe for all patients, regardless of their condition. The first level controlled mode is defined as one in which operating parameters (dB/dt or SAR) reach values that may cause physiological stress, and the second level controlled mode is one in which parameters reach values that may produce significant risks for patients.

The normal operating mode requires only routine monitoring of the patient. The first level controlled mode requires medical supervision. Medical supervision requires a positive assessment by a qualified medical practitioner of the risk versus benefit for the scan, or a decision by a qualified surrogate of the practitioner that the patient satisfies a set of objective criteria formulated by the medical practitioner. Equipment that is capable of operating in the first level controlled mode must display the mode defined by dB/dt and the predicted value of the SAR. When an operating parameter reaches the lower limit of the first level controlled mode, an indication must appear on the console and the operator must take a deliberate action to proceed with the scan. Also, the dB/dt and SAR values must be recorded with the image data.

Operation in the second level controlled mode requires an approved human studies protocol. Security measures (e.g. lock or software password) must be provided to prevent unauthorized operation in this mode.

Prior to this guidance, FDA has cleared equipment for market which incorporates the IEC operating mode scheme, but has not specifically recommended this feature. However, since MR equipment is a world wide market, all manufacturers currently market equipment which conforms to the IEC requirements. With the adoption of this guidance, FDA will begin recommending utilization of the IEC operating mode scheme. However, in the case of time varying gradients (dB/dt), different limits for the operating modes and different measurement methodology will be used.

In the July 1995 version of the IEC standard, the ranges of dB/dt values which define the operating modes do not reflect data obtained in most recent studies. Based on recent data, the lower limit of the first level controlled mode is too low by approximately a factor of two, and the upper limit is well above the pain threshold. On October 11, 1995 CDRH issued an "MRI Guidance Update for dB/dt" in which the limits for the operating modes were based on physiological testing. The operator is to be notified when dB/dt approached the peripheral nerve stimulation threshold and scanning is not permitted above the pain threshold.

Also, in the present version of the IEC standard, only the component of the gradient in the direction of the main static field (the component used to spatially encode the image) is measured in the determination of dB/dt. Since other gradient components may be significant, the October 11, 1995 MRI Guidance Update recommends the use of d |B| /dt (the maximum rate of change of the magnitude of the gradient field) as a measure of the likelihood of peripheral nerve stimulation. NEMA MS 7 has been recently revised to include a standard method for measuring d |B| /dt.

An IEC working group was convened in September 1997, with the objective of revising the measurement methods and operating mode limits for dB/dt. Until this work is completed, CDRH will use the October 11, 1995 Guidance to define the operating mode limits, i.e. the upper limit of the normal operating mode will correspond to the threshold of peripheral nerve stimulation and the upper limit of the first level controlled operating mode will correspond to the threshold of severe discomfort or pain. The revised version of NEMA MS 7 will be the recommended method for measuring d |B| /dt.

Because the technology of MRDDs is still developing, it is expected that further revisions to the IEC standard will be required in the future. However, the international standards-setting procedure is often protracted. In order to ensure that technologically advanced devices which may benefit patients are not kept from the market, CDRH will continue to offer the option of demonstrating safety by showing that the physiological response of the patient is within safe limits (see Attachment A).

3. Other Standards

In addition to the NEMA and IEC particular standards the following standards are also applicable to magnetic resonance diagnostic devices:

a. IEC 60601-1, International Electrotechnical Commission, Medical Electrical Equipment, Part 1: General Requirements for Safety - This is the general standard for medical electrical equipment. IEC 60601-2-33 specifies additional requirements for MRDDs.

b. UL 2601-1, Medical Electrical Equipment, Part 1: General Requirements for Safety - This is the UL version of IEC 60601-1.

c. UL 94 Tests for Flammability of Plastic Materials for Parts in Devices and Appliances - This standard applies to the flammability of plastics used in various MRDD components, e.g. pads, coil enclosures, etc..

d. DICOM (Digital Imaging and Communications in Medicine) - This standard specifies formats for the exchange of radiology and other medical images.

e. Regulations under 21 CFR Subchapter J - Radiological Health - These regulations have been promulgated under the Radiation Control for Health and Safety Act of 1968 and include performance standards relating to radiation emitted by electronic consumer and medical products, including TV monitors and lasers used in electronic data storage devices.

IV. Information Required in a Premarket Notification

Information required under 21 CFR 807.87 for MR diagnostic devices is listed and discussed in detail below.

A. General Information

1. Name and address of manufacturer.
2. Establishment registration number (if not available, registration application should be submitted).
3. Name, title, phone number, fax number and E-mail of contact.
4. Tradename and common name of device.
5. Type of submission (special, abbreviated or traditional)
6. Classification and class of device (21 CFR 892.1000, class II), and product code (LNH, LNI or MOS)
7. Intended use (general purpose of device per 21 CFR 892.1000)
8. Applicable standards (e.g. NEMA and IEC).

B. Administrative Information

1. 510(k) Summary of Safety and Effectiveness or Statement (see 21 CFR 807.92 and 807.93)
2. FDA Indications for Use Form (specific diagnostic use of device, i.e. the anatomical region and/or disease/condition which the device is intended to diagnose)
3. Truthful and Accurate Statement (see 21 CFR 807.87(j))
4. Declarations of Conformity to Consensus Standards (Abbreviated 510(k) only)
5. Declaration of Conformity to Design Controls (Special 510(k) only)
6. Software certification (see section IV.I below)

C. Device Description

1. Hardware and Software

For new MRI systems the device description should list the principal components of the system, a brief description of the purpose of each component, and a diagram illustrating their interconnections. The following specific information should also be included where appropriate:

a. Type of installation (fixed, mobile or transportable)
b. Type of main magnet (superconducting, resistive or permanent)
c. RF amplifier maximum power and duty cycle
d. Description of gradient coil design including an illustration, dimensions, maximum gradient strength and slew rate
e. Complete list and description of RF Coils
    i. Type of coil (transmit, receive, transmit/receive)
    ii. Intended use (resonant nucleus, anatomical region of interest, specific disease or condition)
    iii. Description of the coil design (e.g. linear, quadrature, phased array, etc.)
    iv. Illustration of coil design and location of individual elements
    v. Circuit diagram
    vi. Decoupling method
f. Complete list and description of pulse sequences available on system and range of important sequence parameters
    i. Type of sequence (e.g. spin echo, gradient echo, fast spin echo, etc.)
    ii. Intended use (anatomical regions of interest, specific disease or condition)
    iii. Contrast characteristics (e.g. T1, T2, weighting, etc.)
    iv. Pulse timing diagram
    v. Number of slices (multislice), slice thickness and spacing
    vi. Acquisition and display matrix size
    vii. Image acquisition time
g. Gating/Triggering methods and associated accessories
h. A complete list of image processing functions (e.g. multiplanar reconstruction, maximum intensity projection, etc.) and a description of the purpose of each function

For systems with spectroscopy capabilities, the following additional information should be included:

i. Resonant nuclei
j. Compounds and tissues of interest
k. Description of specialized spectroscopic hardware (e.g. transmitter and coils)
l. Description of specialized spectroscopic software (e.g. localization and postprocessing)
m. Shimming techniques
n. Solvent suppression methods

o. Peak assignment methods
p. Signal enhancement techniques (e.g. proton decoupling)
q. Acquisition times

2. Safety

A summary of recommendations relating to the safety characteristics of MRDDs is contained in Attachment A. The following descriptive parameters relating to the safety of the device should be provided:

a. Static field strength
b. Peak and A-weighted acoustic noise
c. Description of operational modes of system
    i. Safety parameter displays
    ii. Operating mode access requirements
a. Maximum SAR for each transmit coil
b. Maximum dB/dt and gradient coil dimensions
c. Potential emergency conditions and means provided for shutdown
d. Biocompatibility of materials (new material or invasive use)

3. System Modifications and New Components

Submissions for system modifications should identify the system being modified and provide a list and description of all significant hardware and software changes. Modifications that influence safety or performance characteristics should be clearly identified. Also, any changes in the items listed above as provided in the previous premarket notification for the system should be identified.

Submissions for new components, accessories or software should identify the systems for which the components or accessories are intended, and provide a description of the functions and technological characteristics of each component or accessory. Any applicable information in the listing above for specific types of components, accessories or software should be included. In all cases any new technological characteristics should be explained, and pertinent literature references should be included.

4. Drug or Biologic Components

Submissions should clearly state if a drug (e.g. contrast agent) or biologic is utilized in conjunction with the device (e.g. sequence) for which clearance is being sought. In cases where a drug or biologic is utilized, a package insert or other clear statement of its approved use should be included. The intended use of the device must be consistent with the approved use of the drug or biologic with which it is to be used.

D. Laboratory Testing

Testing to all applicable NEMA standards (listed in Section III.C.1 above) or equivalent, should be conducted for each new system, component or modification. In each case, the pertinent test documentation specified in the NEMA standard should accompany the results.

The NEMA standards include descriptions of the test hardware, scan conditions and measurement procedures which are to be utilized. If alternate hardware, conditions or procedures are utilized, the reasons for their use should be clearly explained. Also, the alternate procedures should be described in detail and sample calculations provided.

1. Performance

a. Imaging

For a new whole body MRI system the following NEMA or equivalent tests should generally be conducted:

NEMA MS 1 - Signal-to-Noise Ratio - all volume coils provided with the system

NEMA MS 2 - Geometric Distortion - body coil

NEMA MS 3 - Image Uniformity - all volume coils provided with the system

NEMA MS 5 - Slice Profile/Thickness/Spacing - body coil

NEMA MS 6 - Characterization of Special Purpose Coils - all coils designed with spatially dependent sensitivity

The manufacturer should also provide a test of system high contrast spatial resolution using the body coil, spin echo sequence and suitable commercial phantom. This test should demonstrate that the spatial resolution is limited by the pixel size.

It is not necessary to repeat all of these tests for every new component, sequence or modification, since not all of these tests are affected by each change. The following are examples of tests that should be submitted for major component changes:

Magnet - SNR, geometric distortion, image uniformity, slice profile/thickness/spacing using body coil

Gradient System - geometric distortion, image uniformity, slice profile/thickness/spacing using body coil

RF Transmit Coils - SNR, image uniformity, slice profile/thickness/spacing

RF Receive Coils - SNR, image uniformity, characterization of special purpose coils

Sequences - SNR

Copies of the phantom images obtained in the course of these tests may be requested by the agency.

b. Spectroscopy

No standardized tests have been developed for magnetic resonance spectroscopy performance. The following types of tests are suggested for spectroscopy systems. Manufacturers should provide a description of their procedures for each test including the sequences and coils utilized, and the geometry and composition of all phantoms.

Spatial Localization Accuracy - comparison of desired and actual volume

Peak Assignment Accuracy - comparison of frequency assigned to peak and actual frequency

Spectral Resolution - full-width-half-maximum of peak

Signal-to-noise ratio - ratio of peak amplitude to standard deviation of background

Solvent suppression - ratio of area of solvent peak with and without suppression

Decoupling - comparison of SNR with and without decoupling

2. Safety

Static field strength, acoustic noise, dB/dt, specific absorption rate (SAR) and biocompatibility have been identified as MR safety concerns and data should be provided in appropriate cases as specified below.

a. Static Field Strength

No standardized method for determining static field strength has been developed by NEMA. However, since static field strength is evident from the frequency of operation of the system no measurements are required.

Marketing clearance has been granted to MRDDs up to 2 tesla. Submissions for systems operating above 4 tesla should include data demonstrating substantially equivalent safety.

b. Acoustic Noise

Acoustic noise is primarily influenced by the main magnet and gradients. Consequently, this test need only be done for new systems, or when the main magnet or gradients are modified. Both the peak impulse sound pressure level, L_{peak}, and the time integral of the A-weighted sound pressure level, L_{eq}, should be measured and reported in accordance with NEMA MS 4.

c. dB/dt

Since dB/dt is only affected by the gradients this parameter need only be measured for new systems, or when the gradient power supply or coils are modified. Measurement of dB/dt should be done in accordance with the FDA "Guidance Update for dB/dt" or the recent revision of NEMA MS 7. Both of these documents describe methods for determining d |B| /dt. NEMA MS 7 permits the measurement of the rate of change of the imaging component of the gradient, dB_z/dt, in cases where it is less than 20 T/sec.

d. RF Heating

SAR is determined by RF power and the RF coils used for transmission. Consequently, this parameter need only be measured for new systems or when the RF power supply or an RF transmit coil is modified. Whole body and head SAR should be measured and reported in accordance with NEMA MS 8 for cases where the body coil or head coil are used for RF transmission. For special purpose transmit/receive coils other than head coils, an estimate of local SAR should be provided. No standardized method has been developed for estimating local SAR. Sponsors should provide a detailed explanation of the method they use to measure or calculate local SAR, including copies of all relevant technical publications.

e. Biocompatibility

Biocompatibility data should be provided for devices which employ new materials which contact the skin, or that have invasive uses in accordance with ISO-10933, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing".

E. Clinical Testing

1. Sample Clinical Output

For a new system, sample clinical images should be provided for all receive coils. Each image should be accompanied by a description of the anatomical site and scan parameters.

For a new receive coil, sample clinical images in all three planes should be provided using a representative sequence.

For a new sequence, a sample clinical image should be provided using a representative coil.

2. Clinical Studies

Submissions which involve a new indication for use or a new claim should be accompanied by clinical study data to support the indication or claim. In some cases the agency may request that a manufacturer identify the clinical utility of a new device, and clinical data may be requested to demonstrate this clinical utility.

Past indications for MR devices have been for general diagnostic use (e.g. whole body imaging), for imaging a specific anatomic region, or for a specific disease. Almost all current MR systems have been cleared for general diagnostic use. Specialty coils have generally been cleared for use in a specific anatomical region. Only a few devices have been cleared for specific disease conditions (e.g. sequences for the detection of silicone leakage in the breast, diffusion weighted imaging for stroke detection).

Manufacturers who plan to market a product with a new indication for use, a new claim or where clinical utility may be in question are encouraged to contact the agency prior to submission of a 510(k). A pre-IDE submission may be useful in obtaining agency opinion regarding whether a study protocol will support the proposed indication or claim. Pre-IDE submissions were recently instituted by CDRH as a means for companies to obtain informal agency opinion regarding a study protocol. Reviews are generally completed within 60 days.

A special case where clinical data are required is for a gradient system that produces dB/dt values in excess of the current IEC limits for the normal operating mode (i.e. in excess of 20 T/sec for dB/dt pulses longer than 120 usec). In such cases the current "Guidance Update for dB/dt" dated October 11, 1995 recommends manufacturers conduct volunteer studies to determine if peripheral nerve stimulation is possible. If so, these studies should ascertain the level at which the operator should be notified of this possibility. In cases where a gradient system is modified, a manufacturer need not repeat these volunteer studies if patient response to the modifications can be reliably predicted based on the initial series of tests. As noted above, sections of the IEC standard relating to dB/dt are currently undergoing revisions. When these revisions have been completed it is anticipated that the revised IEC standard will replace the "Guidance Update for dB/dt".

F. Substantially Equivalent Devices

The sponsor must identify at least one class II legally marketed device to which equivalence is claimed. The substantially equivalent device may have been brought to market by the 510(k) process or may be a device described by one of the thirteen petitioners for reclassification (Federal Register, Vol. 53, No. 46, March 9, 1988). The following information relating to the predicate should be supplied:

1. Manufacturer, Tradename and 510(k) number,
2. A brief description of the important similarities and differences between the device and predicate,
3. A tabular comparison of features and specifications of the device and predicate,
4. Promotional material for the predicate and any other relevant labeling.

In cases where the features of a new product are not found in a single predicate, equivalence may be claimed to specific features in several different predicate devices. The important similarities and differences to be discussed should specifically address any differences in technology (hardware or software) and intended use.

G. Modified Devices

In accordance with 21 CFR 807.87(g), when a manufacturer intends to introduce a device into commercial distribution that has undergone a significant modification that could significantly affect the safety or effectiveness of the device, or the device is to be marketed for a new or different indication for use, a premarket notification must be submitted, including appropriate supporting data showing that the manufacturer has considered the consequences of the changes on the safety and effectiveness of the device.

Further information to assist manufacturers in deciding if a 510(k) is required is contained in 510(k) Memorandum #K97-1, entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device", dated January 10, 1997. This memorandum is available on the CDRH web site (http://www.fda.gov/cdrh/ode/510kmod.html). The types of changes addressed in this document include labeling changes, technology or performance specifications changes, and materials changes.

Under the New 510(k) Paradigm a "Special 510(k): Device Modification" may be submitted if the modification does not affect the intended use of the device or alter the fundamental scientific technology. Otherwise, a traditional 510(k) should be submitted. Under this option, the manufacturer should conduct a risk analysis and the necessary verification and validation activities to demonstrate that the design outputs of the modified device meet the design input requirements. After the manufacturer has completed this process, a "Special 510(k): Device Modification" may be submitted

H. Labeling

The labeling for an MR device consists of a Summary Specifications Sheet (i.e. a product data sheet), promotional material, instructions for use and site planning information.

CDRH has recently issued a draft label guidance entitled "Medical Device Labeling—Suggested Format and Content" which is available on the agency web site (http://www.fda.gov/cdrh/ode/labeling.html). Although this document is not in final form, the concepts described in this document should be utilized to the extent possible.

1. Summary Specifications Sheet

The Summary Specifications Sheet for a complete MR system should provide a description of the system applications, its configuration and components, and a list of parameters which characterize the device. This parameter list should include the following information:

a. Magnet - type (superconducting, resistive, permanent), field strength, shim method, shielding, weight, cryogen types and boiloff rates (if applicable), temporal field stability (ppm/hr), spatial homogeneity, bore dimensions, and extent of fringe fields (location of 5 gauss line)
b. Patient Space - size, ventilation, communications and lighting
c. Patient Table - dimensions, positioning accuracy and maximum weight
d. Gradients - amplitude, rise time and slew rate, shielding and cooling
e. RF System - amplifier peak rms power, preamplifier noise and bandwidth
f. Coils - list of coil types and their applications
g. Other Features - sequences, reconstruction speed**,** data storage (types and capacity), image processing features, image display and filming

2. Promotional Material

Claims contained in the promotional material should be consistent with the statements in the FDA "Indications for Use" form.

3. Users Manual

Instructions which should be included in the users manual for a MRDD are summarized in Attachment B.

4. Site Planning Information

The site planning information should contain the following recommendations and information in accordance with IEC 60601-2-33, Clause 6.8.3:

a. Audio and Visual Contact with Patient - Provision should be made in the design of the scan room and equipment to enable audio and visual contact with the patient during the examination.

b. Magnetic Fringe Field - Magnetic field plots should be provided which describe a typical installation. The plots should represent (1) the plane through the magnet isocenter, perpendicular to the main field, and (2) the plane through isocenter parallel to the main field and parallel to the floor for a horizontal field magnet, or in the direction of the longest magnet dimension for a vertical field magnet. Each plot should contain at least the iso-magnetic contours with values of 0.5 mT, 1 mT, 3 mT, 5 mT,

10 mT, 20 mT, 40 mT and 200 mT, as well as a distance scale and a superimposed outline of the magnet.

c. Liquid Cryogens and Cryogenic Gases - For superconducting magnets a venting system should be provided which is connected to outside the examination room and which is designed to withstand a quench. The oxygen concentration in accessible areas should not be allowed to go below acceptable levels. A means, e.g. a grid in the door, should be provided so that pressure build-up during a quench will not prevent the door from being opened if the venting fails.

d. Decay Characteristics of Magnetic Field - For superconducting and resistive magnets the decay characteristics of the magnetic field in the event of a quench or emergency field shut-down should be provided to enable the user to implement adequate life supporting and other safety procedures. These characteristics should indicate the time from activation of the emergency field shut-down unit to the moment at which the field strength in the center of the magnet has fallen to 20 mT. Instructions should also be given regarding where and how to install the actuator of the emergency field shut-down unit.

I. Software

General software information is contained in the "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices" issued on May 20, 1998.

The software for MR devices that is used to perform image reconstruction or image processing is considered to be a minor level of concern. New sequences would also generally be considered to be in this category. In such cases the following information is sufficient:

1. Software version or release number
2. A list and brief description of the functions performed by the software.
3. A description of the software development methods (e.g. list or diagram of steps in development and responsible departments).
4. A list of hazards related to the software functions, and the means taken to mitigate these hazards.
5. A description of the test procedures.
6. A certification by a responsible company official that the software information provided in this notification is correct, and that the same procedures will be used to retest and revalidate the software when it is revised.

Software which performs scan control functions, such as regulating the output of the RF or gradients or estimating the SAR or dB/dt, are considered moderate level of concern for those systems which are capable of reaching the first or second level controlled operating modes as described in IEC 60601-2-33. In such cases the agency will require a detailed description of the algorithms utilized to estimate SAR and dB/dt and the results of

laboratory measurements conducted in accordance with NEMA MS 7 and MS 8 (or equivalent methods).

Material previously submitted in a 510(k) that is common to more than one device, such as the description of the development process, need not be duplicated in subsequent submissions. Inclusion by reference is acceptable. However, all unique material specific to the device must be included.

Attachment A

Recommended Safety Characteristics for a Magnetic Resonance Diagnostic Device

The following are recommended safety characteristics for magnetic resonance diagnostic devices with respect to static field strength, RF heating (SAR), time varying magnetic fields (dB/dt) and acoustic noise. If levels cited in this guidance are exceeded, valid scientific evidence should be provided to establish the safety of operating at the intended levels.

A.1 Static Field Strength

Operation above 4 tesla should only be done under an approved Investigational Device Exemption (IDE).

Reference - "Guidance for Magnetic Resonance Diagnostic Devices - Criteria for Significant Risk Investigations" dated September 29, 1997

A.2 Acoustic Noise

A magnetic resonance diagnostic device should not produce noise having an unweighted peak sound pressure level higher than 140 dB. The method of measurement is specified in NEMA MS 4.

Reference - IEC Clause 26.

A.3 Operating Modes

Magnetic resonance diagnostic devices capable of values of dB/dt and/or SAR above the upper limits of the normal controlled operating mode should provide an indication of the mode defined by the maximum dB/dt value for the scan. The prediction of the value of SAR that will be used during the scan should be displayed on the operator's console.

If the value of dB/dt or SAR is such as to enter the first level controlled operating mode, a clear indication of this should be displayed on the console and a deliberate action of the operator should be required to start the scan. A record of the values should be inseparable from the image data.

A means should be provided to ensure that the values of dB/dt and SAR do not exceed the upper limits of the first level controlled operating mode. This means of control should be independent of the operator input regarding patient size, weight or position.

Equipment which is capable of operating in the second level controlled operating mode should have specific security measures which allow entry into this mode. These measures should indicate to the operator that the conditions are potentially hazardous and should not be applied for routine clinical use. The security measures should involve a key lock, combination lock, software password or other protective devices.

Reference - IEC Clause 51.101

A.3.1 Operating Mode Limits for RF Power

Whole body SAR is the value of SAR averaged over the entire body of the patient over any period of 15 minutes. The normal and first level controlled operating modes comprise values of whole body SAR not higher than 1.5 W/kg and 4 W/kg, respectively. The second level controlled operating mode comprises values above 4 W/kg.

Head SAR is the value of SAR averaged over the head of the patient for any period of 10 minutes. The normal operating mode comprises values of head SAR not higher than 3 W/kg. The second level controlled operating mode comprises values higher than 3 W/kg.

Local tissue SAR is the value of SAR averaged over any gram of tissue over any period of 5 minutes. The normal operating mode comprises values of local tissue SAR not higher than 8 W/kg in the head or torso, or 12 W/kg in the extremities. The second level controlled operating mode comprises values which exceed the normal operating mode.

There is no first level controlled operating mode for head or local tissue SAR.

Reference - IEC Clause 51.103. If revisions to this section of the IEC document are made, the levels specified above are to be adjusted to conform to the revised IEC levels.

The method of measurement of SAR is specified in NEMA MS 8.

As an alternative, evidence may be submitted that RF heating is insufficient to produce a core temperature increase in excess of 1 degree centigrade, or localized heating to greater than 38 degrees in the head, 39 degrees in the trunk and 40 degrees in the extremities.

A.3.2 Operating Mode Limits for Time Varying Gradients

The normal operating mode comprises peak values of dB/dt which are insufficient to produce peripheral nerve stimulation. The first level controlled operating mode comprises peak values of dB/dt which may produce peripheral nerve stimulation, but which do not produce severe discomfort or painful stimulation.

Systems which are incapable of producing peak values of dB/dt in excess of 20 T/sec are considered to be limited to the normal operating mode. Currently, manufacturers of systems which are capable of producing peak values of dB/dt in excess of 20 T/sec are

requested to conduct limited human volunteer studies (at least 20 subjects) to determine if stimulation is possible, and if so, the threshold value for mild peripheral nerve stimulation. If painful stimulation can be induced, the threshold of painful stimulation should also be determined. The upper limits of the normal and first level controlled operating modes should be set below the thresholds of mild peripheral nerve stimulation and painful stimulation, respectively.

References - “MRI Guidance Update for dB/dt” dated October 11, 1995 and NEMA MS 7

When revisions to IEC 60601-2-33 relating to dB/dt have been completed, the IEC provisions relating to dB/dt will replace the “MRI Guidance update for dB/dt”.

A.4 Emergency Shutdown

A magnetic resonance diagnostic device which utilizes a superconducting or resistive magnet should be provided with an emergency field shutdown unit . All devices should be provided with means to stop the scan by interrupting operation of the gradients and RF power.

Reference - IEC Clause 49.

Attachment B

Recommended User Instructions for a Magnetic Resonance Diagnostic Device

The users manual should contain the following instructions in accordance with IEC 60601-2-33, Clause 6.8.2:

B.1 Screening -

Recommendations should be included relating to screening of patients who could be at risk due to professional activity, past medical history, present medical state and physical environment of the equipment. The following classes of patients should be mentioned: patients for whom exams are contraindicated, patients having a likelihood of emergency medical treatment independent of the equipment, and patients having a likelihood of emergency treatment due to the elevated fields when operating in the first level controlled mode.

The Rationale (Annex BB) for this requirement states that magnetic resonance examination is usually considered to be contraindicated for patients who have metallic implants or electrically, magnetically or mechanically activated implants (e.g. cardiac pacemakers) because the magnetic and electromagnetic fields may produce strong attraction and/or torque to the implant or may interfere with the operation of these devices. This applies also to patients who rely on electrically, magnetically or mechanically activated life support systems.

Scanning patients with intracranial aneurysm clips is contraindicated unless the physician is certain that the clip is not magnetically active.

Examination requires particular caution in the following cases:

a. Patients with implanted surgical clips (haemostatic clips) or other ferromagnetic material,
b. Patients engaged in occupations or activities which may cause accidental lodging of ferromagnetic materials, or who may have imbedded metal fragments from military activities,
c. Neonates and infants (for whom data establishing safety are lacking),
d. Patients with permanent (tattoo) eye-liner or with facial make-up (severe eye irritation has been reported),
e. Patients with compromised thermoregulatory systems (e.g. neonates, low birth weight infants, certain cancer patients),
f. Patients with metallic implants, because they may cause artifacts in diagnostic images due to magnetic field distortion,
g. Patients with implanted prosthetic heart valves, and

h. Pregnant patients (the safety of magnetic resonance examination has not been completely established for embryos and fetuses).

B.2 Level of Supervision -

Recommendations should be provided to the user to establish a program for the supervision of patients appropriate to their conditions and the modes of operation of the equipment. The recommendations should state that all patients should receive at least routine monitoring (audio or visual contact). When operating in the first level controlled mode, medical supervision is to be provided. When operating in the second level controlled mode an approved investigational human studies protocol is needed.

In terms of the need for medical supervision, particular caution is required in performing examinations in the following cases:

a. Patients with greater than normal potential for cardiac arrest,
b. Patients who are likely to develop seizures, or claustrophobic reactions,
c. Decompensated cardiac patients, febrile patients, and patients with impaired ability to perspire,
d. Patients who are unconscious, heavily sedated or confused, and with whom no reliable communication can be maintained, and
e. Examinations which are carried out at room temperature above 24 degrees C or relative humidity above 60%.

B.3 Emergency Procedures -

Instructions should be included to the user to define and implement specific emergency medical procedures which take into account the high magnetic field, so that medical treatment can be given as soon as possible if the patient feels ill during the examination. These procedures should include a means to remove the patient rapidly from the field (using an emergency field shut-down unit if necessary).

B.4 Excessive Noise -

Instructions should state that hearing protection is required for patients if the equipment can exceed 99 dBA. Also, the noise level at the control panel should comply with local rules.

B.5 Controlled Access Area -

Instructions should state that it is necessary to establish a controlled access area such that outside this area the field does not exceed 5 gauss.

The size and shape of the area should be specified, accompanied by a sketch.

The need to establish adequate rules for controlling access to the controlled access area should be explained in terms of the potential risk from the attraction of objects containing iron or other magnetically active materials, or from torque on metallic materials, and the potential risk to persons inadvertently entering the area who may be affected by the possible dysfunction of their medical implants.

Recommendations should be given on how the controlled access area is to be indicated (e.g. markings, barriers or signs).

The controlled access area should be labeled “Danger - High Magnetic Field” at all entries.

Operators should be warned by appropriate signs about the presence of magnetic fields and their force and torque on magnetic materials, and that loose ferrous objects should be excluded.

Access control and labeling of fringe fields should be carried out by the user. For safe operation of pacemakers a 5 gauss limit should be kept.

A list of equipment and tools recommended for use in the controlled access area should be provided by the manufacturer. For all equipment or tools listed, a description should be given of any special measures needed for their installation, or any special precautions which should be taken regarding their use.

It should be clearly stated that peripheral equipment, including patient monitoring, life support and emergency care equipment, which are not recommended for use in the controlled access area, may be disturbed by the RF field or magnetic fringe field, and this equipment may also disturb the scanner.

B.6 Liquid Cryogens -

Instructions should require adequate provisions for the supply of cryogens, recommend that refilling be performed by trained personnel, provide information on maintenance and inspection of the magnet and minimum cryogen levels, and require that frequent checks of the cryogen level be carried out by the user.

Information should be given on potential hazards and proper handling of cryogens including protective clothing, procedures to be used after gas release, precautions against lack of oxygen, use of non-magnetic containers for cryogens, and procedures to be followed if flammable materials are found near cryogen containers.

B.7 Operating Modes -

Information should be provided on the meaning of the operating modes, and that the level of exposure and need for patient monitoring should be based on medical judgement regarding risk vs. benefit.

Instructions should state that only routine monitoring is needed in the normal mode.

For equipment which can operate in the first level controlled mode, the instructions should describe the indications displayed by the system and deliberate actions required by the operator, and should state that medical supervision is required.

For equipment which can operate in the second level controlled mode security measures should be provided to prevent unauthorized operation. Operation in this mode is only permitted under an approved human studies protocol.

Information should be provided concerning gradients and RF fields.

For equipment which operates in the first or second level mode for dB/dt the instructions should explain the possible effects on the peripheral nervous system and heart, the range of values of dB/dt which the system can generate, and note that the equipment will indicate when dB/dt exceeds the normal mode.

Instructions should explain that the definitions of the operating modes for whole-body SAR assume that the examination room temperature is not more than 24 degrees C and the relative humidity is not more than 60%, and that for higher temperature and humidity the limits in the definitions of the operating modes for whole-body SAR should be reduced. The relationship between ambient temperature, relative humidity and SAR should be described in the instructions.

For equipment which operates in the first or second level mode for SAR, instructions should explain the effects on patients who may have reduced thermoregulatory capability and increased sensitivity to elevated body temperature (e.g. febrile and cardiac decompensated patients, those with compromised ability to perspire and pregnant women).

The range of values of SAR which can be generated by the system should be given along with the accuracy of the predicted SAR.

B.8 Auxiliary Equipment -

Instructions should warn the patient that auxiliary equipment, such as patient monitoring and gating equipment and RF coils, that have not been specifically tested and approved for use in the magnetic resonance environment, may result in burns or other injuries to the patient.

Instructions should also warn that even auxiliary devices labeled as compatible with MR equipment may be capable of causing injury if the manufacturer's instructions, especially with respect to electrical lead positioning, are not followed.

B.9 Emergency Shutdown -

Instructions should state when and how the emergency field shutdown unit should be operated. Examples of situations which require emergency field shut-down should be provided.

B.10 Fire Precautions -

Instructions should recommend that fire precautions should be discussed with the local fire department and that emergency procedures should be established.

In addition, the FDA recommends that the following information be included in the manual:

B.11 Prescription Use -

A statement should be included which states that "Federal law restricts this device to sale, distribution and use by or on the order of a physician", and "The device is limited by Federal Law to investigational use for indications not in the Indications Statement".

B.12 Recommended Training -

Instructions should describe the recommended training needed by the physician to interpret the images and by the operator to learn to operate the device safely and effectively.

B.13 Quality Assurance -

Instructions should describe the quality assurance procedures recommended for the user, including a detailed specification of all phantoms to be used.

B.14 Maintenance -

Instructions should include the recommended maintenance schedules for the equipment, including a designation of whether they should be performed by the user or company service personnel.

B.15 Cleaning and Disinfection -

Instructions for cleaning and disinfection should be included for components which come into contact with the patient or are intended for invasive use, and are reusable (e.g. endocavitary coils).