This guidance was written prior to the February 27, 1997 implementation of FDA's Good Guidance Practices, GGP's. It does not create or confer rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both. This guidance will be updated in the next revision to include the standard elements of GGP's.

MRI Guidance Update for dB/dt 4-21-95

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The Center for Devices and Radiological Health (CDRH) has not officially updated the "Guidance for the Content and Review of a Magnetic Resonance Diagnostic Device 510(k) Application" since this document was first released on August 2, 1988. Since then, a number of developments have occurred in magnetic resonance diagnostic devices which require revision of the original Guidance.

An issue of immediate concern is the development of fast imaging methods, such as echo planar techniques. As a result of the increase in gradient strength and dB/dt associated with these techniques, 510(K) notifications have been submitted for MRI devices which produce dB/dt values exceeding current Guidance levels of concern. The Guidance states that if levels of concern are exceeded, a manufacturer must provide valid scientific evidence to establish the safety of operating at the intended levels. However, no specific requirements regarding evidence of safety beyond the levels of concern are provided by the Guidance.

This document contains draft revisions of the MRI Guidance relating to dB/dt beyond the current levels of concern, and the rationale for these changes. We would like to obtain the opinion of MRI manufacturers, users, technical experts and other interested parties before finalizing these changes, and welcome any individual or collective comments you may wish to submit. Draft revisions relating to other current issues, such as interventional MRI, will be circulated in the near future for comment.

I. Background

The original MRI guidance provided three options for manufacturers to show that the gradient rate of change is below a level of concern:

a) demonstrate that the maximum dB/dt is 6T/sec or less,

b) for axial gradients demonstrate that
dB/dt < 20 T/sec for tau > 120 usec,
< 2400/tau T/sec for 12 usec < tau < 120 usec

< 200 T/sec for tau < 12 usec

where tau is the pulse width in microseconds of a rectangular dB/dt pulse or the half period of a sinusoidal dB/dt pulse.

For transverse gradients dB/dt was permitted to be three times the above limits for axial gradients.

c) demonstrate that the gradient rate of change is not sufficient to cause peripheral nerve stimulation by an adequate margin of safety (at least a factor of three).

The guidance did not specify a method for measuring dB/dt. However, the NEMA MRI Technical Committee later developed a draft measurement procedure, which has also been incorporated into the draft standard IEC-601-2. This procedure only describes the measurement of dB_z/dt, which is the component necessary to MR imaging if the static field is in the z direction.

As dB/dt levels have risen it has become increasingly difficult for CDRH to evaluate whether new systems will cause peripheral nerve stimulation. The difficulties have arisen both from the lack of sufficient neurostimulation data, and uncertainties in measurement methodology. The only published study of threshold values over a range of pulse durations is that of Budinger et al. (J. Comput. Assist. Tomogr., 15(6):609-614). Also, Budinger's study and other research has revealed that components other than dB_z/dt may be principally responsible for stimulation. Thus, there is a need for alternative methods of characterizing gradient fields.

Under these circumstances the Agency has attempted to make marketing clearance decisions on a case-by-case basis. However, a more standardized method is needed so that manufacturers have a clear indication of Agency requirements prior to preparing their submissions.

II. Proposed Revisions

A. Laboratory Data

1. Requirements

Manufacturers of systems which produce dB/dt values in excess of current levels of concern would be required to provide an estimate of the maximum value of $|B|$ produced by each gradient coil (x, y and z) which could be experienced by a patient, where $|B|$ denotes the magnitude of the vector sum of the field components (B_x, B_y, and B_z). The location of

the maximum value of |B| for each gradient coil, and the values of the individual field components at that location would be reported. Samples of the field plots used in these determinations would be included in the submission.

Manufacturers would provide worst case sequence timing information and utilize this to estimate the shape and amplitude of the worst case d|B|/dt pulse for each gradient coil. Measurements would be made and submitted to verify these estimates.

2. Rationale

The purpose of the laboratory data would be to characterize the magnetic field produced by each gradient coil, including the components which are not related to imaging. The field plots needed to do this are generally available as part of the coil design process, and should be readily available to manufacturers. The volume to be examined for maximum |B| would be limited to regions which could be occuppied by a patient.

Studies of peripheral nerve stimulation have been reported in terms of magnetic field strength (flux density), time rate of change of magnetic field (dB/dt) and pulse duration. The required laboratory data is intended to provide all of this information, which will facilitate relating the characteristics of the system under evaluation to the available peripheral nerve stimulation data. This is not possible with the dB_z/dt data provided by the NEMA test.

A limitation of the proposed laboratory data requirement is that it would not provide information to characterize the simultaneous operation of the gradient coils, which was addressed by the NEMA method. Comments are specifically solicited regarding the importance of this limitation, and suggested alternative or additional data which would compensate for this deficiency.

B. Clinical Studies

1. Requirements

Manufacturers of systems which produce values of dB/dt in excess of current levels of concern would be required to submit limited volunteer studies of peripheral nerve stimulation using equipment which is as similar as possible to the system submitted for marketing clearance. The studies would consist of at least 20 volunteers and would include conditions (patient position and scan parameters) which produce the maximum dB/dt based on laboratory data.

For those systems which are found to produce stimulation in these limited volunteer studies, more extensive data would be required. The purpose of these additional studies would be to provide a preliminary estimate of the relationship between operating parameters (e.g. dB/dt pulse duration and amplitude) and the percentage of patients which experience peripheral nerve stimulation. The effect of different patient positions and gradient directions would also be examined in these additional studies.

2. Rationale

The purpose of the limited volunteer studies would be to provide information on physiological response to supplement the laboratory data required above. For those interested in statistics, there is a 95% chance that the true stimulation rate is below 14% if no volunteers out of the twenty are stimulated. However, a statistical model may not be appropriate here.

The limited volunteer studies, laboratory data, previously published studies, and any other information available to the Agency would be used to decide if the system has the potential for inducing stimulation. Systems which are judged to have the potential for producing stimulation would be subject to labeling requirements described in Section C below.

For those systems found to be capable of producing stimulation in the limited volunteer studies, the additional studies to determine the relationship between operating parameters and frequency of stimulation would be used to support the operational characteristics of the devices provided for operator notification/deliberate action described in Section D below.

The intent here is to place the labeling requirements (i.e. patient information/reporting) on all systems which could possibly produce stimulation, even if it is not observed in the limited volunteer studies. The reason for this is that the limited studies will not be large enough to determine if a device produces stimulation in a very small percentage of patients. If it turns out that stimulation is not produced in clinical use, a company could ask that the labeling requirements be removed.

The operator notification/deliberate action requirements would be initially limited to systems which produce stimulation in the limited volunteer studies.

C. Labeling

1. Requirements

a. Manufacturers of systems which have the potential for producing peripheral nerve stimulaton would be required to include instructions to the operator which describe the types of imaging techniques available on the system (e.g. echo planar) which may potentially produce this phenomenon. A description of the sensation of peripheral nerve stimulation would be included in these instructions. Instructions describing the operation of any related special equipment features (e.g. monitors or displays) would also be required.

b. The operator would also be instructed that when techniques which may produce peripheral nerve stimulation are utilized he should:

i) inform the patient that peripheral nerve stimulation may occur,

ii) describe the nature of the sensation to the patient,

iii) instruct patients not to clasp their hands, since this may create a conductive loop which will increase the possibility of stimulation,

iv) maintain constant contact with the patient,

v) terminate the scan if the patient reports or appears to be experiencing stimulation, and

vi) complete a report of any incidents of stimulation and the associated circumstances (imaging parameters, level of stimulation, etc.) and submit this report immediately to the company.

2. Rationale

a. The purpose of the items relating to operator information is to familiarize the operator with the phenomenon of peripheral nerve stimulation, the general types of scans which may produce stimulation, and the related safety features of the system. This is necessary since equipment which can produce stimulation is new to the market and operators have little or no prior experience.

It is felt that a general description of the types of scan which may produce stimulation will be more meaningful to the operator than a technical description of dB/dt levels. However, additional technical information may be included at the discretion of the company.

The description of the types of techniques which may produce stimulation should include all possible techniques, which may, in the company's experience and the Agency's judgement, have any chance of producing stimulation. The reminder to the operator provided by the device (Section D below) would address those operating conditions under which stimulation is considered more likely.

b. The purpose of items i) and ii) is to ensure that the patient is informed regarding the possibility of peripheral nerve stimulation, so that he or she will not be startled. This information could conveniently be given to patients during positioning, when they are told not to clasp their hands (item iii).

Item iv) requiring the operator to maintain contact with the patient is intended to ensure that the operator watches the patient and is not performing other tasks while the scan is in progress.

Item v) requiring the operator to terminate the scan if the patient reports or appears to be experiencing stimulation is intended to ensure patient safety. The operator would be permitted to adjustment scan parameters to settings which produce no stimulation.

The purpose of the reports required under item vi) is to allow the company and FDA to monitor the clinical experience with the device. This will enable an assessment of the adequacy of any monitor settings, and evaluation of how system engineering parameters relate to patient physiological response. After the system has been in use for some length of time it may be appropriate to suspend the reporting requirement, or limit it to more serious cases (e.g. incidents where pain is induced). Companies would be allowed to request revision of their reporting criteria as an amendment to their 510(k).

In conjunction with the stimulation reports, manufacturers should also keep track of the total number of patients who are imaged with procedures which have the potential for producing stimulation. This will enable an estimate of the percentage of patients who experienced stimulation. Means for compiling this information could be written into the system software.

D. Device Characteristics

1. Requirements

Manufacturers of systems which are known to produce peripheral nerve stimulation would be required to provide

means to notify the operator when there is a possibility of peripheral nerve stimulation. Deliberate action by the operator would be necessary to proceed with the scan.

2. Rationale

It is felt that when operating parameters reach a level where peripheral nerve stimulation becomes a real possibility, the operator should be notified, and should be asked to acknowledge this notification. This would serve as a backup reminder to the operator to provide the required instructions to the patient listed in the labeling requirements above.

The intent here is to establish a requirement similar to that of the current draft of IEC-601-2, but at a level above the current upper limit of the IEC normal operating mode. Based on most recent studies, the current IEC limits appear to be too conservative. This will lead to excessive repetition of the notification, which may cause some operators to ignore it. Also, the IEC levels could require some systems to have unnecessary features which may add to their cost.

The level at which peripheral nerve stimulation would be considered a possibility should be conservative, i.e. where fewer than 1% of patients experience this effect. The system parameters associated with this level would be determined based on premarket testing and the reports received after the product was placed in general clinical service.