Draft Guidance for Industry and FDA Staff

Class II Special Controls Guidance Document: Full Field Digital Mammography System

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.
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Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Alternatively, electronic comments may be submitted to http://www.fda.gov/dockets/ecomments. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

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When final, this document will supersede Guidance for the Premarket Application for Digital Mammography Systems, issued February 16, 2001

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, and Radiological Devices
Office of Device Evaluation

Division of Imaging and Applied Mathematics
Office of Science and Engineering Laboratories

Preface

Additional Copies

Additional copies are available from the Internet at: http://www.fda.gov/cdrh/ode/guidance/1616.html. You may also send an e-mail request to dsmica@fda.hhs.gov to receive an electronic copy of the guidance or send a fax request to 240-276-3151 to receive a hard copy. Please use the document number (**1616**) to identify the guidance you are requesting.

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Class II Special Controls Guidance Document: Full Field Digital Mammography System

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

1. Introduction

This draft guidance document was developed as a special controls guidance to support the reclassification of the Full Field Digital Mammography (FFDM) System from class III (premarket approval) to class II (special controls). The device is intended to produce digital x-ray images of the breast. This draft guidance will be issued in conjunction with a Federal Register notice announcing the proposal to reclassify this device type. This guidance is issued for comment purposes only. If a final rule to reclassify this device type is not issued, this guidance document will not be issued as a special control.

Following the effective date of a final rule reclassifying the device, any firm submitting a 510(k) for an FFDM system will need to address the issues covered in this special control guidance. However, the firm need only show that its device meets the recommendations of the guidance or in some other way provides equivalent assurances of safety and effectiveness.

The Least Burdensome Approach

This draft guidance document reflects our careful review of what we believe are the relevant issues related to an FFDM System and what we believe would be the least burdensome way of addressing these issues. If you have comments on whether there is a less burdensome approach, however, please submit your comments as indicated on the cover of this document.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are

cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

2. Background

FDA believes that special controls, when combined with the general controls, will be sufficient to provide reasonable assurance of the safety and effectiveness of an FFDM system. Thus, a manufacturer who intends to market a device of this generic type must (1) conform to the general controls of the Federal Food, Drug, and Cosmetic Act (the Act), including the premarket notification requirements described in 21 CFR 807 Subpart E, (2) address the specific risks to health associated with FFDM Systems identified in this guidance, and (3) obtain a substantial equivalence determination from FDA prior to marketing the device. (See also 21 CFR 807.85.)

This special control guidance document identifies the classification regulation and product code for the FFDM System (please refer to **Section 4. Scope)**. In addition, other sections of this special control guidance document list the risks to health identified by FDA and describe measures that, if followed by manufacturers and combined with the general controls, will generally address the risks associated with FFDM Systems and lead to a timely 510(k) review. This document supplements other FDA documents regarding the specific content requirements of a premarket notification submission. You should also refer to 21 CFR 807.87, the guidance, **Format for Traditional and Abbreviated 510(k)s**,[1] and the section of CDRH's Device Advice, **Premarket Notification 510(k)**.[2]

As described in the guidance entitled, **The New 510(k) Paradigm - Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications; Final Guidance**,[3] a manufacturer may submit a Traditional 510(k) or has the option of submitting either an Abbreviated 510(k) or a Special 510(k). FDA believes an Abbreviated 510(k) provides the least burdensome means of demonstrating substantial equivalence for a new device, particularly once FDA issues a class II special controls guidance document. Manufacturers considering certain modifications to their own cleared devices may lessen the regulatory burden by submitting a Special 510(k).

3. The Content and Format of an Abbreviated 510(k) Submission

An Abbreviated 510(k) submission must include the required elements identified in 21 CFR 807.87, including the proposed labeling for the device sufficient to describe the device, its intended use, and the directions for its use. In an Abbreviated 510(k), FDA may consider the contents of a summary report to be appropriate supporting data within the meaning of 21 CFR

[1] http://www.fda.gov/cdrh/ode/guidance/1567.html.
[2] http://www.fda.gov/cdrh/devadvice/314.html.
[3] http://www.fda.gov/cdrh/ode/parad510.html.

807.87(f) or (g); therefore, we recommend that you include a summary report. The report should describe how you may have incorporated the recommendations of this special control guidance document during the device development and testing. The report should also briefly describe the methods or tests used and a summary of the test data or description of the acceptance criteria applied to address the risks identified in this document, as well as any additional risks specific to your device. This section suggests information to fulfill some of the requirements of section 807.87 as well as some other items that we recommend you include in an Abbreviated 510(k).

Coversheet

The coversheet should prominently identify the submission as an Abbreviated 510(k) and cite the title of this special controls guidance document.

Proposed Labeling

Proposed labeling should be sufficient to describe the device, its intended use, and the directions for its use. (Please refer to **Section 10. Labeling** for specific information that should be included in the labeling for devices of the type covered by this guidance document.)

Summary Report

We recommend that the summary report contain the following information.

Description of the Device and its Intended Use

We recommend that you describe the performance specifications and, when appropriate, include detailed, labeled drawings of the device. (Please refer to **Section 5**. **Device Description** for specific information that we recommend you include in the device description for devices of the type covered by this guidance document.) You should also submit an "indications for use" enclosure.[4]

Description of Device Design Requirements

We recommend that you include a brief description of the device design requirements.

Identification of the Risk Analysis Method

We recommend that you identify the risk analysis method(s) you used to assess the risk profile, in general, as well as the specific device's design and the results of this analysis. (Please refer to **Section 6. Risks to Health** for the risks to health generally associated with the use of this device that FDA has identified.)

[4] Refer to http://www.fda.gov/cdrh/ode/indicate.html for the recommended format.

Discussion of the Device Characteristics

We recommend that you discuss the device characteristics that address the risks identified in this class II special controls guidance document, as well as any additional risks identified in your risk analysis.

Description of the Performance Aspects

We recommend that you include a brief description of the test method(s) you have used or intend to use to address each performance aspect identified in **Section 8** of this class II special controls guidance document. If you follow a suggested test method, you may cite the method rather than describing it. If you modify a suggested test method, you may cite the method but should provide sufficient information to explain the nature of and reason for the modification. For each test, you may either (1) briefly present the data resulting from the test in clear and concise form, such as a table, **or** (2) describe the acceptance criteria that you will apply to your test results.[5] (See also 21 CFR 820.30, Subpart C - Design Controls for the Quality System Regulation.)

Reliance on Standards

If any part of the device design or testing relies on a recognized standard, we recommend that you include either:

- a statement that testing will be conducted and meet specified acceptance criteria before the device is marketed or
- a declaration of conformity to the standard.[6]

Because a declaration of conformity is based on results from testing, we believe you cannot properly submit a declaration of conformity until you have completed the testing the standard describes. For more information, please refer to section 514(c)(1)(B) of the Act and the FDA guidance, **Use of Standards in Substantial Equivalence Determinations; Final Guidance for Industry and FDA**.[7]

If it is not clear how you have addressed the risks identified by FDA or additional risks identified through your risk analysis, we may request additional information about aspects of the device's performance characteristics. We may also request additional information if we need it to assess the adequacy of your acceptance criteria. (Under 21 CFR 807.87(l), we may request any

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[5] If FDA makes a substantial equivalence determination based on acceptance criteria, the subject device should be tested and shown to meet these acceptance criteria before being introduced into interstate commerce. If the finished device does not meet the acceptance criteria and, thus, differs from the device described in the cleared 510(k), FDA recommends that submitters apply the same criteria used to assess modifications to legally marketed devices (21 CFR 807.81(a)(3)) to determine whether marketing of the finished device requires clearance of a new 510(k).

[6] See Required Elements for a Declaration of Conformity to a Recognized Standard (Screening Checklist for All Premarket Notification [510(k)] Submissions), http://www.fda.gov/cdrh/ode/reqrecstand.html

[7] http://www.fda.gov/cdrh/ode/guidance/1131.html

additional information that is necessary to reach a determination regarding substantial equivalence.)

As an alternative to submitting an Abbreviated 510(k), you can submit a Traditional 510(k) that provides all of the information and data required under 21 CFR 807.87 and described in this guidance. A Traditional 510(k) should include all of your methods, data, acceptance criteria, and conclusions. Manufacturers considering certain modifications to their own cleared devices should consider submitting Special 510(k)s.

The general discussion above applies to any device subject to a special controls guidance document. The following is a specific discussion of how you should apply this special controls guidance document to a premarket notification submission for an FFDM System.

4. Scope

The scope of this document is limited to FFDM systems.[8] If the reclassification is finalized, it will be codified at 21 CFR 892.1715, and the device will have the product code MUE.

> **21 CFR 892.1715 – Full field digital mammography system.**
>
> *(a) Identification*. A full field digital mammography system is a device intended to produce full field digital x-ray images of the breast. This generic type of device may include one or more of the following: digital mammography software, full field digital image receptor, acquisition workstation, and signal analysis programs.
>
> *(b) Classification*. Class II (special controls). The special control for the device is FDA's guidance document entitled "Class II Special Controls Guidance Document: Full Field Digital Mammography System." See § 892.1(e) for the availability of this guidance document.

Mammographic x-ray producing equipment (x-ray generator, x-ray control, x-ray tube, collimator, beam filter, and breast compression system) are regulated under 21 CFR 892.1710 as class II devices (special controls).

This guidance does not cover display accessories to an FFDM System, i.e., softcopy output devices (monitors), hardcopy output devices (printers), and review workstations. These devices are classified as class II (see 21 CFR 892.2040 and 21 CFR 892.2050).[9]

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[8] FFDM systems must also meet the applicable requirements of 21 CFR Part 900, including 900.12(b) and 21 CFR 900.12(e).

[9] For softcopy (monitors) and hardcopy (printers) output devices, image review manipulation software, and review workstations, please refer to the FDA guidance: **Display Accessories for Full-Field Digital Mammography Systems - Premarket Notification (510(k)) Submissions** http://www.fda.gov/cdrh/ode/guidance/1617.html.

5. Device Description

You should identify your device by the regulation (21 CFR 892.1715) and product code (MUE) described in **Section 4. Scope**. We recommend that you provide a description of all components of the FFDM system with associated pictorial representations of the layout, interconnection of the different components, and geometric characteristics, including the following:

- source to image receptor distance (SID);
- source to patient support device distance; and
- alignment to chest wall.

We also recommend you provide a description of each functional component of the FFDM system, including the x-ray unit, the x-ray scatter grid, the breast compression system, the detector, and the image acquisition workstation, as described below.[10,11]

X-ray Unit

For the x-ray tube, we recommend you describe the following:

- target materials;
- x-ray filter materials type and thickness;
- window material and thickness; and
- focal spot sizes.

For the x-ray generator, we recommend you describe the following:

- trade name if manufactured by a third party;
- type, range, and accuracy of technique factors (x-ray tube voltage, x-ray tube current, exposure time, and mAs) for all combinations of anode materials and focal spot sizes, as appropriate; and
- automatic exposure control (AEC) systems.

X-ray Scatter Grid

For the x-ray scatter grid, we recommend you describe the following:

- grid ratio; and

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[10] Radiographic equipment used with FFDM systems must comply with 21 CFR 1020.30 and 21 CFR 1020.31 in accordance with 21 CFR 900.12(b).

[11] Image output devices used with a FFDM system are classified as one of the device types described in 21 CFR 892.2040 and 21 CFR 892.2050. The guidance, **Display Accessories for Full-Field Digital Mammography Systems-Premarket Notification 510(k) Submissions**, available at http://www.fda.gov/cdrh/ode/guidance/1617.html, describes our recommendations for image output devices used with FFDM systems.

- Bucky factor, whether stationary or reciprocating.

Breast Compression System

For the breast compression system, we recommend you describe the following:

- paddle types, sizes, geometries, and materials;
- power-driven, hands-free compression control system (if applicable);
- fine adjustment compression control system;
- compression override capability;
- continuous display of force capability;
- manual or automatic emergency compression release features; and
- maximum compression force.

Detector

For the x-ray detector, we recommend you describe the following:

- type such as thin-film transistor (TFT) array, or array of charge coupled devices (CCDs) optically coupled to thallium activated cesium iodide (CsI:Tl) scintillator plate;
- x-ray interaction materials and thicknesses, or the real mass density of the materials;
- interaction efficiency;
- scanning rate (for systems using a slot scanning system);
- data correction algorithms; and
- relevant temporal characteristics, such as decay rate of the phosphor afterglow for indirect detectors, latent image decay, and ghosting resulting from storage phosphor and charge trapping.

For detectors intended to be used with conventional mammographic x-ray systems, as direct replacements for the screen-film cassette (such as computed radiography (CR) plate/reader/display systems), we recommend you provide a description of the x-ray system characteristics and performance needed to function properly with the digital image receptor.

Image Acquisition Workstation

For the image acquisition workstation, we recommend you provide the specifications of the computer operating system. For the associated image acquisition software, we recommend you describe the analog to digital conversion, including bit depth, matrix size, and pixel width.

For image processing algorithms, we recommend you provide:

- the methods for assessing and choosing among the available image processing algorithms (i.e., suitability and selection);

- name and characteristics of the platform for the software; and
- description of the algorithm, including detailed flowcharts.

For each step of your algorithm, we recommend you describe the assessment methodology and indicate whether readers were involved, the number of readers who participated, and their qualifications.

In addition, we recommend you describe the algorithm and the assessment methodology used for the image acquisition and processing for any special views available on your FFDM system, such as magnification view or spot compression view. For patients with breast implants, we recommend you describe how the algorithm assures the image quality.

Principles of Operation

The principles of operation should discuss the methods used to select the technique factors on the x-ray system, including the following:

- rationale for using any automatic exposure control (AEC) systems for controlling the x-ray exposure;
- technique chart for manual exposures; and
- a description of how the exposure factors are controlled and limited by the system.

We also recommend you describe the method of controlling breast compression, including how the level of compression is displayed and limited.

In addition to the above, we recommend that you submit the information for software-controlled devices described in **Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices**[12] and in **Guidance for Off-the-Shelf Software Use in Medical Devices; Final**.[13] The kind of information we recommend you submit is determined by the "level of concern," which is related to the risks associated with software failure. The level of concern for a device may be minor, moderate, or major. The level of concern for an FFDM system is usually moderate.

We also recommend you provide a summary of the training program for mammography facility staff.

6. Risks to Health

In Table 1 below, FDA has identified the risks to health generally associated with the use of the device type addressed in this document. The measures recommended to mitigate these identified risks are given in this guidance document, as shown in the table below. We recommend that you also conduct a risk analysis, before submitting your 510(k), to identify any other risks specific to

[12] http://www.fda.gov/cdrh/ode/guidance/337.html.
[13] http://www.fda.gov/cdrh/ode/guidance/585.html.

your device and include the results of this analysis in your 510(k). If you elect to use an alternative approach to address a particular risk identified in this document, or have identified risks additional to those in this document, then you should provide sufficient detail to support the approach you have used to address that risk.

Table 1: Risks to Health Identified for the FFDM System Device

Identified Risk	Recommended Mitigation Measures
Electrical hazards	7. Electrical Safety
Corrupted or non-diagnostic image	8. Physical Laboratory Testing 9. Clinical Studies
Incorrect patient positioning	9. Clinical Studies
Excessive x-ray exposure	8. Physical Laboratory Testing
Excessive breast compression	8. Physical Laboratory Testing
Infection, skin irritation	10. Labeling

7. Electrical Safety

We recommend that you evaluate the electrical safety of your device. We recommend that you evaluate your device as described in one of the following standards or equivalent methods.

- International Electrotechnical Commission (IEC) 60601-1 Medical Electrical Equipment – Part 1: General Requirements for Safety
- Underwriters Laboratories Inc. (UL) 2601-1 Amendment 1 Medical Electrical Equipment: General Requirements for Safety

8. Physical Laboratory Testing

As part of the physical laboratory testing, we recommend you describe the following:

- all phantoms;
- the test protocols; and
- the FFDM system settings used to determine the imaging performance.

If the test object (phantom) is readily available in the imaging community (e.g., Society of Motion Picture and Television Engineers (SMPTE) test pattern), a reference to the test object is generally appropriate.

We recommend you report all exposure techniques, i.e., x-ray filtration, kVp, and mAs settings used in your imaging performance testing.

We recommend you provide the uncertainty (standard deviation or 95% confidence intervals) on each measure used to assess the imaging performance. If applicable, we recommend you report the trade name, characteristics, and accuracy of all proprietary measuring instruments used for performing the quantitative tests.

We also recommend you assess the imaging characteristics of your system as described below. We recommend you provide quantitative data, representative graphs when applicable, and a comparison of these results to the imaging characteristics of a legally marketed FFDM device.

Quantum Limited Operation

For quantum limited performance, i.e., noise added by the FFDM system does not exceed the quantum noise when operated in the normal range of exposures, we recommend you provide data showing that the device operates in a quantum limited mode at the exposure levels typical for mammography. If not quantum limited, we recommend you provide the range of exposures where quantum limited operation is not achieved.

Sensitometric Response

We recommend you provide quantitative data on the sensitometric response of the image acquisition system, i.e., the digital value versus radiation exposure curve.

Spatial Resolution

We recommend you provide a quantitative measure of the spatial resolution properties of the image acquisition system, i.e., the modulation transfer function (MTF).

Signal-to-Noise Ratio Transfer

We recommend you provide a quantitative measure of the efficiency of signal-to-noise ratio (SNR) transfer of the image acquisition system. This is measured by using the detective quantum efficiency (DQE) as a function of spatial frequency. For systems using flat-field correction, we recommend you measure the impact of flat-field correction on DQE and noise equivalent quanta (NEQ). We recommend you perform SNR analysis using different acrylic or other tissue-equivalent phantom thicknesses for the anode and filter combinations available and at different exposure levels, i.e., kVp and mAs settings that result in exposure levels covering the range normally encountered in mammography.

Dynamic Range

We recommend you provide a quantitative measure of the dynamic range of the image acquisition system. This is measured by using the NEQ, DQE, or both, as a function of spatial frequency and radiation exposure level. We recommend you present these measurements at multiple exposure levels typical for mammography.

Phantom Testing

We recommend you perform the image quality factor (IQF) evaluation as described in Thomas, *et al*.[14] and calculate the IQF at a diameter no larger than 1.8 mm and thicknesses no larger than 0.25 μm. According to Thomas, the k factor is the product of the thickness and the diameter of the smallest correctly identified disks in the phantom. If you follow this methodology, we recommend using k factor of 60 μm^2, but not greater than 80 μm^2. We recommend that multiple readers examine multiple images of the phantom and score each of them independently. We also recommend you estimate the error bars on your results. In addition, we recommend you perform these scoring tests at multiple exposure levels typical for mammography.

We recommend you provide the protocol and test results using an appropriate phantom, such as a contrast-detail (CD) phantom. We recommend the observers participating in the rating experiment be qualified personnel under the Mammography Quality Standards Act (MQSA) regulations (21 CFR Part 900) or have equivalent qualifications (please describe). We also recommend you provide the complete characteristics of the soft-copy display system or the hard-copy system if a film printout is used.

Image Erasure and Fading

For systems using a delayed readout of image data such as a photostimulable phosphor, we recommend you provide a description and results of the following:

- image erasure and fading tests as a function of time and temperature; and
- retention of image information as a function of the number of erasures and exposures.

We recommend you provide information on fogging and depletion of charge after exposure to room light. We recommend you include results of an image fading test at 50˚C, if the system is intended for batch processing in a mobile facility.

Repeated Exposure Test

We recommend you provide results of 100 or more repeated exposures and erasures showing that there are no residual trapped charges that can give false information such as multiple exposures or ghost images. A test for assessing image ghosting as described in *Addendum on Digital Mammography: The European Protocol for the Quality Control of the Physical and Technical Aspects of Mammography Screening, version 1.0, November 2003*[15], may be used.

In addition, we recommend you determine the life of a detector and the criteria for its replacement, i.e., the recommended number of exposures or time frame prior to replacement.

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[14] Thomas, J. A., Chakrabarti, K., Kaczmarek, R., and Romanyukha, A., "Contrast Detail Phantom Scoring Methodology," **Med. Phys.** Vol 32 (3), pp 807-814, 2005.

[15] Available at www.euref.org

Defect Characteristics

We recommend you describe the following:

- type and quantity of detector defects and whether their location overlaps the imaged breast;
- methods of compensation or blanking that you use to compensate or correct these detector defects;
- criteria for defect limits and how these limits are determined; and
- tests that will be performed during production to assure that the criteria for defect limits are met.

For the location of the detector defects, we recommend you provide a graphical map showing location and frequency.

For any compensation or correction, we recommend you describe pixel-to-pixel variations in, for example, sensitivity and offset.

Noise Analysis

We recommend you perform noise analysis as described in Maidment, *et al*.[16] and provide a quantitative measure of the noise properties of the image acquisition system. Noise properties can be derived from the noise power spectrum (NPS) as a function of spatial frequency and exposure level.

We recommend you provide the test protocols for all parameters used to calculate your estimated DQE. In addition, we recommend you indicate whether you use 1- or 2-dimensional NPS in the estimation of the noise.

Patient Radiation Dose

We recommend you provide a quantitative estimate of the patient radiation dose using phantom testing as described below. This estimate should be expressed as the average glandular dose delivered during a single craniocaudal view of the standard breast simulated by the appropriate phantom. Your phantom testing should simulate 2, 4.0, 6.0, and 8.0 cm thick, compressed breasts consisting of 30, 50, and 70 percent glandular and 70, 50, and 30 percent adipose tissue, as illustrated in Table 2 below. We recommend you describe the phantom and specify all the conditions of operation of the FFDM system during your testing, including kVp, mAs, x-ray filtration, exposure level at the detector, and patient radiation dose.

[16] Maidment, A. D. A., Albert, M., Bunch, P. C., Cunningham, I. A., Dobbins, J. T., III, Gagne, R. M., Nishikawa, R. M., Van Metter, R. L., Wagner, R. F., "Standardization of NPS measurement: interim report of AAPM TG16," Proceedings of SPIE - Volume 5030, **Medical Imaging** 2003: Physics of Medical Imaging, Yaffe, M. J., Antonuk, L. E., Editors, June 2003, pp. 523-532.

Table 2: Recommended Patient Radiation Dose Testing Using Phantoms

Percent Glandular/Adipose Tissue	**Simulated Breast Thickness (cm)**			
	2.0	4.0	6.0	8.0
30/70				
50/50				
70/30				

We also recommend you describe how the patient radiation exposure is controlled and limited by the system.

Automatic Exposure Control Performance

We recommend you provide evaluation results of each of the automatic exposure control (AEC) modes available in your system. We recommend that the AEC performance be evaluated by acquiring data sets with various kVp settings and various thicknesses of a homogeneous tissue-equivalent material for the standard mode and the magnification mode, if available. Tests should include contrast noise ratio (CNR) and dose values at each thickness to ensure that AEC is capable of maintaining adequate image contrast as the material thickness is varied.

Breast Compression System

We recommend you report testing results of the compression force, accuracy, and limits of the breast compression system.

In accordance with 21 CFR 807.87(l), we may request that you provide representative phantom images acquired with your FFDM system.

9. Clinical Testing

In accordance with the Act, the agency will rely upon well-designed bench and/or animal testing and limited clinical testing rather than requiring large-scale multi-reader multi-case (MRMC) clinical studies unless there is a specific justification for asking for clinical information to support a determination of substantial equivalence. While, in general, large-scale MRMC clinical studies will not be needed for most FFDM systems, FDA may recommend that you collect additional clinical data for an FFDM system with any one of the following:

- indications for use dissimilar from legally marketed devices of the same type;
- designs dissimilar from legally marketed designs; or
- new technology, i.e., technology different from that used in legally marketed devices of the same type.

FDA will always consider alternatives to the clinical testing discussed below (the mammographic feature analysis) when the proposed alternatives are supported by an adequate scientific rationale.

Mammographic Feature Analysis

Certain imaging features present on clinical mammograms cannot be adequately evaluated by testing physical characteristics of the device (e.g., detection of small low-contrast lesions obscured by overlying breast tissue; characterization of small microcalcifications; subtle imaging features of the margins of mass lesions; architectural distortion). Furthermore, while physical laboratory testing evaluates individual device characteristics, a combination of individual characteristics may interact in a complex manner. FDA recommends that you conduct a mammographic feature analysis to provide a stress test to your FFDM device. A stress test is designed to study differences between competing imaging systems using cases selected to challenge those differences. If the cases are properly selected and contain the mammographic, clinical, and pathologic characteristics described below, the number of cases evaluated should be limited.

The stress testing results should provide an estimate of the true screening and diagnostic performance of the device, including the following:

- detect microcalcifications;
- discriminate benign from malignant microcalcifications;
- detect regions of architectural distortion; and
- discern subtle irregularities in otherwise smooth mass margins and thereby discriminate between benign and malignant masses.

We recommend the mammographic feature analysis be performed by radiologists certified under MQSA current regulations[17] or having equivalent qualifications. Each radiologist should examine and score patient images obtained with your FFDM system and a legally marketed device. We recommend collecting mammograms with the following characteristics:

- all patient lesions less than 1.0 cm in size and non-palpable;
- all breast compositions but predominantly (i.e., at least 75%) an equal number of heterogeneously dense and homogeneously dense;
- even distribution of masses, clusters of microcalcifications, and architectural distortions (majority malignant but a sufficient number benign);
- a distribution of clusters of microcalcifications that includes different types of benign and malignant microcalcifications;
- at least one retroareolar mass, one retroareolar cluster of microcalcifications, and one retroareolar architectural distortion; and

[17] See 21 CFR Part 900.

- a small number of normal mammograms.

If cases are not obtained using double x-ray exposure of patients, we recommend you demonstrate equivalence between two different datasets obtained from your FFDM system and the legally marketed device with respect to breast compositions, lesion types and sizes, diagnoses (normal, benign, and malignant), x-ray acquisition techniques, and other pertinent imaging features and patient characteristics. We recommend a comparative features analysis using two reading sessions, one for each system and separated by an appropriate period of time to avoid memory bias. If cases are obtained using double x-ray exposure of patients, we recommend you perform side-by-side comparisons. In either circumstance, each reader should compare or score the following features[18] for each case:

- ACR Breast Imaging Reporting and Data System (BIRADS) assessment category for each finding;
- confidence to make a diagnosis of normal, benign, and malignant, using at least a 10-point scale;
- lesion conspicuity for masses, microcalcifications, and architectural distortions, separately;
- ability to discern subtle irregularities in otherwise smooth mass margins;
- ability to determine the type of microcalcification in accordance with the ACR BIRADS lexicon;
- image contrast for differentiation of subtle tissue density differences;[19]
- sharpness, assessing the edges of fine linear structures, tissue borders, calcifications, and spiculations;
- tissue visibility at the skin line;
- noise, i.e., noise obscuring breast structures or suggestive of structures not actually present;
- artifacts due to image processing, detector failure, and other factors external to the breast on the hard-copy and the soft-copy displays;
- breast positioning, including separately assessing coverage of the breast on the craniocaudal and the mediolateral oblique views;
- exposure, including separately assessing visualization of the fibroglandular tissue and visualization of the breast tissue underlying the pectoralis muscle;
- breast compression, including assessing overlapping breast structures, non-uniform exposure of the fibroglandular tissues, poor penetration of the thicker portions of the breast, overexposure of the thinner areas, and motion unsharpness; and

[18] Mammography Quality Control Manual, *Clinical Image Quality*, **American College of Radiology**, 1999, pp. 79-112.

[19] In the case of soft-copy display, it may be appropriate to adjust the window and level settings when you perform the image contrast assessment.

- overall clinical image quality.

In addition, we recommend you provide the following:

- a description of the study design, including a discussion of how your study avoids bias due to the reader's familiarity with images from a particular acquisition system;
- a copy of the protocol and data analysis plan;
- details on the number of readers and their qualifications, i.e., certification under MQSA current regulations (21 CFR Part 900) or equivalent;
- description of the reader training paradigm for the mammographic feature analysis;
- description of the guidelines given to the readers for comparing or scoring features including details of the comparison or scoring technique used,[20] i.e., scale and definition for each feature;
- trade name and characteristics of the legally marketed predicate device;
- details of the data sets collected on your FFDM system and on the legally marketed device (see below)
- description of the randomization scheme;
- description and specifications of the soft-copy and the hard-copy display used;
- sensitivity and specificity analysis based on ACR BIRADS assessment category for each finding and for each reader;
- comparison or scoring analysis and results for each feature using the soft-copy21 display and the hard-copy display, separately; and
- sub-analyses of each feature, including stratification by reader, breast density type, lesion type and size, x-ray acquisition setting (kVp, mAs, AEC and manual mode, separately), and breast compression setting.

The details of the data sets collected on your FFDM system and on the legally marketed device listed above should include:

- patient demographics (age, ethnicity)
- number of normal patients
- number of patients identified as having a benign or a malignant breast abnormality
- number of patients stratified by breast composition, lesion type, and size.

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[20] Destouet J. M., Bassett L. W., Yaffe M. J., Butler P. F., Wilcox P. A., "The ACR's Mammography Accreditation Program: Ten Years of Experience Since MQSA," **J. Am. Coll. Radiol.** (2) pp. 585-594, 2005.

[21] For the soft-copy display, the feature analysis should be done twice: one analysis should not allow any display adjustment of the window level for the brightness and contrast, and one analysis should allow the reader to adjust the window level for the brightness and contrast.

For the side-by-side feature analysis, we recommend you use a 5-point scale to rate the superiority when applicable. Otherwise, we recommend you use a 5-point scale to rate "presence," "relevance," and "acceptability" for screening and diagnostic purposes of each applicable mammographic feature. We recommend you provide the scoring definition and training to the readers prior to the clinical testing. Reader training should consist of scoring an independent image set collected from your FFDM system and the legally marketed device to achieve self-consistency.

Multi-Reader Multi-Case Study

FDA may also recommend a multi-reader multi-case (MRMC) study to compare sensitivity, specificity, and receiver operating characteristic (ROC) curves between your FFDM device, especially if the results of the physical laboratory testing and the mammographic feature analysis raise concerns or if the design of your device is dissimilar from legally marketed designs. FDA will always consider alternatives to the MRMC study when the proposed alternatives are supported by an adequate scientific rationale.

The Radiological Devices Branch in the Division of Reproductive, Abdominal, and Radiological Devices is available to discuss any questions you may have about mammographic feature analysis or MRMC studies before you initiate your clinical testing.

If a clinical study is needed to demonstrate substantial equivalence, i.e., conducted prior to obtaining 510(k) clearance of the device, the study must be conducted under the Investigational Device Exemptions (IDE) regulation, 21 CFR Part 812. FDA believes that the FFDM system device addressed by this guidance document is a non-significant risk device, therefore the study is subject to the abbreviated requirements of 21 CFR 812.2(b).[22] In addition to the requirements of section 21 CFR 812.2(b), sponsors of such trials must comply with the regulations governing institutional review boards (21 CFR Part 56) and informed consent (21 CFR Part 50).

10. Labeling

The premarket notification must include labeling in sufficient detail to satisfy the submission requirements of 21 CFR 807.87(e). The following suggestions are intended to assist you in preparing labeling that satisfies 21 CFR 801.[23]

Your user manual should include the information described below.

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[22] See http://www.fda.gov/oc/ohrt/irbs/devices.html#risk

[23] Although final labeling is not required for 510(k) clearance, final labeling must comply with the requirements of 21 CFR Part 801 before a medical device is introduced into interstate commerce. In addition, final labeling for prescription medical devices must comply with 21 CFR 801.109. Labeling recommendations in this guidance are consistent with the requirements of Part 801.

Indication for Use

We recommend the indication for use address how the device will be used, for example:

> The device is intended to be used for screening and diagnosis of breast cancer. The device is to be used in the same clinical applications as a traditional mammographic screen-film system.

Directions for Use

We recommend submitting clear and concise instructions for use that delineate the technological features of the specific device and how the device is to be used. Instructions should encourage local/institutional training programs designed to familiarize users with the features of the device and how to use it in a safe and effective manner. As a prescription device, under 21 CFR 801.109, the device is exempt from having adequate directions for lay use.

Warnings

The warnings should address MQSA certification of the facility, for example:

> The device should be used only in facilities MQSA certified for digital mammography systems.

Precautions

The precautions should discuss the potential for adverse events associated with the use of the device. The adverse events should include: the following

- excessive breast compression;
- excessive x-ray exposure;
- electric shock;
- infection; and
- skin irritation, abrasions, or puncture wounds.

Device Description

We recommend you describe the technical characteristics and specifications of the major components of your system, including the following:

- x-ray system;
- detector;
- x-ray control;
- breast compression system;
- acquisition workstation; and
- compatible image display monitor and printer.

Device Information

We recommend you include the following:

- an overview of the device;
- the principles of operation for the device;
- the technical specifications of the device;
- the performance criteria;
- instructions on how to calibrate the automatic exposure control (AEC);
- technique chart for manual exposures;
- information on exposure factors;
- standards of good practice;
- instructions on safety control; and
- instructions on maintenance.

Summaries of the Physical Laboratory Testing

We recommend that you provide brief summaries of your physical laboratory testing results, including graphs or tables, as appropriate, for the following:

- quantum limited operation;
- sensitometric response;
- spatial resolution;
- signal-to-noise ratio transfer;
- dynamic range;
- phantom testing;
- image erasure and fading;
- repeated exposure test;
- defect characteristics;
- noise analysis;
- patient radiation dose; and
- automatic exposure control performance.

Clinical Studies

We recommend you include a summary of the clinical studies performed with your device that includes the following:

- study objectives;
- study design;

- patient demographics (age, ethnicity);
- number of patients with normal mammograms (ACR BIRADS category 1);
- number of patients identified as having a benign or a malignant breast abnormality;
- number of patients stratified by breast composition, lesion type, and size;
- description of the methodology used in gathering clinical information;
- description of the statistical methods used to analyze the data; and
- study results.

Additional Information

We also recommend you include:

- the life of the detector and the criteria for replacement, i.e., the number of exposures between replacing detectors;
- a full description of the quality assurance tests (and action limits), including detailed procedures for performing these tests, if applicable, and the frequency of testing;
- description of the tests that the facility should perform to ensure that image quality is maintained for images generated using the AEC mode and for those obtained in the manual mode;
- instructions for cleaning and disinfecting equipment surfaces that contact the patient and all equipment surfaces likely to become soiled during use to prevent disease transmission to the patient;[24]
- the trade name of the recommended cleaning solution;[25]
- types of accessories compatible with your system;
- x-ray exposure unit instructions in order to operate the device safely;
- conformity to any voluntary standards;
- manufacturer's contact information; and
- a description of personnel authorized to service the system.

In addition, instructions for maintenance of the system performance (quality assurance processes) should include:

- instructions on how to calibrate the digital image detector; and
- information on the tools needed to calibrate the digital image detector.

[24] http://www.fda.gov/cdrh/ode/198.pdf

[25] Recommended cleaning solutions should be those that are legally marketed in the United States, e.g., registered with the U.S. Environmental Protection Agency.