Draft Guidance for Industry and Food and Drug Administration Staff

Pediatric Information for X-ray Imaging Device Premarket Notifications

DRAFT GUIDANCE

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For questions regarding this document, contact Thalia Mills at thalia.mills@fda.hhs.gov or (301) 796-6641.

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

Office of *In Vitro* Diagnostic Device Evaluation and Safety (OIVD)
Division of Radiological Devices

Office of Communication, Education and Radiation Programs (OCER)
Division of Mammography Quality and Radiation Programs

Office of Science and Engineering Laboratories (OSEL)
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Pediatric Information for X-ray Imaging Device Premarket Notifications

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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 guidance document about the Food and Drug Administration's (FDA's or the Agency's) current thinking on information that should be provided in premarket notifications for x-ray imaging devices with indications for use in pediatric populations. The Agency intends for this guidance to minimize uncertainty during the premarket review process of 510(k)s for x-ray imaging devices for pediatric use, to encourage the inclusion of pediatric indications for use for x-ray imaging device premarket notifications, and to provide recommendations on information to support such indications.

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. Scope

This guidance applies only to complete x-ray imaging devices that could be used on pediatric patients. Table 1 lists devices covered by this guidance according to the corresponding regulations and product codes. This document does not apply to imaging equipment sold as components or accessories (such as tube-housing assemblies, tables, or detectors).

Table 1. X-ray imaging systems: regulations and product codes

Regulation	Product Codes
21 CFR 892.1600 – Angiographic x-ray system	IZI – System, X-Ray, Angiographic
21 CFR 892.1650 – Image-intensified fluoroscopic x-ray system	MQB – Solid-State X-ray Imager (Flat Panel/Digital Imager) JAA – System, X-ray, Fluoroscopic, Image-Intensified OWB – Interventional Fluoroscopic X-ray System OXO – Image-Intensified Fluoroscopic X-ray System, Mobile
21 CFR 892.1660 – Non-image-intensified fluoroscopic x-ray system	JAB – System, X-ray, Fluoroscopic, Non-Image-Intensified
21 CFR 892.1680 – Stationary x-ray system.	MWP – Cabinet, X-Ray System KPR – System, X-Ray, Stationary
21 CFR 892.1720 – Mobile x-ray system	IZL – System, X-Ray, Mobile
21 CFR 892.1740 – Tomographic x-ray system	IZF – System, X-Ray, Tomographic
21 CFR 892.1750 – Computed tomography x-ray system	JAK – System, X-ray, Tomography, Computed OAS – X-ray, Tomography, Computed, Dental
21 CFR 872.1800 – Extraoral source x-ray system	EHD – Unit, X-Ray, Extraoral With Timer MUH – System, X-Ray, Extraoral Source, Digital
21 CFR 872.1810 – Intraoral source x-ray system	EAP – Unit, X-Ray, Intraoral

This guidance should be used in conjunction with other guidance specific to your type of x-ray imaging device (e.g., x-ray computed tomography (CT), general radiography and dental radiography, and diagnostic and interventional fluoroscopy devices) that addresses how you should meet premarket notification (510(k)) submission requirements under 21 CFR part 807.

This guidance supplements other FDA documents regarding the general content and format requirements of a 510(k) submission. You should refer to 21 CFR 807.87, the guidance entitled "Format for Traditional and Abbreviated 510(k)s,"[1] and the section of CDRH's Device Advice entitled "Premarket Notification (510k)."[2]

X-ray imaging devices are subject not only to the medical device requirements in the Federal Food, Drug, and Cosmetic Act (FD&C Act), but must also comply with the Electronic Product Radiation Control (EPRC) provisions of sections 531-542 of the FD&C Act and 21

[1] http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084365.htm
[2] http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/default.htm

CFR Subchapter J on radiological health.[3] Many of the requirements found in regulations issued under the EPRC provisions relate to limiting radiation exposure. See 21 CFR 1020.30-1020.33 ("Diagnostic x-ray systems and their major components;" "Radiographic equipment;" "Fluoroscopic equipment;" and "Computed tomography (CT) equipment").

3. Background

Currently, most x-ray imaging devices are marketed with a general indication for use (IFU) statement.[4] Many general use x-ray imaging devices neither address the unique issues associated with pediatric use nor contain labeling specific for use on pediatric patients, even though many (if not all) of these devices are used or could be used to image pediatric patients.

Exposure to ionizing radiation is of particular concern in pediatric patients for three reasons: 1) younger patients are more radiosensitive than adults (i.e., the cancer risk per unit dose of ionizing radiation is higher for younger patients);[5] 2) younger patients have a longer expected lifetime for the effects of radiation exposure to manifest as cancer; and 3) use of equipment and exposure settings designed for adult use can result in excessive radiation exposure for the smaller patient. The third point is of special concern because many pediatric imaging exams are performed in facilities lacking specialized expertise in pediatric imaging.[6]

In 2004, the Agency issued general pediatric guidance entitled "Premarket Assessment of Pediatric Medical Devices."[7] The guidance, which applies to all devices, defines pediatric subpopulations and the general information that should be provided for different types of premarket submissions for devices intended for use in pediatric populations. In 2007, Congress passed The Food and Drug Administration Amendments Act of 2007[8] (FDAAA) (Pub. L. 110-85) that included Title III, the Pediatric Medical Device Safety and Improvement Act [9] (PMDSIA). PMDSIA requires submission of information on pediatric

[3] http://www.fda.gov/Radiation-EmittingProducts/ElectronicProductRadiationControlProgram/LawsandRegulations/default.htm

[4] See the guidance entitled "General/Specific Intended Use" (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073945.pdf). See also the draft guidance entitled "510(k) Device Modifications: Deciding When to Submit a 510(k) for a Change to an Existing Device" (issued July 27, 2011) at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm265274. When finalized, this guidance will represent the Center's current thinking on this topic.

[5] NAS National Research Council Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation. 2006. *Health risks from exposure to low levels of ionizing radiation: BEIR VII phase 2*. Washington, D.C.: National Academy of Sciences, National Academies Press.

[6] Larson, D.B. *et al*., "Rising Use of CT in Child Visits to the Emergency Department in the United States, 1995-2008," *Radiology*, vol. 259(3), pp. 793-801, 2011.

[7] http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM089742.pdf

[8] http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FoodandDrugAdministrationAmendmentsActof2007/FullTextofFDAAALaw/default.htm

[9] http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_public_laws&docid=f:publ085.110

subpopulations that suffer from the disease or condition that the device is intended to treat, diagnose, or cure for certain types of device applications and supplements.

In February 2010, the FDA launched an "Initiative to Reduce Unnecessary Radiation Exposure from Medical Imaging"[10] and on March 30-31, 2010, the Agency held a public meeting entitled “Device Improvements to Reduce Unnecessary Radiation Exposure from Medical Imaging.”[11] At the meeting, the FDA sought advice on "steps that manufacturers of CT and fluoroscopic devices could take to reduce unnecessary radiation exposure through improved product design, enhanced labeling, or improved instructions and training for equipment use and quality assurance at medical imaging facilities."[12] The Agency asked whether manufacturers should incorporate special provisions for pediatric patients, particularly with regard to hardware and software features.[13] Recommendations received by FDA, which apply to all general-use x-ray imaging modalities, included making available pediatric protocols and control settings, targeted instructions and educational materials emphasizing pediatric dose reduction, quality assurance tools for facilities emphasizing radiation dose management, and dose information applicable to pediatric patients. Many of the recommendations from pediatric experts focused on expanding the flexibility or range of features already available on x-ray imaging devices, which may also improve adult imaging for non-standard applications.

Experts have commented that many radiological devices are sold without the design features or labeling information that would help users optimize benefit (clinically-usable images) in comparison to risk (radiation exposure) for pediatric imaging.[14,15] Imaging professionals can safely use existing equipment that may not have specific features or instructions for pediatric use by consulting recommendations provided by the Alliance for Radiation Safety in Pediatric Imaging (ARSPI)[16] and other organizations. FDA has reviewed the recommendations from ARSPI and believes they are appropriate. Because of the special concerns about excessive exposure to radiation in children, FDA believes that new x-ray

[10]FDA's white paper entitled "Initiative to Reduce Unnecessary Radiation Exposure from Medical Imaging" is available at http://www.fda.gov/Radiation-EmittingProducts/RadiationSafety/RadiationDoseReduction/ucm199994.htm.

[11]Agenda and transcripts are available at: http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm201448.htm. Public docket submissions are available at: http://www.regulations.gov/#!docketDetail;rpp=10;po=0;D=FDA-2010-N-0080.

[12]See 75 FR 8375, 8376 (Feb. 24, 2010) (http://www.regulations.gov/#!documentDetail;D=FDA-2010-N-0080-0001)

[13] The federal register notice lists all the questions asked at the meeting (See 75 FR 8375-8377 (2010); http://edocket.access.gpo.gov/2010/2010-3674.htm).

[14]http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm201448.htm (see transcripts links)

[15] The principles of radiation protection in medicine, including "optimization" are described in: International Commission on Radiological Protection. 2007. ICRP Publication 105: Radiological Protection in Medicine. *Ann. ICRP*, *37*(6). Optimization of radiation exposure for x-ray imaging means the following: Examinations should use techniques that are adjusted to administer the lowest radiation dose that yields an image quality adequate for diagnosis or intervention (i.e., radiation doses should be "As Low as Reasonably Achievable" (ALARA)).

[16]http://www.pedrad.org/associations/5364/ig/

imaging devices should be demonstrated to be appropriate for pediatric use or use in pediatric populations should be cautioned against. The end user can then make more informed decisions about use of the device on pediatric patients.

Manufacturers seeking marketing clearance for a new x-ray imaging device with a pediatric indication should provide data supporting the safety and effectiveness of the device in pediatric populations. Manufacturers who seek marketing clearance only for general indications or do not submit adequate data to the FDA to support a pediatric indication for use for x-ray imaging devices where pediatric use is likely should label their x-ray imaging device with the statement "*CAUTION: Not for use on patients less than approximately <insert patient size (e.g., body part thickness or height and weight appropriate to your device)>*." as part of the IFU statement. This statement should also be prominently displayed on the device itself (e.g., control panel).[17] The statement should be revised depending on the size subgroups (see section 4) for which manufacturers submit data. FDA is particularly concerned about the imaging of smaller pediatric patients with sizes that do not overlap with adult size ranges.

In the sections below, the guidance discusses the information that should be included in premarket notifications for x-ray imaging devices with pediatric indications for use.

4. Pediatric population

The FDA's Center for Devices and Radiological Health defines the age of the pediatric population as birth through 21 years.[18] While the risk of radiation-induced cancer depends on age, patient size (not age) is a more important factor for optimizing image quality and radiation dose for x-ray imaging exams. Because the focus of this guidance is on device design and evaluation of x-ray imaging equipment, this guidance divides the pediatric population into subgroups based on patient size rather than age.

Pediatric patients can range in weight from less than 500 grams (1 lb) to more than 120 kg (265 lb). Thus a device designed for pediatric use will cover the entire size range of the adult general population; conversely, devices designed only for adults may not be optimized for use on many smaller patients.

[17]Under section 513(i)(1)(E)(i) of the FD&C Act, when determining that a device is substantially equivalent to a predicate device, FDA may require limitations in the device labeling about off-label use of the device when "there is a reasonable likelihood" of such use and if "such use could cause harm." FDA believes these conditions generally apply to use of x-ray imaging devices with general indications for use on pediatric populations. Such determinations are made on a case by case basis and other requirements must be met, including a consultation between FDA and the 510(k) submitter, before such limitations can be required. FDA's policy on when a device may be found "substantially equivalent with limitations" is discussed further in the guidance entitled "Determination of Intended Use for 510(k) Devices; Guidance for CDRH Staff (Update to K98-1)." (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm082162.htm).

[18]See the guidance entitled "Premarket Assessment of Pediatric Medical Devices" (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM089742.pdf).

In the design of x-ray imaging devices, we recommend sponsors consider at least the following subgroups defined according to age and approximate average height and weight measurements: neonate/birth-1 month [1-2 kg (2.2-4.4 lb) low end estimate], 1 year old [~11 kg (24 lb); recumbent length 100 cm (39.4 in.)], 5 year old [~21 kg (46 lb); 113 cm (44.5 in) standing height], 12 year old [~52 kg (115 lb); 156 cm (61.5 in) standing height] and adult [~80 kg (176 lb); standing height 170 cm (67.0 in)].[19,20,21] These subgroups are listed as a general guide. Different subgroups that still cover the broad size range expected for pediatric patients may be appropriate. While height and weight are readily available metrics in describing "average" patients, patient thickness is the most useful metric for x-ray imaging.[22,23]

It is important to note that there is considerable overlap between the sizes of larger pediatric and smaller adult patients. For example, the 5th percentile U.S. adult female [51 kg (112 lb.); 151 cm (59 in) standing height] is similar in size to an average 12 year old.[24] Therefore, a well-designed adult device that takes account of a broad individual size variation should be able to competently image average pediatric patients 12 years old and above.

5. Indications for Use

The 510(k) submission should clearly define the indication(s) for use, including pediatric populations for whom the device is intended, at the beginning of the submission and in the labeling. If use in pediatric populations is not intended, the Indications for Use statement

[19] Size measurements are based on approximate mean values (averaged across males and females) from: McDowell, M.A., C.D. Fryar, C.L. Ogden, and K. M. Flegal. 2008. Anthropomorphic Reference Data for Children and Adults, United States, 2003-2006. *National Health Statistics Reports*, *10*, 1-48. Available for download at: http://www.cdc.gov/nchs/data/nhsr/nhsr010.pdf. The weight given for the neonate subgroup is lower than the average to ensure that a broad range of sizes is adequately covered.

[20] These suggested subgroups fall within the age groups identified in the guidance entitled "Premarket Assessment of Pediatric Medical Devices" (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM089742.pdf): neonate (birth-1 month), infant (1 month-2 yrs.), child (2-12 yrs.), adolescent (12-21 yrs.). For design and evaluation of radiological devices, patient size (i.e. height, weight, thickness) is a better indicator.

[21] Based on reports of the lifetime incidence of cancer vs. age of exposure data, these pediatric subgroups defined by the Agency cover the region where the largest age dependence is expected for cancer risk. Risk decreases much less steeply as a function of age for individuals over 21 years old. [See NAS National Research Council Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation. 2006. *Health risks from exposure to low levels of ionizing radiation: BEIR VII phase 2*. Washington, D.C.: National Academy of Sciences, National Academies Press.]

[22] The following reference gives current data for anteroposterior and transverse body diameter for pediatric patients ranging in age from 0.5 to 20 years: Kleinman, P. L., K. J. Strauss, D. Zurakowski, K. S. Buckley, and G. A. Taylor. 2010. Patient size measured as a function of age at a tertiary care children's hospital. *American Journal of Roentgenology*, *194*, 1611-1619.

[23] The following reference used cylindrical phantoms with diameters of 8, 16, 24, and 32 cm to represent a neonate, 5 year old, 12 year old, and adult patient respectively: Siegel, M. J., et al. 2004. Radiation dose and image quality in pediatric CT: effect of technical factors and phantom size and shape. *Radiology*, *233*(2), 515-522.

[24] McDowell, M.A., C.D. Fryar, C.L. Ogden, and K. M. Flegal. 2008. Anthropomorphic Reference Data for Children and Adults, United States, 2003-2006. *National Health Statistics Reports*, *10*, 1-48. Available for download at: http://www.cdc.gov/nchs/data/nhsr/nhsr010.pdf.

should include the statement "*CAUTION: Not for use on patients less than approximately <insert patient size (e.g., body part thickness or height and weight appropriate to your device)>*."

This statement should be revised depending on the size subgroups (see section 4) for which you submit data. FDA is particularly concerned about imaging of smaller pediatric patients with sizes that do not overlap with adult size ranges. See also section 11B of this guidance on contraindications, warnings, and precautions.

6. Pediatric device features

All x-ray imaging devices with an indication for use in pediatric imaging should be designed for that purpose. The device description should describe those features specifically included to allow for imaging smaller patients. The Agency recommends consultation with knowledgeable pediatric imaging specialists (physicians, physicists, and technologists) and human factors specialists[25] during the design phase to ensure the device is suitable for pediatric use.

Examples of pediatric use features to consider for x-ray imaging equipment are:

- specific pre-set pediatric control settings that are appropriate for the intended patient;
- automatic exposure control (AEC) designed and tested for a broad range of patient sizes, including pediatric;
- pediatric procedures, labeling, and protocols that are designed to minimize radiation exposure while providing image quality of acceptable clinical value;
- display and recording of patient dose or dose index and ability to record other patient information, e.g., age, height, and weight (either manual entry or automatic calculation);[26] while this recommendation also applies to adult imaging, it is especially important to include for pediatric imaging so estimates of patient-specific dose can be made reliably without assuming a "typical" or "standard" patient size, which are often based on adults; and
- software interface features that alert the end user to important pediatric use issues (e.g., interactive software pop-ups that remind users of special pediatric issues when setting up the image acquisition).

All of the features listed above may not be appropriate for every device. For example, a CT scanner will likely have a more sophisticated software interface and capabilities for pre-

[25]See the FDA guidance entitled "Medical Device Use-Safety: Incorporating Human Factors Engineering into Risk Management." (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm094460.htm) and the standard AAMI /ANSI HE75:2009, *Human factors engineering - Design of medical devices.* See also the draft guidance entitled "Applying Human Factors and Usability Engineering to Optimize Medical Device Design" (issued June 22, 2011) at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm259748.htm. When finalized, this guidance will represent the Center's current thinking on this topic.

[26]Appendix, Table 2 entry "dose measurement, display, and documentation" includes relevant dose metrics and FDA-recognized standards for different modalities.

programmed protocols than a general radiography or dental imaging device. However, basic information on device settings to be used as a starting point for typical pediatric exams should still be provided.

While the focus of this guidance is pediatric use, many recommendations in this guidance would also improve adult imaging (e.g., better dose display and recording; availability of default protocols and dose reduction features suitable for a broad range of sizes; instructions emphasizing clear explanations of dose reduction features and any special issues for patients that are not of average size).

7. Risk Assessment

The Agency recommends that the device's risk assessment be expanded to include additional hazards and means of mitigation specific to pediatric use of the device. When developing features or user instructions aimed at reducing radiation exposure to pediatric patients, the sponsor should ensure that the resulting images are of adequate quality for the desired clinical task. An exam with poor image quality could result in a missed diagnosis or in a repeated exam (involving additional radiation exposure to the patient). Examples of hazardous situations that could result in unnecessary radiation exposure or poor image quality specific to pediatric patients are:

- use of adult settings or protocols instead of appropriate pediatric settings or protocols;
- design features that do not allow proper positioning of pediatric patients (e.g., a deep patient cradle interfering with lateral x-ray of a small patient); and
- automatic controls that are not calibrated for pediatric patients.

The above examples are not a comprehensive list. Consultation during the design phase with professionals who are knowledgeable regarding pediatric imaging may help identify other risks and situations specific to pediatric use.

8. Protocols

The term "protocol" in this document means, but is not limited to, a set of imaging system settings, programs, and algorithms used to image patients. Pediatric-appropriate protocols for common procedures appropriately adjusted for the patient's size and weight should be available. In some cases (e.g., general radiography), these protocols may simply consist of instructions (e.g., exposure chart) on how to appropriately configure the equipment and adjust parameters for the patient weight, body habitus, and clinical indication; sponsors should provide such information as part of a dedicated guide to pediatric use of their device (see also section 11 of this guidance). In other cases (e.g., CT), it may be appropriate to pre-program the protocols into software. Also, in the design of protocols, special hardware design issues that affect safety and effectiveness of pediatric populations should be addressed. For example, if use of automatic exposure control is recommended on pediatric patients, this feature should be designed and calibrated for that purpose.

A list summarizing the available pre-configured, default pediatric protocols should be provided in the 510(k) submission. This list should include the protocol name, brief description of exam purpose, anatomical region, intended size of patient, and the acquisition parameters used as starting points. As discussed in the following section, representative dose information (applicable to pediatrics) associated with each protocol should also be provided.

9. Laboratory Image Quality and Dose Assessment

An assessment of image quality and estimation of radiation dose should be performed to demonstrate the pediatric use of the new device. The appendix of this guidance lists relevant common tests and applicable standards used to evaluate the performance of x-ray imaging systems. In general, testing should be performed under conditions that match the intended routine clinical use of the system, including radiation dose.

If these tests already have been performed during evaluation of the device for use in the general adult population, they do not need to be repeated on a pediatric population to demonstrate acceptable pediatric use.[27] However, the sponsor should ensure that the range of settings and conditions for testing include those that would normally be used during pediatric imaging. Any equipment features or settings that are expected to vary depending on patient size should be evaluated for acceptable outcomes. Of special concern are features that automatically adjust clinical exposure settings based on patient size such as AEC and tests of temporal resolution (especially important for interventional or cardiac imaging).

For image quality or dose measurements that involve discrete measurements in phantoms, testing should include, at a minimum, a range of phantoms that represent birth-1 month, 1 year old, 5 year old, 12 year old, and adult sizes (see section 4 of this guidance for subgroup details). Extrapolation from one subgroup to another may be possible, eliminating the need to test in all subgroups. The submission should include a rationale for the chosen size/age subgroups and testing procedures.

The 510(k) submission should include the following:

- a summary of the results of the tests, including a description of the phantoms used and explanation of why the phantoms are appropriate for pediatric measurements;
- the test protocols and system settings used to determine imaging performance (e.g., exposure settings such as tube voltage, tube current, and use of AEC); and
- the measurement uncertainty, the trade name, characteristics, and accuracy of the measuring instruments used for performing the quantitative tests, if applicable.

[27] Although the focus of this guidance is on pediatrics, the Agency recommends that devices be designed and tested to enable optimized imaging for a broad range of adult sizes. The adult range includes small females (5th percentile U.S. female is ~51 kg, 151 cm standing height) up to large males (95th percentile U.S. adult male is ~123 kg, 189 cm standing height). A small adult female is similar in size to an average 12 year old pediatric patient. [Data source: McDowell, M.A., C.D. Fryar, C.L. Ogden, and K. M. Flegal. 2008. Anthropomorphic Reference Data for Children and Adults, United States, 2003-2006. *National Health Statistics Reports, 10*, 1-48. Available for download at: http://www.cdc.gov/nchs/data/nhsr/nhsr010.pdf.]

If the testing method has been described in the literature, a reference may be sufficient instead of providing a full description in the 510(k) submission.

10. Clinical Image Quality Assessment

Clinical images will only be requested when laboratory testing is insufficient to demonstrate substantial equivalence. If any images are provided to the Agency, they should be accompanied by corresponding dose information, exposure settings, and clinical background (e.g., type of exam, age, size, and sex of patient, and clinical indications).

For questions regarding the need for images of pediatric patients, sponsors are encouraged to request a meeting prior to 510(k) submission.[28]

11. Labeling

In addition to information describing the general operation of the device, the user manual should contain the following information specific to pediatric use:[29]

A. Indications for use

Labeling should include the indications for use (see section 5 of this guidance).

B. Contraindications, warnings, and precautions

Contraindications, warnings, and precautions for devices indicated for use on pediatric populations should clearly address the potential risks and their association with the age, size, and condition of the pediatric subject and alert the user to specific hazards associated with the use of the device in the target population.[30] The contraindications, warnings, and precautions should address the risks specific to pediatric use that were identified in the risk assessment report.

If the device is not indicated for pediatric use, the labeling should contain a caution statement against use in pediatric populations as well as a prominent physical label on the device itself.

[28]For more on the appropriate protections for pediatric populations, see the guidance entitled "Premarket Assessment of Pediatric Medical Devices" (2004) [http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM089742.pdf].

[29]The premarket notification must include labeling in sufficient detail to satisfy the submission requirements of 21 CFR 807.87(e). 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.

[30]See the guidance entitled "Premarket Assessment of Pediatric Medical Devices" (2004); http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM089742.pdf

- The label[31] on the device (e.g., control panel) should be visible from at least four feet away and should state "*CAUTION: Not for use on patients less than approximately <insert patient size (e.g., body part thickness or height and weight appropriate to your device)>.*"
- The following is an example of a full statement in the labeling (e.g., user manual) for a device with information submitted supporting use in patients larger than approximately 50 kg (110 lb) in weight and 150 cm (59 in) in height: "*CAUTION: This device is not intended for use on patients less than approximately 50 kg (110 lb) in weight and 150 cm (59 in) in height; these height and weight measurements approximately correspond to that of an average 12 year old or a 5th percentile U.S. adult female[32]. Use of equipment and exposure settings designed for adults of average size can result in excessive radiation exposure for a smaller patient. Studies[33] have shown that pediatric patients may be more radiosensitive than adults (i.e., the cancer risk per unit dose of ionizing radiation is higher), and so unnecessary radiation exposure is of particular concern for pediatric patients.*"

The approximate height, weight, and age ranges in this statement may need to be revised depending on the subgroups (see section 4) for which you submit data. FDA is particularly concerned about the imaging of smaller pediatric patients with sizes that do not overlap with adult size ranges.

C. Device description

The device description should be expanded to include a list of the hardware and software features designed specifically for pediatric use. When different options are available for purchase, the labeling should describe the various options recommended for use in pediatric subgroups and, when feasible, present these options in tabular form by age, weight, or other appropriate criteria.

D. Instructions for use

Under 21 CFR 807.87(e), the 510(k) submission shall include directions for its use. These instructions for use should delineate the technological features of the specific device and how the device is to be used on patients. Instructions for how to properly configure the device for pediatric use (and how this may differ from adult use) should also be provided.

The instructions for use should address radiation dose reduction strategies for pediatric patients. All user-configurable imaging parameters should be clearly explained, including

[31]The content, placement, and format (size, color, etc.) of this caution statement should follow the recommendations in the standard: ANSI Z535.4-2007 *American National Standard for Product Safety Signs and Labels*.

[32]McDowell, M.A., C.D. Fryar, C.L. Ogden, and K. M. Flegal. 2008. Anthropomorphic Reference Data for Children and Adults, United States, 2003-2006. *National Health Statistics Reports, 10,* 1-48. Available for download at: http://www.cdc.gov/nchs/data/nhsr/nhsr010.pdf.

[33]NAS National Research Council Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation. 2006. *Health risks from exposure to low levels of ionizing radiation: BEIR VII phase 2*. Washington, D.C.: National Academy of Sciences, National Academies Press.

their impact on patient dose. Combinations of certain parameters that can provide for optimal image quality/minimal dose under unusual circumstances (i.e., a difficult or obese patient) may be suggested but should be clearly indicated as such. Screenshots of the user interface software controls should be provided in the labeling, explaining how different parameters affect dose and image quality, particularly for pediatrics. To mitigate the risk of user error, the following should be considered:

- User's manuals in downloadable electronic form with easily searchable interfaces, in addition to paper copies; and
- Leave-behinds/just-in-time educational material such as checklists that include any special pediatric issues during pre-acquisition, acquisition, and post-acquisition steps.[34]

Instructions should consider the likely educational background of the end-user; for example, equipment likely to be used by professionals other than radiologists or radiologic technologists (e.g., dental x-ray or devices designed for cardiac imaging) should include information targeted at the appropriate professional groups (e.g., dentists, cardiologists, etc.).

E. Quality control testing recommendations

As stated in 21 CFR 1020.30(h)(1)(ii), manufacturers of x-ray equipment are required to provide users with a schedule of the maintenance necessary to keep the equipment in compliance with 21 CFR 1020.30-1020.33. The device labeling should include a section on recommended quality control testing. These recommendations should be accompanied by instructions/guidelines to the user on how to ensure its continued proper operation. Quality control recommendations should include any tests (acceptance testing, annual and continuous testing) that ensure the device functions properly when used on pediatric populations; time intervals for such testing should also be included.

F. Additional information

The end-user documentation should include a means to obtain additional information regarding the system design and unique operating principles of the device pertaining to pediatric use.

A summary of the physical laboratory tests (see section 9 of this guidance) characterizing the performance of the device for pediatric use should be provided. Users can then employ this information in their evaluation of the importance of any tradeoffs between different characteristics of imaging performance.

A summary of pediatric protocols (brief description of purpose, acquisition parameters, and intended size of patient) should be provided in a separate section. Dose information for each

[34] An example is the Image Gently/FDA "Digital Radiography Safety Checklist" (http://www.pedrad.org/associations/5364/files/Attachment%20D.CR.DR%20%20checklist.pdf).

protocol should be included in the labeling and displayed by the software, where appropriate.[35]

If literature is used in support of particular pediatric design features and protocols, a summary should be available to users (e.g., table with references and pediatric use topics or applications and equipment settings covered in each).

12. Training and testing materials for users and manufacturers' personnel

A training program emphasizing production of acceptable quality images at a reasonable radiation dose should be provided to the clinical end user.[36] The user's manual may be considered part of this training program.

This training program should emphasize equipment-specific training and the optimal use of all built-in dose reduction and image quality improvement features.[37] It should explain clearly how to use the specific features of the equipment. Training should be accessible, practical, and targeted at all different types of end users. Any testing questions that accompany training sessions should address an understanding of pediatric use issues (e.g., dose saving features for children). In order to facilitate continuous learning, a DVD that includes the content of any in-person training sessions could be provided to the facility or made available in another format (e.g., as online modules).

The 510(k) submission should include a description of the training materials for the device, whether included with the equipment purchase or available at extra cost. The description should point out any pediatric-specific topics covered.

13. Summary

Where appropriate, the 510(k) submission should include the following information in support of a pediatric indication for use of the device:

- documentation of design features and risk mitigation strategies specific to pediatric use;
- specifications for pediatric protocols/settings with accompanying dose documentation and a summary of any supporting literature used in protocol design;
- laboratory tests for dosimetry and image quality covering the conditions of operation used for typical pediatric patients;

[35]Appendix, Table 2 entry "dose measurement, display, and documentation" includes relevant dose metrics and FDA-recognized standards for different modalities.

[36]A model for such a training program for ultrasound devices (not covered by this guidance) is: *Medical Ultrasound Safety*, 2nd ed. (2009) published by the American Institute of Ultrasound in Medicine (http://www.aium.org/).

[37]Examples of training materials emphasizing pediatric dose reduction are available at the Alliance for Radiation Safety in Pediatric Imaging website (http://spr.affiniscape.com/associations/5364/ig/).

- instructions and educational materials directed to technologists, radiologists, physicists, and other imaging professionals (e.g., cardiologists and dentists) regarding pediatric-specific imaging aspects of the equipment, including available dose reduction features and the specific procedures for configuring such dose-reducing features; and
- means by which individual facilities can contact the sponsor for assistance when developing pediatric dose reduction protocols and procedures.

Appendix: General Laboratory Image Quality and Dose Assessment, Tests and Standards

Compliance testing for required performance characteristics is specified in 21 CFR 1020.30-1020.33 ("Diagnostic x-ray systems and their major components;" "Radiographic equipment;" "Fluoroscopic equipment;" and "Computed tomography (CT) equipment"). In addition to this required testing, recognized standards specify additional methods for assessment of image quality and dose that should be consulted.

This appendix lists common laboratory tests and the applicable standard for each modality; it is included for reference and is not intended to be exhaustive. The tests listed focus on ensuring the imaging device is capable of producing acceptable quality images at a reasonable dose. The information may also be included in device-specific guidance, which should also be consulted. Inclusion of this list does not imply that all of these standards must be followed for every device or that every applicable test and associated standard has been listed. For additional standards applicable to specific devices, please refer to the Recognized Consensus Standards Database.[38]

The guidance entitled "Recognition and Use of Consensus Standards"[39] describes how the agency will use information on conformance with recognized standards to satisfy premarket review requirements. 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 standard. If a 510(k) 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. Instead of following a recognized standard, a firm may choose to submit alternative equivalent information demonstrating safety and effectiveness.

Some, but not all, of these tests and standards specifically address pediatric use issues. Therefore, in the design of a new device, it is recommended that a manufacturer consult an expert in pediatric imaging.

[38] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm
[39] http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm077274.htm

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Test and brief description	Modality	Relevant standard or more detailed instructions
Sensitometric Response: The output digital signal value versus the radiation exposure curve provides the sensitometric response of the image acquisition system.	General radiography (excludes dynamic imaging/fluoroscopy and CT)	IEC 62220-1 ed1.0 (2003-10) *Medical electrical equipment- Characteristics of digital x-ray imaging devices- Part 1: Determination of the detective quantum efficiency*
	Dynamic imaging x-ray devices (e.g., fluoroscopic or cardiac imaging)	IEC 62220-1-3 ed1.0 (2008-06) *Medical electrical equipment - Characteristics of digital X-ray imaging devices - Part 1-3: Determination of the detective quantum efficiency - Detectors used in dynamic imaging*
Modulation Transfer Function (MTF): Provides a quantitative measure of the spatial resolution properties of the image acquisition system.	CT	IEC 61223-3-5 ed1.0 (2004-08) *Evaluation and routine testing in medical imaging departments–Part 3-5: Acceptance tests–Imaging performance of computed tomography X-ray equipment*; Corrigendum 1 (2006-03) and IEC 6122[illegible]2-6 ed2.0 (2006-11) *Evaluation and routine testing in medical imaging departments – Part 2-6: Constancy tests – Imaging performance of computed tomography X-ray equipment*
	General radiography (excludes dynamic imaging/fluoroscopy and CT)	IEC 62220-1 ed1.0 (2003-10) *Medical electrical equipment- Characteristics of digital x-ray imaging devices- Part 1: Determination of the detective quantum efficiency*
	Dynamic imaging x-ray devices (e.g., fluoroscopic or cardiac imaging)	IEC 62220-1-3 ed1.0 (2008-06) *Medical electrical equipment - Characteristics of digital X-ray imaging devices - Part 1-3: Determination of the detective quantum efficiency - Detectors used in dynamic imaging*
Noise Power Spectrum (NPS): As a function of spatial frequency and exposure level, this test provides a quantitative measure of the noise properties of the image acquisition	General radiography (excludes dynamic imaging/fluoroscopy and CT)	IEC 62220-1 ed1.0 (2003-10) *Medical electrical equipment- Characteristics of digital x-ray imaging devices- Part 1: Determination of the detective quantum efficiency*

system.	Dynamic imaging x-ray devices (e.g., fluoroscopic or cardiac imaging)	IEC 62220-1-3 ed1.0 (2008-06) *Medical electrical equipment - Characteristics of digital X-ray imaging devices - Part 1-3: Determination of the detective quantum efficiency - Detectors used in dynamic imaging*
Detective Quantum Efficiency (DQE): This test provides a quantitative measure of the efficiency of signal-to-noise ratio (SNR) transfer of the image acquisition system. This measure is obtained by calculating the detective quantum efficiency (DQE) as a function of spatial frequency. SNR analysis should be performed using exposure levels covering the range normally encountered using your system to provide the dynamic range of the system.	General radiography (excludes dynamic imaging/fluoroscopy and CT)	IEC 62220-1 ed1.0 (2003-10) *Medical electrical equipment- Characteristics of digital x-ray imaging devices- Part 1: Determination of the detective quantum efficiency*
	Dynamic imaging x-ray devices (e.g., fluoroscopic or cardiac imaging)	IEC 62220-1-3 ed1.0 (2008-06) *Medical electrical equipment - Characteristics of digital X-ray imaging devices - Part 1-3: Determination of the detective quantum efficiency - Detectors used in dynamic imaging*
Image Erasure and Fading: For systems using a delayed readout of image data, such as photostimulable phosphor, tests should include image decay as a function of time and temperature and signal retention as a function of the number of exposures and exposures.	General radiography and fluoroscopy	For testing recommendations also appropriate for radiographic and fluoroscopic systems, please see section 8 of the guidance entitled "Class II Special Controls Guidance Document: Full-Field Digital Mammography System."[40]
Repeated Exposure test for ghosting: Tests for quantitatively assessing residual images/ghosts are described in IEC standards as "lag effect" tests.	General radiography	IEC 62220-1 ed1.0 (2003-10) *Medical electrical equipment- Characteristics of digital x-ray imaging devices- Part 1: Determination of the detective quantum efficiency*
	Dynamic imaging x-ray devices (e.g., fluoroscopic or cardiac imaging)	IEC 62220-1-3 ed1.0 (2008-06) *Medical electrical equipment - Characteristics of digital X-ray imaging devices - Part 1-3: Determination of the detective quantum efficiency - Detectors used in dynamic imaging*
Automatic exposure control (AEC) performance: A demonstration of the degree of control intended with respect to tube current modulation on non-uniform phantoms or with respect to temporal gating should be	CT: Specifies that CT scanners provide an AEC feature, but does not specify any test of AEC performance.	IEC 60601-2-44 ed3.0 (2009-02) *Medical electrical equipment – Part 2-44: Particular requirements for the basic safety and essential performance of X-ray equipment for computed tomography*; Corrigendum 1 (2010-05)

[40] http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm107552.htm

performed for a range of exam conditions (phantom sizes or time sequences).	Radiography and fluoroscopy	The following standard also applies to interventional fluoroscopy (with exceptions and additions noted in IEC 60601-2-43): IEC 60601-2-54 ed1.0 (2009-06) *Medical electrical equipment - Part 2-54: Particular requirements for the basic safety and essential performance of X-ray equipment for radiography and radioscopy*[41]
Dose or exposure index measurement, display, automatic reporting of values, and documentation	CT: Dose indices based on Computed Tomography Dose Index 100 ($CTDI_{100}$) and radiation dose structured reporting standards	IEC 60601-2-44 ed3.0 (2009-02) *Medical electrical equipment – Part 2-44: Particular requirements for the basic safety and essential performance of X-ray equipment for computed tomography*; Corrigendum 1 (2010-05)
	Radiography and fluoroscopy: defines reference air kerma and reference air kerma rate	IEC 60601-2-54 ed1.0 (2009-06) *Medical electrical equipment - Part 2-54: Particular requirements for the basic safety and essential performance of X-ray equipment for radiography and radioscopy*
	Interventional fluoroscopy: defines reference air kerma, reference air kerma rate, dose area product; describes range of operating conditions for dose measurements; defines skin dose as air kerma for display purposes	IEC 60601-2-43 ed2.0 (2010-03) *Medical electrical equipment - Part 2-43: Particular requirements for the basic safety and essential performance of X-ray equipment for interventional procedures*
	Exposure index standard for general radiography	IEC 62494-1 ed1.0 (2008-08) *Medical electrical equipment - Exposure index of digital X-ray imaging systems - Part 1: Definitions and requirements for general radiography*
	Radiation dose structured reporting for radiography and fluoroscopy	IEC/PAS 61910-1 ed1.0 (2007-07) *Medical electrical equipment - Radiation dose documentation - Part 1: Equipment for radiography and radioscopy*
	Reproducibility of radiation output for dental x-ray devices	IEC 61223-3-4 ed1.0 (2000-03) *Evaluation and routine testing in medical imaging departments - Part 3-4: Acceptance tests - Imaging performance of dental X-ray equipment*
Modality-specific tests not specified	Dental x-ray imaging:	IEC 61223-3-4 ed1.0 (2000-03)

[41]Subclause 203.6.3.2.102 of IEC 60601-2-54 does not mention pediatrics specifically but it does specify a range of different-sized phantoms (10, 15, 20 cm thickness) for testing of automatic exposure control for direct radiography.

in above categories (examples included for reference; not exhaustive)	Line pair resolution; Low contrast resolution; Image homogeneity	*Evaluation and routine testing in medical imaging departments - Part 3-4: Acceptance tests - Imaging performance of dental X-ray equipment*
	CT: Sensitivity Profile; Patient-Support Positioning and Accuracy; Tomographic Section Thickness; Noise; Uniformity; Mean CT Numbers	IEC 61223-3-5 ed1.0 (2004-08) *Evaluation and routine testing in medical imaging departments–Part 3-5: Acceptance tests–Imaging performance of computed tomography X-ray equipment*; Corrigendum 1 (2006-03) and IEC 61223-2-6 ed2.0 (2006-11) *Evaluation and routine testing in medical imaging departments – Part 2-6: Constancy tests – Imaging performance of computed tomography X-ray equipment* and IEC 60601-2-44 ed3.0 (2009-02) *Medical electrical equipment – Part 2-44: Particular requirements for the basic safety and essential performance of X-ray equipment for computed tomography*; Corrigendum 1 (2010-05)
	Fluoroscopy and radiography: Additional tests are specified in the standards on the right (some of these tests are also included in the FDA performance standards).	IEC 60601-2-54 ed1.0 (2009-06) *Medical electrical equipment - Part 2-54: Particular requirements for the basic safety and essential performance of X-ray equipment for radiography and radioscopy* and IEC 60601-2-43 ed2.0 (2010-03) *Medical electrical equipment - Part 2-43: Particular requirements for the basic safety and essential performance of X-ray equipment for interventional procedures*

Pediatric issues that are specifically addressed by the standards referenced in Table 2 are listed in Table 3. (Note that the items below are design features, not tests, but the list is included here for completeness.)

Table 3. Specific pediatric issues addressed by applicable standards

Standard	Modality	Pediatric issues specified
IEC 60601-2-43 ed2.0 (2010-03) *Medical electrical equipment - Part 2-43: Particular requirements for the basic safety and essential performance of X-ray equipment for interventional procedures*	Interventional fluoroscopy	• The anti-scatter grid should be removable without tools for interventional x-ray equipment specified for pediatric applications (subclause 203.6.6; p. 30). • The last image-hold feature is especially important for pediatric applications (Annex AA, p. 42).
IEC 60601-2-54 ed1.0 (2009-06) *Medical electrical equipment - Part 2-54: Particular requirements for the basic safety and essential performance of X-ray equipment for radiography and radioscopy*	Radiography and fluoroscopy	• The anti-scatter grid should be removable for x-ray equipment specified for pediatric applications (subclause 203.6.6; p. 39). • X-ray equipment specified for pediatric applications should have a means of placing an added filter not less than 0.1 mm Cu or 3.5 mm Al (subclause 203.7.1; p. 4[illegible]).
IEC/PAS 61910-1 ed1.0 (20[illegible]-07) *Medical electrical equipment - Radiation dose documentation - Part 1: Equipment for radiography and radioscopy*	Radiation dose structured reporting for radiography and fluoroscopy	Recommends a higher level of conformance (level 2) to the radiation dose structured report for dedicated pediatric equipment (p. 8).