ACR
American College of Radiology
Quality is Our Image

acr.org

June 26, 2019

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2013-N-0134 – Mammography Quality Standards Act; Amendments to Part 900 Regulations; Comments of the American College of Radiology

The American College of Radiology (ACR)—a professional association representing more than 38,000 diagnostic radiologists, interventional radiologists, radiation oncologists, nuclear medicine physicians, and medical physicists —appreciates the opportunity to provide comments to the U.S. Food and Drug Administration (FDA) regarding the proposed modifications to MQSA regulations. The ACR has a longstanding record of commitment to quality in breast imaging; as the only nationally-approved MQSA accreditation body, ACR shares FDA's commitment in updating MQSA regulations to reflect changes in technology, breast imaging practices, and the experience garnered in implementing MQSA over the years.

ACR's comments were developed with input from a broad representation of relevant ACR commissions, committees and interested members and focus on those areas of the proposed rule for which we suggest modifications. For ease of FDA's consideration, our comments are presented to align with the order and structure set forth in the NPRM.

Definitions of Mammography and Mammographic Modality

ACR is comfortable with FDA's proposal to amend the definition of "mammography" to exclude computed tomography of the breast and the definition of "mammographic modality" to delete the reference to "xeromammography". However, by failing to incorporate stereotactic breast biopsy procedures as part of MQSA regulations, we believe FDA has missed an important opportunity to improve the quality of breast cancer diagnosis. **ACR urges FDA to incorporate stereotactic breast biopsy procedures under MQSA by revising the "Definitions" section of the regulation §900.2((aa)(1) as follows:**

(aa) *Mammography* means radiography of the breast, but, for the purposes of this part, does not include:

(1) Radiography of the breast performed during invasive interventions for localization ~~or biopsy procedures~~; or

Stereotactic breast biopsy is a critical component of breast cancer diagnosis. Poorly executed stereotactic procedures due to inadequate equipment or insufficient training can result in missed cancers and unnecessary patient complications. Although FDA opted not to regulate it in the initial MQSA rulemaking, FDA acknowledged in the preamble of the final rule: "Since the publication of the proposed regulations on April 3, 1996, significant progress has occurred in the professional community and FDA now believes that there is enough information to begin the development of interventional mammographic regulations." ACR concurs with that sentiment, noting that breast biopsy under x-ray guidance is a mature and widely performed procedure and already accredited on a voluntary basis. Inclusion of breast biopsy as part of MQSA has been recommended by the National Mammography Quality Assurance Advisory Committee (NMQAAC). Likewise, the IOM's 2005 report stated, "FDA should remove the exemption on interventional mammographic procedures such as stereotactic breast biopsy…"

Repeated Failure of Accreditation

Conceptually, ACR supports FDA's proposal to prohibit an accreditation body from accepting an application for accreditation from a facility that has failed to become accredited after multiple attempts until 1 year after the most recent failed attempt (proposed §900.4(a)(6)(ii)); however, we believe the language should be revised to avoid unintended consequences. **ACR strongly recommends that FDA revise and clarify this proposal to state four consecutive attempts of accreditation granting cycles, as opposed to three consecutive attempts.** Remembering that accrediting bodies perform an on-site survey for facilities after multiple failed attempts, if FDA retains the language "three consecutive attempts," this will result in every facility that requires a Scheduled On Site Survey to cease performing mammography for a year before being able to participate in the SOSS or the post-SOSS reinstatement. We presume that the intent of the FDA is to prohibit a facility from performing mammography if they failed the post-SOSS reinstatement, which would be the fourth attempt, rather than the third attempt. In addition, **we strongly recommend that the final rule provide FDA discretion to enforce this provision on a case-by-case basis, in consultation with the accrediting body.**

Enforcement discretion would be particularly important for facilities with multiple units, when one unit has been unsuccessful four times, but other units remain fully accredited. For example, a facility has three mammography units. Two of those units are fully approved with no failures. The third unit has four attempts. **ACR recommends that as a general rule, a facility that has four consecutive unsuccessful attempts on one unit but retains full accreditation on other units, should be able to continue to provide services with the two approved units.**

Further, in order to ensure the benefits of the proposed provision are realized and that the requirement is applied equitably, facilities must not be permitted to switch accrediting bodies to avoid this requirement. **ACR recommends that the proposed language be revised to further clarify that if a facility switches from one accrediting body to another, failures issued by both accrediting bodies would count toward the "four consecutive attempts" threshold.** For

example, if a facility has four unsuccessful attempts with a state accreditation program, subsequently seeks accreditation from ACR and fails again, then neither accreditation body (AB) should be allowed to accept another application from the facility until 1 year after the most recent unsuccessful attempt.

Retention and Provision of Personnel Records

ACR agrees it is important that personnel be able to obtain copies of facility records that document their qualifications to work at additional or new facilities. We are concerned that use of the term "reasonable request" could be problematic from a regulatory perspective due to the subjectivity of the term "reasonable". We also think it is important to clarify that facilities' responsibility for retention of former employees' credentials is not indefinite. **ACR recommends revising proposed §900.12(a)(4)) as follows:**

(4) *Retention of personnel records*. Facilities shall maintain records of training and experience relevant to their qualification under MQSA for personnel who work or have worked at the facility as interpreting physicians, radiologic technologists, or medical physicists. These records must be available for review by the MQSA inspectors. Records of personnel no longer employed by the facility must be maintained at least until the next annual inspection has been completed and FDA has determined that the facility is in compliance with the MQSA personnel requirements. The facility shall provide copies of these personnel records to current or former interpreting physicians, radiologic technologists, and medical physicists upon their ~~reasonable~~ written request for as long as the facility retains the records (as per 900.12(a)(4)). Before a facility closes or ceases to provide mammography services, it must make arrangements for access by personnel to their MQSA personnel records. This access may be provided by the permanent transfer of these records to the personnel or the transfer of the records to a facility or other entity that will provide access to these records for a period of at least 24 months.

ACR's proposed 24 month retention period is consistent with the documentation time period required under MQSA for personnel continuing experience (e.g., 900.12(a)(1)(ii)(A)). If a facility closes and personnel start working at another facility, this would ensure that they have similar access to the required documentation as is afforded personnel whose prior facility has not closed.

Equipment and Quality Control

The ACR generally agrees with the proposed requirement of allowing use of only digital accessory components that were either approved or cleared by FDA specifically for mammography, or approved or cleared by FDA for a use that could include mammography. However, we also recognize this proposed change may create a fiscal and implementation burden for those facilities that would need to purchase new equipment to come into compliance. Therefore, **ACR strongly recommends the final rule provide a grace period of 24 months, from the effective date of the rule, to allow facilities to make this transition.** This would be consistent with the grace period FDA granted for equipment updates as part of the prior final rule.

Quality Assurance Testing for Equipment Other the Screen-Film

ACR agrees with the proposed inclusion of this requirement, however **we propose that the referenced section (§ 900.12(e)(6)) also be modified as follows:**

"(6) Quality control tests--other modalities. For systems with image receptor modalities other than screen-film, the quality assurance program shall be substantially the same as the quality assurance program recommended by the image receptor manufacturer, or the quality assurance program of the ACR Digital Mammography Quality Control Manual, except that the maximum allowable dose shall not exceed the maximum allowable dose for screen-film systems in paragraph (e)(5)(vi) of this section."

The ACR Digital Mammography Quality Control Manual has been approved by FDA as an alternative standard and should be recognized in this context as well.

Mammographic Assessment Categories

As a general comment, we note that the explanatory language associated with each assessment category is not required to be reported with the BI-RADS assessment. In other words, a facility that uses only the text corresponding to the overall assessment category – "Incomplete: Need Additional Imaging Evaluation," "Negative," "Benign," "Probably Benign," "Suspicious," "Highly Suggestive of Malignancy," and "Known Biopsy-Proven Cancer" word – is compliant with MQSA requirements. **ACR recommends that this policy be explicitly preserved in the current rulemaking to avoid confusion.**

It should also be noted that the proposed "Post-Procedure Mammograms for Marker Placement" is already included in the alternative standard, though in that context it is not clear that the category also applies to mammograms done for preoperative localizations. Because localizations are now done with a variety of devices (wires, radioactive seeds, radiofrequency devices etc.), **ACR recommends that the term "position of a localization needle" be changed to "position of a localization device". Additionally, because the category will be used for multiple indications, ACR proposes the category title be changed to: "Post-Procedure Mammograms for Marker or Localization Device Placement." In order to avoid confusion in implementation, the proposed rule should clarify that this assessment category does not have a numeric value associated with it, and should be excluded from auditing.**

With respect to the third proposed category, "Incomplete: Need prior mammogram for comparison, ACR notes that this assessment category is encompassed within BI-RADS 0. The currently accepted verbiage is "Category 0: Incomplete – need additional imaging evaluation and/or comparison with prior examination(s)". Because it is sometimes important to get prior ultrasound in addition to, or instead of, prior mammograms for comparison before a final assessment can be issued, **ACR recommends substituting the more general phrase "breast imaging" for the more specific "mammogram" in titling this proposed category.** (The use of the term, "imaging", would be consistent with FDA's current incomplete category, "Incomplete: Need additional imaging evaluation.") **The regulations or FDA guidance should make clear that the current BI-RADS 0 verbiage, "Category 0: Incomplete – need additional imaging**

evaluation and/or comparison with prior examination(s)", is also acceptable in categorizing incomplete evaluations.

As a final comment, ACR notes that the use of BI-RADS 4 sub-categories (4a, 4b, 4c) is currently not permitted under MQSA – only the generic "4" with its associated terminology**. ACR recommends that the proposed rule be revised to allow or even encourage reporting in these BI-RADS 4 sub-categories (4a, 4b, 4c).** Inclusion of the subcategories provides more complete information on the likelihood of cancer on a biopsy, and transmits important risk information to the physician performing the biopsy, pathologist reviewing the tissue, and the surgeon. (Breast Imaging Reporting and Data System, BI-RADS: Mammography, 5th edition. Reston, VA: American College of Radiology. 4a - ≥ 2 - < 10% 4B ≥ 10 to < 50, 4C ≥ 50 to < 95). It is also important for concordance evaluation and improves the ability to understand and improve audit results. (Mai Elezaby, MD, Geng Li, PhD, Mythreyi Bhargavan-Chatfield, PhD, Elizabeth S. Burnside, MD, MPH, MS Wendy B. DeMartini, MD. ACR Bi-RADs assessment category 4 subdivisions in Diagnostic Mammography: *Radiology:* Volume 287: Number 2—May 2018.)

Deadline for Provision of Lay Summary to Patient and Report to Provider

ACR notes that the timeline proposed for communicating results under (§900.12(c)(2) and (c)(3) [mammography assessment that is "suspicious" or "Highly suggestive of malignancy] appears to be inconsistent with the proposed timeline under Proposed § 900.12(c)(1)(v)(B)) for the assessment category "Incomplete: Need prior mammograms for comparison". More specifically, if comparison with prior mammograms is required, proposed § 900.12(c)(1)(v)(B)) would provide facilities up to 30 days from the date of the mammogram to issue a final assessment. However, in a scenario in which the interpreting physician determines prior mammograms are required but doesn't receive the prior mammograms until more than 14 calendar days after the date of the mammogram and, upon comparing prior images issues an assessment of "suspicious" or "highly suggestive of malignancy", the facility would have exceeded the "in no case later than 14 calendar days from the date of the mammogram" requirement specified in ((§900.12(c)(2) and (c)(3)) for the assessment category "Incomplete: Need prior mammograms for comparison". Proposed § 900.12(c)(1)(v)(B)). **ACR suggests that in such cases, the facility should have 14 and 21 days from the receipt of the comparison images to issue the "suspicious" or "highly suggestive of malignancy" report to the referring physician or the lay letter to the patient respectively.**

Breast Density Notification

The ACR supports providing patients and their doctors with accurate, actionable information to better diagnose and treat those in our care. In keeping with this, ACR supports the proposed mandate that patient's breast density be included in the mammography report that must be provided to the patient's referring or named healthcare provider (Proposed §900.12(c)(1)(vi)), and we concur with the use of four BI-RADS-consistent categories for reporting breast tissue density in the mammography report (Proposed § 900.12(c)(1)(vi)).

The ACR recognizes that density information included in the lay summary women receive from their mammography examination may be helpful in encouraging an informed dialogue on this

topic between the patient and her physician. However, we have a number of concerns with the FDA's proposed approach to patient breast density notification as well as the language specified for inclusion in the lay summary. Specifically:

ACR recommends against requiring density language in the lay summary for women with density classifications "Breasts are almost entirely fatty" or "Scattered areas of fibroglandular density." Such information is not actionable and could lead to unnecessary confusion and even cause undue concern. For example, in a lay letter to women who do not have dense breasts, it is confusing to include an explanation of the fact that dense tissue can mask cancers. Moreover, such a statement could be incorrectly construed as giving reassurance that cancers in these women are never missed. Also, to advise women whose breasts are not dense to discuss breast density with their health care providers does not seem appropriate and might exacerbate underutilization of screening mammography. **If FDA ultimately decides to require reporting of breast density to women for "Breasts are almost entirely fatty" or "Scattered areas of fibroglandular density" breasts, the verbiage regarding the implications of having dense tissue should only be conveyed to women with dense tissue.**

ACR is also concerned the some of the terminology used in the proposed lay letter verbiage, is both incomplete and somewhat inaccurate. **We suggest that "not dense" and "dense" rather than the terms "low density" and "high density" are more appropriate terms for the lay summary;** patients may mistakenly conflate the level of density with the level of breast cancer risk. We note that dense tissue can be fibrous, glandular, or a combination of both, not necessarily glandular alone and that "dense" does not necessarily mean "more glands than fat" as the proposed language purports. **Importantly, the lay letter conveying density information should explicitly state that dense breasts are <u>not</u> abnormal.**

Rather than suggesting edits to the lay letter language proposed in the NPRM, **ACR recommends that FDA adopt the BI-RADS language copied below. We recommend that the requirement to include such language apply to the lay summary of women with "Heterogeneous fibroglandular tissue" or "Extreme fibroglandular tissue" only:**

> **"The mammogram shows that your breast tissue is dense. Dense breast tissue is very common and is not abnormal, but dense breast tissue can make it harder to find cancer on a mammogram. Also, dense breast tissue may increase your breast cancer risk. This information about the result of your mammogram report is given to you to raise your awareness. Use this report when you talk to your doctor about your own risks for breast cancer, which include your family history. At that time, ask your doctor if more screening tests might be useful, based on your risk."**

<u>Federal Preemption of State Breast Density Requirements</u>

ACR has heard from several members and one state chapter stressing the importance of federal preemption of state breast density reporting requirements. Although some states may prefer that their own density reporting language be used in mammography reports and the proposed NPRM purports to set only minimum standards, in practice, it may be difficult to determine whether a state statute is "stricter" and thus whether state- or federal- required language must be used. In any event, asking facilities to comply with different federal and state requirements

could be burdensome, and confusing to imaging facilities and patients alike. Neither facilities nor accrediting bodies should be expected to make independent legal determinations as to whether compliance with state or federal reporting (or both) is required. **Accordingly, ACR recommends that there be a clear statement of federal preemption of breast density reporting requirements in the final rule.**

Mammography Medical Outcomes Audit

ACR recognizes the value of medical outcomes audits as a quality improvement tool in mammography. We are concerned, however, that the specifications set forth in the NPRM may limit the effectiveness of the proposed audit requirement. We also note that the proposal to require cancer detection rate (CDR) and positive predictive value (PPV) for screening exams will require mammography facilities to track outcomes for all category 0 assessments, a new requirement that will impose a significant burden on facilities; the financial costs of this do not appear to be reflected in FDA's regulatory burden analysis. **We recommend FDA reconsider the proposed Medical Outcomes Audit section consistent with the comments that follow.**

As a general comment, in order to be meaningful an audit must have strict definitions of terms. The proposal for medical outcomes audit outlined in the NPRM does not sufficiently define terms or provide adequate guidance to facilities for performing an audit that accurately reflects performance. Among ACR's concerns:

- BI-RADS® is the current medical standard for medical audits and the methodology has been coded into most current medical audit software. The 2013 edition points out that there are 3 definitions for positive predictive value (PPV):
    - PPV_1 (abnormal findings at screening) = TP/(number of positive screening examinations)
      OR
      = TP/(TP + FP_1) [where FP_1 is no known tissue diagnosis of cancer within 1 year* of a positive screening examination (BI-RADS Category 0, 3, 4 or 5)]
    - PPV_2 (biopsy recommended) = TP/(number of screening or diagnostic examinations recommended for tissue diagnosis)
      OR
      TP/(TP+FP_2) [where FP_2 is no known tissue diagnosis of cancer within 1 year* after recommendations for tissue diagnosis or surgical consultation on the basis of a positive examination (BI-RADS Category 4 or 5)
    - PPV_3 (biopsy performed) = TP/(number of biopsies)
      OR
      TP/(TP+FP_3) [where FP_3 is a concordant benign tissue diagnosis (or discordant benign tissue diagnosis and no known tissue diagnosis of cancer) within 1 year* after recommendation for tissue diagnosis on the basis of a positive examination (BI-RADS Category 4 or 5)

  It is not clear from the proposed regulations which PPV metric is being required. We strongly suggest that the FDA require that all 3 PPVs (PPV_1, PPV_2 and PPV_3) be

calculated as outlined in BI-RADS Table 2. (See below.)

*Note that BI-RADS 2013 acknowledges that a few facilities may recommend less stringent screening intervals (rather than the ACR-recommended annual screening interval). In these cases, the actual screening interval should be used for the audit rather than 1 year for determination of cancer. See below:

> "Cancer — This is tissue diagnosis of either ductal carcinoma in situ (DCIS) or any type of primary (not metastatic) invasive breast carcinoma. For auditing purposes, positive truth is defined as a tissue diagnosis of cancer within an interval after breast imaging examination equal in length to the recommended screening interval. ***In the definitions listed later in this section (true-positive, true-negative, etc.), as well as in the subsequent examples, the recommended screening interval is assumed to be 1 year (365 days) because this is by far the most frequently recommended interval in the United States. One should substitute a 2-year (or longer) interval in these definitions, if appropriate.***"

- Likewise, the proposed definition of CDR is vague. For screening exams, CDR denominator is the total # of screening exams. For diagnostic exams, the definition is total # of diagnostic exams. The CDR ascertainment interval should parallel the routinely recommended screening interval.

- The term "positive mammograms" is not adequately defined. Previously, FDA had defined this as those mammograms for which biopsy is recommended. The NPRM appears to include category 0 exams as well. BI-RADS has different definitions for "positive": screening = categories 0, 3, 4, and 5; diagnostic = categories 4 and 5 (See BI-RADS Figure 1 below).

- For audit to be a useful measure for PPV, it is important that screening and diagnostic studies be evaluated separately. PPV of patients with symptoms is very different from those without. Failure to distinguish between screening and diagnostic data would preclude meaningful comparison to the literature or other available benchmarks. Accordingly, we recommend the final rule reflect the importance of this.

The BI-RADS atlas contains definitions and detailed instructions for performing a basic audit. **We strongly encourage the FDA to be more specific in its requirements, using current accepted terminology to prevent confusion among facilities as well as MQSA inspectors and to minimize inappropriate non-compliances.** See BI-RADS Table 2 below on the basic clinically relevant audit.

Figure 1. References for Biopsy Results — Screening and Diagnostic

		BIOPSY RESULTS	
		Positive (tissue diagnosis of cancer within 1 year)	Negative (concordant benign tissue diagnosis, or no tissue diagnosis of cancer within 1 year)
SCREENING	Breast imaging positive (BI-RADS® categories 0, 3, 4, 5)[a]	**TP**	**FP**
	Breast imaging negative (BI-RADS® categories 1, 2)	**FN**	**TN**
Sensitivity = TP/(TP + FN)			

		BIOPSY RESULTS	
		Positive (tissue diagnosis of cancer within 1 year)	Negative (concordant benign tissue diagnosis, or no tissue diagnosis of cancer within 1 year)
DIAGNOSTIC	Breast imaging positive (BI-RADS® categories 4,5)[a]	**TP**	**FP**
	Breast imaging negative (BI-RADS® categories 1, 2, 3)	**FN**	**TN**
Sensitivity = TP/(TP + FN) Specificity = TN/(TN + FP) PPV = TP/(TP + FP)			

[a] *For mammography — usually involves category 0 assessments but also includes rare category 4 or 5 assessments (use discouraged). For breast US — effectively involves category 0 assessments. For breast MRI — usually involves category 4 or 5 assessments; includes all category 3 assessments made at screening for mammography, US, and MRI.*

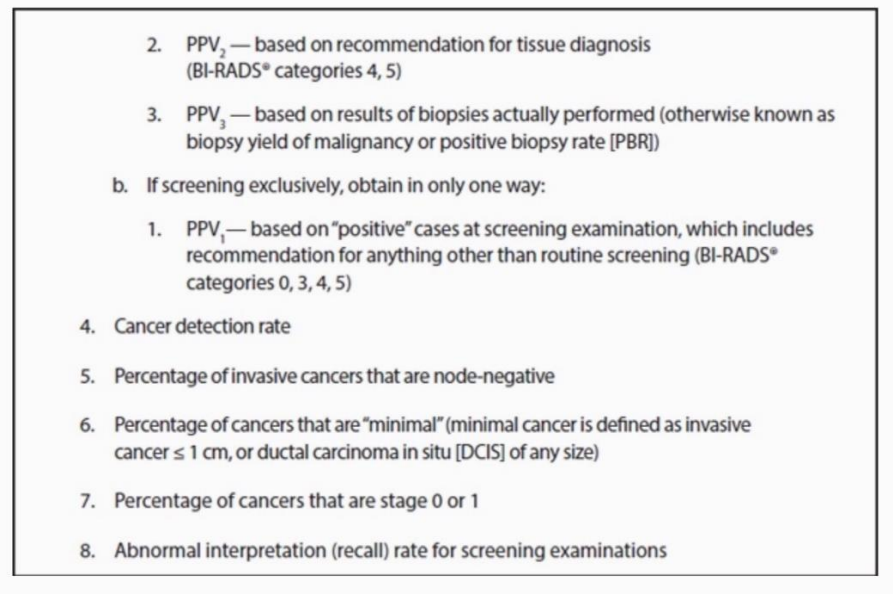
Table 2. The Basic Clinically Relevant Audit

A. Data to Be Collected

1. Modality or modalities.
2. Dates of audit period and total number of examinations in that period.
3. Number of screening examinations; number of diagnostic examinations (separate audit statistics should be maintained for each).
4. Number of recommendations for additional imaging evaluation (recalls) (ACR BI-RADS® category 0 — "Need Additional Imaging Evaluation").
5. Number of recommendations for short-interval follow-up (ACR BI-RADS® category 3 — "Probably Benign").
6. Number of recommendations for tissue diagnosis (ACR BI-RADS® category 4 — "Suspicious" and category 5 — "Highly Suggestive of Malignancy").
7. Tissue diagnosis results: malignant or benign, for all ACR BI-RADS® category 0, 3, 4 and 5 assessments (ACR suggests that you keep separate data for fine-needle aspiration/core biopsy cases and for surgical biopsy cases). MQSA Final Rule requires that an attempt is made to collect tissue diagnosis results for those mammography examinations for which tissue diagnosis is recommended.[2]
8. Cancer staging: histologic type, invasive cancer size, nodal status, and tumor grade.
9. MQSA Final Rule also requires analysis of any ***known*** false-negative mammography examinations by attempting to obtain surgical and/or pathology results and by review of negative mammography examinations.[2]

B. Derived Data to Be Calculated

1. True-positives (TP)
2. False-positives (FP_1, FP_2, FP_3)
3. Positive predictive value (PPV_1, PPV_2, PPV_3)
   a. In a screening/diagnostic facility, PPV may be obtained in one or more of three ways:
      1. PPV_1 — based on positive cases at screening examination, which includes recommendation for anything other than routine screening (BI-RADS® categories 0, 3, 4, 5)



2. PPV_2 — based on recommendation for tissue diagnosis (BI-RADS® categories 4, 5)
3. PPV_3 — based on results of biopsies actually performed (otherwise known as biopsy yield of malignancy or positive biopsy rate [PBR])

b. If screening exclusively, obtain in only one way:

1. PPV_1— based on "positive" cases at screening examination, which includes recommendation for anything other than routine screening (BI-RADS® categories 0, 3, 4, 5)

4. Cancer detection rate
5. Percentage of invasive cancers that are node-negative
6. Percentage of cancers that are "minimal" (minimal cancer is defined as invasive cancer ≤ 1 cm, or ductal carcinoma in situ [DCIS] of any size)
7. Percentage of cancers that are stage 0 or 1
8. Abnormal interpretation (recall) rate for screening examinations

Proposed Effective Date

The NPRM proposes an effective date of 18 months after the date of publication of the final rule in the Federal Register. As noted in the NPRM, facilities will need time to become familiar with the new requirements and to add breast density notification to their reporting systems. ACR notes that there are many changes proposed in the NPRM that would directly impact mammography software vendors as well as facilities. ACR's experience with vendors working to incorporate current-edition BI-RADS changes into their software suggests that 18 months will not be enough time for vendors to develop and implement new FDA requirements into existing software and to push the updates out to all their customers. **ACR encourages FDA to consult with applicable vendors and adopt an implementation timeframe that ensures adequate time for vendors and facilities to come into compliance with new requirements.** ACR is happy to work with FDA in assessing a reasonable timeframe for adoption and implementation of the proposed requirements by licensed BI-RADS vendors.

As always, the American College of Radiology welcomes continued dialogue with FDA on matters of shared interest. Please contact Gloria Romanelli, JD, ACR Senior Director of Legislative and Regulatory Relations at (202) 223-1670/gromanelli@acr.org with questions or concerns.

Sincerely,

Geraldine B. McGinty, MD, MBA, FACR
Chair, Board of Chancellors
American College of Radiology