



March 5, 2021

Submitted via regulations.gov

Attn: Dan Barry
U.S. Department of Health and Human Services
(on behalf of the Food and Drug Administration)
200 Independence Ave. SW
Washington, DC 20201

Subject: (RIN: 0991-ZA52) *Making Permanent Regulatory Flexibilities Provided During the COVID-19 Public Health Emergency by Exempting Certain Medical Devices From Premarket Notification Requirements; Request for Information, Research, Analysis, and Public Comment on Opportunities for Further Science and Evidence-Based Reform of Section 510(k) Program; Comments of the American College of Radiology, Radiological Society of North America, and Society for Imaging Informatics in Medicine*

The American College of Radiology (ACR),¹ Radiological Society of North America (RSNA),² and Society for Imaging Informatics in Medicine (SIIM)³ appreciate the opportunity to comment on the notice and request for information (RFI) signed by Alex M. Azar II, former Secretary of Health and Human Services, and published in the Jan. 15, 2021 *Federal Register* on behalf of the Food and Drug Administration (FDA), titled, *Making Permanent Regulatory Flexibilities Provided During the COVID-19 Public Health Emergency by Exempting Certain Medical Devices From Premarket Notification Requirements; Request for Information, Research, Analysis, and Public Comment on Opportunities for Further Science and Evidence-Based Reform of Section 510(k) Program* (RIN: 0991-ZA52; Document Number: 2021-00787; 86 FR 4088).

The notice/RFI described the intention of the U.S. Department of Health and Human Services (HHS) to permanently exempt seven class I devices for which 510(k) premarket review had been temporarily waived by FDA during the COVID-19 public health emergency. HHS also discussed the possibility of

¹ The **American College of Radiology (ACR)** is a professional association representing over 40,000 diagnostic radiologists, interventional radiologists, radiation oncologists, nuclear medicine physicians, and medical physicists. ([ACR.org](https://www.acr.org)).

² The **Radiological Society of North America (RSNA)** is an association of radiologists, radiation oncologists, medical physicists and related scientists promoting excellence in patient care and health care delivery through education, research and technologic innovation. The Society is based in Oak Brook, Illinois. ([RSNA.org](https://www.rsna.org)).

³ The **Society for Imaging Informatics in Medicine (SIIM)** is the leading healthcare professional organization for those interested in the current and future use of informatics in medical imaging. The Society's mission is to advance medical imaging informatics across the enterprise through education, research, and innovation in a multi-disciplinary community. ([SIIM.org](https://www.siim.org))

permanently exempting 83 class II devices and 1 unclassified device class from the 510(k) requirements for which it inaccurately stated premarket review had been “waived” during the public health emergency. The list of proposed class II devices included several radiology products under 21 CFR §892 used by physicians in radiology patient care, including artificial intelligence/machine learning (AI/ML)-enabled software:

- Lung CT System, Computer-Aided Detection (OEB - §892.2050)
- Chest X-Ray Computer Aided Detection (OMJ - §892.2050)
- Computer-Assisted Diagnostic Software For Lesions Suspicious For Cancer (POK - §892.2060);
- Radiological Computer-Assisted Triage And Notification Software (QAS - §892.2080)
- Radiological Computer Assisted Detection/Diagnosis Software For Fracture (QBS - §892.2090)
- Radiological Computer Assisted Detection/Diagnosis Software For Lesions Suspicious For Cancer (QDQ - §892.2090)
- Radiological Computer-Assisted Prioritization Software For Lesions (QFM - §892.2080)
- X-Ray Angiographic Imaging Based Coronary Vascular Simulation Software Device (QHA - §892.1600)
- Automated Radiological Image Processing Software (QIH - §892.2050)
- Image Acquisition And/Or Optimization Guided By Artificial Intelligence (QJU - §892.2100)
- And more.

General Comments

The ACR, RSNA, and SIIM are deeply concerned by the former Secretary’s proposal to significantly broaden the limited scope of the temporary policies for certain radiology product modifications described in FDA’s April 2020 document, *Enforcement Policy for Imaging Systems During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency*, and to permanently exempt the aforementioned product types from 510(k) premarket notification requirements. The described approach would undermine FDA’s critical role in providing reasonable assurance of the safety and effectiveness of radiology software used in patient care.

The Jan. 15 notice/RFI inaccurately described the scope of FDA’s temporary enforcement policy and did not offer alternatives to 510(k) requirements to ensure the exempted products would safely perform as intended in clinical environments. If implemented, such a concept would create a gap in oversight that could be detrimental to patients and providers, and potentially counterproductive for the burgeoning, but still relatively new imaging AI market. The described exemption would also contradict FDA’s explicit responsibility to regulate imaging software as clarified by Congress in the 21st Century Cures Act, Section 3060. For these reasons, the ACR, RSNA, and SIIM strongly oppose implementation of the former Secretary’s proposals for the identified class II radiology devices.

Concerns Regarding Mischaracterization of Temporary FDA Enforcement Policy

The Jan. 15 notice/RFI incorrectly described the FDA’s enforcement policies during the COVID-19 public health emergency as a temporary “waiver” from 510(k) premarket notification requirements. The implication was that the identified radiology devices would not need to meet 510(k) requirements during the public health emergency. However, with respect to the identified imaging software products, the actual FDA enforcement policy described in *Enforcement Policy for Imaging Systems During the*

Coronavirus Disease 2019 (COVID-19) Public Health Emergency is limited to modifications to the indications or functionality of software to address urgent COVID-19 image analysis needs where those modifications do not create an undue risk. Thus, the permanent 510(k) exemptions discussed in the HHS notice/RFI would be substantially broader in scope than the referenced FDA enforcement policy.

Concerns Regarding Contradiction with Important FDA Efforts and Needed Enhancements

The FDA and its stakeholders have for several years publicly deliberated on ways to enhance FDA's regulatory pathways and processes to ensure AI/ML-enabled software works as intended in rapidly evolving clinical environments. There has been substantial work within FDA to improve its oversight over AI/ML software, as described in FDA's Jan. 12 *Artificial Intelligence/Machine Learning-Based Software as a Medical Device Action Plan*. Building on the April 2019 discussion paper, *Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning-Based Software as a Medical Device*, the FDA discussed the need to improve transparency and generalizability across the total product lifecycle (TPLC) using good machine learning practices in algorithm development, premarket assurance of safety and effectiveness, real-world performance monitoring, and a pathway for clearance of continuous learning algorithms to improve transparency and generalizability. Unfortunately, the Jan. 15 HHS notice/RFI contradicted FDA's important activities in the digital health domain and its plans for the immediate future.

The FDA continues to face outstanding challenges in ensuring the safety and effectiveness of imaging AI/ML algorithms, even with comparative product assessments enabled by the current 510(k) requirements. AI models can experience brittleness when failing to adapt to conditions substantially different to the environment in which the algorithm was trained. For example:

- Imaging AI/ML algorithms analyze input data from numerous makes, models, and generations of hardware radiology devices. Thus, the presentation of the input data to the algorithm is variable, which can lead to performance inconsistencies within a single user facility as well as across implementations of the same algorithm in different user facilities.
- Patient demographics can vary significantly from institution to institution. As FDA evaluations do not always require comparisons across different user facilities, patient populations, and clinical conditions, there are sometimes open questions about the generalizability of previously cleared algorithms.
- The performance of AI models can degrade over time due to changing equipment, imaging protocols, or patient populations. The FDA has yet to advance post-market AI/ML performance monitoring; however, promising plans for future pilots were mentioned in the Jan. 12 *Artificial Intelligence/Machine Learning-Based Software as a Medical Device Action Plan*.
- Likewise, end-users do not typically have the infrastructure, processes, or wherewithal to systematically monitor the performance of deployed clinical AI on an ongoing basis in lieu of FDA oversight.

Rather than broadly exempting these radiology devices from 510(k) premarket notification requirements and deferring many safety and effectiveness questions about individual products to concerned consumers, FDA should explore ways to enhance its current approaches to overseeing AI/ML-enabled imaging software. This could include ideas such as requiring multisite validation to ensure AI is

generalizable across practices and patient populations, requiring longitudinal performance monitoring to assess real-world algorithm performance, requiring publication of the structured use case used to develop the model, and other approaches that balance safety and effectiveness considerations with ensuring access to promising innovations. Enhanced special controls and increased collaboration with the radiology provider community are key to advancing these goals.

Concerns Regarding Insufficient Justification for Exemptions of Radiology Software

The Jan. 15 notice/RFI cited, as its only justification, the low number of reported medical device reports (MDRs) filed by mandatory reporters for the identified product types and included in the Manufacturer and User Facility Device Experience (MAUDE) database. MAUDE is described by FDA as a *“passive surveillance system [that] has limitations, including the potential submission of incomplete, inaccurate, untimely, unverified, or biased data.”* FDA’s description of MAUDE goes on to warn that *“the incidence or prevalence of an event cannot be determined from this reporting system alone due to under-reporting of events, inaccuracies in reports, lack of verification that the device caused the reported event, and lack of information about frequency of device use.”*

Importantly, safety and effectiveness concerns may not always rise to the death or “serious injury” definition in 21 CFR §803.3 required for individual adverse event reports (e.g., life-threatening, results in permanent impairment/damage, or requires medical or surgical intervention to avoid permanent impairment/damage). This is particularly true for imaging software intended to facilitate detection, diagnoses, triage, or other functions. The negative effects of radiology software underperformance could include misrepresentation of findings, inaccurate measurements, progression of missed diseases or conditions, and exposure of patients to unnecessary procedures. MAUDE’s representation of product safety has been called to question by researchers and consumer groups. For example, a user facility’s report of a serious injury or malfunction filed with the manufacturer may not always be included in MAUDE if the manufacturer disagrees about the device’s contribution to the adverse event. Thus, MAUDE data should not drive policymaking or 510(k) exemptions for any class II devices, much less the identified digital health products for which safety and effectiveness concerns stretch the inherent limitations of the MDR/MAUDE framework.

Setting aside the above concerns with using MAUDE data alone to justify deregulation of class II software medical devices, the nascent nature and limited market penetration of AI/ML-enabled radiology software means a ten-year lookback on reported adverse events for these product types is not especially insightful. Additionally, FDA’s authority is not limited to medical devices with numerous reports of deaths and serious injuries captured by MAUDE, and there are various other safety and effectiveness concerns that must also be addressed by the agency. FDA must not defer its statutory responsibility to ensure devices used in patient care perform as expected as end-users may not always have enough information or expertise to discover potentially ineffective AI models. The impact of diagnostic imaging is such that the negative effects on patients of malfunctioning or ineffective medical devices can be felt years or even decades downstream.

ACR, RSNA, and SIIM Recommendations

Our organizations strongly recommend that HHS and FDA not implement broad and permanent exemptions from 510(k) premarket notification requirements for the identified class II radiology devices

under §892 in the Jan. 15, 2021 notice/RFI. We urge FDA to continue collaborations with the healthcare provider community to enhance clinical validation and real-world monitoring of AI/ML-enabled radiology software to ensure safety and effectiveness, and ultimately help establish trustworthiness and promote clinical adoption of promising innovations.

We welcome further dialog with the HHS and FDA regarding these proposals and all issues of shared interest. For questions or outreach, please contact Gloria Romanelli, JD, ACR Senior Director of Legislative and Regulatory Relations and Legal Counsel, Quality and Safety; and, Michael Peters, ACR Director of Legislative and Regulatory Affairs, at (202) 223-1670 or gromanelli@acr.org | mpeters@acr.org.

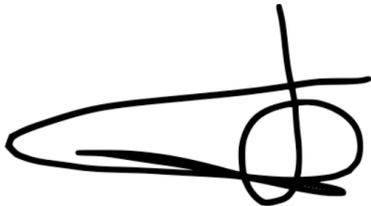
Sincerely,



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