Digital health, device and pathology stakeholders have conflicting views on HHS proposal to exempt devices

Device manufacturers, digital health stakeholders and health care providers recently provided comment on HHS's proposal to exempt 84 medical devices from the FDA's pre-market notification requirements. AgencyIQ has analyzed 56 comments submitted on the rule.

BY LAURA DIANGELO, MPH MAR 26, 2021 12:45 PM EDT

Executive IQ Brief

- **Policy issue(s):** In January 2021, the US Department of Health and Human Services (HHS) issued a notice that it intended to remove premarket submission requirements for 85 medical device products (83 Class II; 1 Unclassified). These products, which are currently required to submit a 510(k) pre-market notification for review and clearance by the FDA before coming to market, were the subject of pandemic-related enforcement discretion policies by the agency. According to HHS, the lack of significant adverse events reported following the enforcement discretion policy indicated that these products did not require pre-market review.
- **Comments closed:** March 15, 2021
- **Comments received:** 56
- **Overall industry sentiment:** Support for the proposal varied based on the product type. In general, stakeholders with digital pathology products supported the proposed 510(k) exemptions for these types of devices, citing overlapping oversight between FDA and CMS, the agency that sets standards for clinical operations in laboratories. However, digital health stakeholders largely did not support the proposal, citing the need for better scientific and regulatory understanding of novel technologies. In addition, some stakeholders raised concerns about the precedent – typically, the FDA (not HHS) conducts a review of devices that should be exempt from 510(k) requirements.

Proposal Overview

Under the Medical Device Amendments (MDA) of 1976, medical devices are stratified into three regulatory classifications based on their intended use and the level of risk they present to a patient. Class III devices are those that present the highest assessed amount of risk, and are those

devices intended to be implanted, life sustaining or life supporting. Class II medical devices are defined as those presenting moderate risk, while Class I devices are low risk products. In general, Class II (and some Class I) sponsors must submit a 510(k) pre-market notification for review and clearance by the FDA before they can legally market their product in the US.

However, not all Class I and Class II medical devices are subject to the 510(k) requirements. The exemption of well-understood, low-risk device types from pre-market requirements has been a priority for both the FDA and for Congress over the past several decades. Under FDAMA, Congress exempted most Class I devices from the 510(k) requirements and established a process by which Class II devices could be exempted from 510(k) requirements on a case-by-case basis.

Under the 21st Century Cures Act of 2016 (Section 3054), Congress directed FDA to conduct a review of the devices for which 510(k)s were currently required and determine if such a requirement was still appropriate for each device. The agency was directed to conduct this review every five years. This expands on FDAMA, which only required the agency to undertake an exemption review on a case-by-case basis.

HHS' Proposal

On January 11, 2021, the US Department of Health and Human Services issued a notice that it would extend the emergency flexibilities for the majority of the device types for which the FDA waived 501(k) requirements during the pandemic.

HHS proposed to exempt 83 Class II medical device types and 1 unclassified device (vestibular analysis apparatus, device code LXV) from 510(k) requirements. This exemption process would require a notice-and-comment period.

HHS's list of proposed exemptions wasn't random. Rather, it listed products that were subject to FDA's enforcement discretion guidelines issued during the COVID-19 pandemic. These devices included a wide variety of product types used to directly respond to the pandemic such as respiratory equipment, cardiopulmonary accessories, sterilizers and disinfection reprocessing instruments, facemasks, personal protective equipment (PPE), airway monitors and infusion accessories.

In addition, HHS proposed to permanently waive the 510(k) requirements for a significant number of remote monitoring, including digital health technologies for mental and behavioral conditions, pathology and imaging devices, computerized diagnostic aids, and cardiac and fetal monitors.

HHS' rationale for these changes was based on a retrospective review of the FDA's adverse events database for medical devices, known as the Manufacturer and Use Facility Device Experience database, or MAUDE. According to the notice, HHS conducted a review of the number of adverse events submitted to MAUDE for each device, by product code, over the last several years. HHS also examined the number of adverse events listed in MAUDE before and after the FDA issued its emergency regulatory flexibility policies. Based on its findings, it determined that the 510(k) requirements were unnecessary, as the Department's review found that the number of listed adverse events for those products did not spike following the issuance FDA's enforcement discretion policies.

HHS concluded the notice with a request for input on the process by which the FDA considers products to be 510(k) exempt, questioning apparent "scientific inconsistencies" in the types of

exempt and reserved devices. The notice highlights the example of manual stethoscopes and thermometers, which are 510(k) exempt, versus electronic versions of these products, which are subject to the 510(k) requirements. According to the Department, “these apparent inconsistencies merit scientific scrutiny. To that end, the Department seeks public comment as to whether other inconsistencies in the medical device regulatory framework exist.”
Industry FeedbackHHS’ docket on the proposal received 56 comments from a variety of stakeholders – including life sciences trade associations, manufacturers and provider organizations. AgencyIQ reviewed and analyzed comments from relevant stakeholders, and highlights from their comments may be found below.

Organization

Comments, suggestions and requests

Life Sciences Associations

Digital Therapeutics Alliance (DTA)

Trade Association

· Does not support long-term regulatory exemption for digital products. DTA cites regulatory oversight as key to ensure public trust in digital health products, patient safety and device quality.

· Does not believe that the exclusive reliance on MAUDE data is appropriate to understand the context of digital health products’ safety profiles.

· Supports the development of new pathways for digital products, which it states are “appropriate and necessary”, after the emergency.

· Cites concerns about the future of already-marketed products once the enforcement discretion comes to an end.

Medical Imaging and Technology Alliance (MITA)

Trade Association

· Cites concerns about the future of already-marketed products once the enforcement discretion comes to an end, and the transition either into removing the products from the market or “into conventional regulatory compliance.”

· Does not support long-term regulatory exemption for digital products. MITA cites regulatory oversight as key to ensure public trust in digital health products, patient safety and device quality, and “ongoing” innovation in certain Artificial Intelligence (AI) based products included in the proposal.

· Does not believe that the exclusive reliance on MAUDE data is appropriate to understand the context of digital health products’ safety profiles.

· Supports continued use and maintenance of the 510(k) pathway for digital health devices, stating that the pathway is “a cornerstone of efficiently bringing safe and effective medical devices to market”.

· Seeks clarity about how this proposed rule would impact FDA commitments under MDUFA.

Digital Pathology Association

Trade Association

· Believes that the exclusive reliance on MAUDE data may not be appropriate to understand the context of digital health products' safety profiles in all circumstances but does state that it is a useful metric for some products.

· Supports 510(k) exemptions for certain digital pathology display products (e.g., product code PZZ , QKQ), citing the expertise of end-user pathology and laboratory professionals.

· Supports 510(k) exemptions for the OEO product code, which are devices that aid in immunohistochemistry (IHC) staining for certain breast cancer biomarkers. However, DPA requests that good manufacturing practice (GMP) requirements remain in effect for these products.

· Supports regulatory reform for whole slide imaging (WSI) digital pathology products (product code PSY), including individualized product code for each hardware and software component within a WSI system. A modularized approach, DPA explains, will help improve interoperability and consistency in practice.

· Outlines concerns about AI products included in the proposed exemption and supports the FDA' s efforts to build upon its AI/ML Action Plan.

Association for Pathology Informatics (API)

Trade Association

· Believes that the exclusive reliance on MAUDE data may not be appropriate to understand the context of digital health products' safety profiles in all circumstances.

· Supports 510(k) exemptions for certain digital pathology display products (under product code PZZ).

· Raises concerns about the proposed 510(k) exemptions for three digital pathology product codes in the proposed rule: Digital Pathology Image Viewing and Management Software (QKQ); Whole Slide Imaging Systems (PSY); and Automated Digital Image Manual Interpretation Microscopes (OEO). Overall, API requests a new system of regulation for product code QKQ, a modularized approach to WSI products that could improve interoperability, and more targeted software-related pathways for products under OEO.

· Highlights the need for "increased regulatory flexibility" for product codes QKQ, PSY and OEO, citing the duplicative oversight between CMS and FDA.

Life Sciences Firms and Manufacturers

Roche Diagnostics

Medical device firm

· Supports the proposal to remove 510(k) requirements from four digital pathology product codes: Whole Slide Imaging Systems (PSY); Digital Pathology Display (PZZ); Digital Pathology Image Viewing and Management Software (QKQ); and Automated Digital Image Manual Interpretation Microscopes (OEO).

· Suggests that post-market requirements including general and special controls and the quality system requirements, should be sufficient to ensure continued safety of these digital pathology products.

· Recommends that the FDA increase its focus on "truly innovative device premarket reviews and regulatory submission approaches" for digital pathology products, and especially AI/ML-based software products.

Orexo

Pharmaceutical/digital health firm

· Supports the general framework used to identify potential 510(k) exemptions, and supports HHS' proposal to exempt products from 510(k) pre-market notification requirements. Specifically, Orexo cites devices under PWE (Computerized Behavioral Therapy Device for Psychiatric Disorders) as devices that should be exempt from 510(k) requirements.

· Requests additional clarity on the transition away from the emergency-related enforcement discretion for products that are currently marketed under these flexibilities.

Baxter Healthcare

Medical device firm

· Does not support 510(k) exemptions for medical devices under product code PHC (Infusion Safety Management Software), citing FDA alerts on adverse events.

· Urges FDA to consider opportunities to create efficiencies in the pre-market submission pathways, such as reviewing components of a system together (e.g., combining review of safety management software with a 510(k) for an infusion pump).

Limbix Health

Medical device firm

· Does not support 510(k) exemptions for devices under product code PWE (Computerized Behavioral Therapy Device for Psychiatric Disorders).

Otsuka Inc.

Pharmaceutical/digital health firm

· Does not believe that the exclusive reliance on MAUDE data is appropriate to understand the context of regulated product safety profiles.

· Does not support the 510(k) exemption proposals, citing concerns with the methodologies used to determine that pre-market notification may no longer be required to ensure safety and efficacy.

· Highlights ongoing challenges with the regulation of novel digital technologies and software-based devices, stating that these products are not yet well-understood enough to merit regulatory exemptions.

GuideStar Medical Devices Inc.

Medical device firm

· Does not support the unilateral 510(k) exemptions included in the proposal.

· Recommends that HHS reverse its proposal, and then “hand pick” certain low-risk devices to reconsider for exemption individually.

AliveCor

Medical device firm

· Does not support the proposed 510(k) exemption for devices under product code QDA (Electrocardiograph Software for Over-The-Counter Use), citing patient safety risks.

Caption Health

Medical device firm

· Does not believe that the exclusive reliance on MAUDE data is appropriate to understand the context of regulated product safety profiles.

· Cites concerns about HHS’ methodology to identify potential exemptions, noting that the FDA enforcement discretion guidelines were limited in scope.

· Recommends that FDA continue to consider 510(k) exemptions on a “case-by-case” basis using the agency’s typical methodology.

· Supports the FDA’s AI/ML Action Plan for software-based products.

MedRhythms, Inc.

Medical device firm

· Does not support the 510(k) exemptions proposed by HHS, especially for software-based digital health products. MedRhythms cites the novelty of these products, which are not yet well understood enough to support 510(k) exemptions.

· Does not believe that the exclusive reliance on MAUDE data is appropriate to understand the context of regulated product safety profiles.

AppliedVR

Digital health firm

· Does not support the 510(k) exemptions proposed by HHS, especially for software-based digital health products.

· Does not believe that the exclusive reliance on MAUDE data is appropriate to understand the context of regulated product safety profiles.

· Raises concerns about the potential for reimbursement from CMS for products that have not been formally granted market access by the FDA. AppliedVR specifically cites the Medicare Coverage for Innovative Technology (MCIT) program, which would grant additional reimbursement options for products that have been designed with Breakthrough Device status. Although this regulation is currently on hold under the new administration, AppliedVR was recently awarded breakthrough status for its virtual reality-based cognitive behavioral therapy tool.

Pear Therapeutics

Digital health/pharmaceutical firm

· Does not support the 510(k) exemptions proposed by HHS, specifically citing devices under product code PWE (Computerized Behavioral Therapy Device for Psychiatric Disorders).

· Cites concerns about HHS' methodology to identify potential exemptions, noting that the FDA enforcement discretion guidelines were limited in scope.

· Does not believe that the exclusive reliance on MAUDE data is appropriate to understand the context of regulated product safety profiles.

· Highlights ongoing challenges with the regulation of novel digital technologies and software-based devices, stating that these products are not yet well-understood enough to merit regulatory exemptions.

Cognoa

Digital health firm

· Does not support the 510(k) exemptions proposed by HHS, especially for software-based digital health products.

· Does not believe that the exclusive reliance on MAUDE data is appropriate to understand the context of regulated product safety profiles.

· Raises concerns about the potential for reimbursement from CMS for products that have not been formally granted market access by the FDA. AppliedVR specifically cites the Medicare Coverage for Innovative Technology (MCIT) program, which would grant additional reimbursement options for products that have been designed with Breakthrough Device status (although this regulation is currently on hold).

Nanosonics Limited

Medical device firm

· Does not support the 510(k) exemptions proposed by HHS, especially for devices used for disinfection or sterilization. Nanosonics specifically cites four product codes included in the proposal as inappropriate for a 510(k) exemption due to potential patient safety issues, technical complexity and downstream risks: OUJ (High Level Disinfection Reprocessing Instrument For

Ultrasonic Transducers, Mist); PSW (High Level Disinfection Reprocessing Instrument For Ultrasonic Transducers, Liquid); KMH (Sterilizer, Dry Heat); and FLF (Sterilizer, Ethylene-Oxide Gas).

Midmark Corporation

Medical device firm

· Supports HHS' proposal to remove 510(k) requirements for medical devices.

· Recommends that the FDA create a new product code for radiological image processing systems for use in dentistry, and exempt these products from the 510(k) pre-market notification requirements. Currently, these products are regulated under product code LLZ.

Corista, LLC

Digital pathology firm

· Supports the proposal to remove 510(k) requirements for digital pathology devices, including: Whole Slide Imaging Systems (PSY); Digital Pathology Display (PZZ); and Digital Pathology Image Viewing and Management Software (QKQ).

· Cites the expertise of end-user pathology and laboratory professionals as a key rational for reducing regulatory burden for these products.

Kanteron Systems

Digital pathology firm

· Supports the proposal to remove 510(k) requirements for digital pathology devices, including: Whole Slide Imaging Systems (PSY); Digital Pathology Display (PZZ); and Digital Pathology Image Viewing and Management Software (QKQ).

Sectra

Digital pathology firm

· Supports the proposal to remove 510(k) requirements for digital pathology devices, including: Whole Slide Imaging Systems (PSY); Digital Pathology Display (PZZ); and Digital Pathology Image Viewing and Management Software (QKQ).

Infrared Cameras Inc. (ICI)

Infrared technology firm

· Raises concerns that camera-based devices used to assess body temperature (i.e., telethermographic systems), for which the FDA has expressed enforcement discretion, are being used inappropriately during the pandemic, increasing risk for individuals and organizations. Supports continued regulatory oversight of these products.

leanRAQA

Regulatory compliance and strategy consultancy

· Encourages a case-by-case reconsideration of the proposed 510(k) exemptions, citing concerns that some of the devices on the list are used in high-risk situations or for life-sustaining, life-supporting care.

Providers and Provider Organizations

American Medical Association (AMA)

Provider Association

· Does not support HHS' proposal to exempt medical devices from the 510(k) pre-market notification requirements.

· Raises concerns about "unilateral action by HHS and the precedent it may set", recommending that the FDA continue to consider case-by-case 510(k) exemptions.

· Does not believe that the exclusive reliance on MAUDE data is appropriate to understand the context of regulated product safety profiles.

American College of Radiology, Radiological Society of North America, and Society for Informatics in Medicine

Provider Associations

· Does not support HHS' proposal to exempt medical devices from the 510(k) pre-market notification requirements.

· Cites concerns about HHS' methodology to identify potential exemptions, noting that the FDA enforcement discretion guidelines were limited in scope.

· Highlights ongoing challenges with the regulation of novel digital technologies and software-based devices, stating that these products are not yet well-understood enough to merit regulatory exemptions. The associations go on to note that the proposed exemptions would conflict with FDA's work to improve regulatory pathways for digital health products, including the AI/ML Action Plan.

Cardinal Health

Provider Organization

· Supports the exemption of certain surgical gloves (product code OPA) from 510(k) requirements.

American Society of Anesthesiologists (ASA)

Provider Association

· Does not support HHS' proposal to exempt medical devices from the 510(k) pre-market notification requirements, especially AI/ML software-based digital health products and medical devices used to provide life support.

· Recommends a more flexible regulatory approach for “useful medical technologies that have encountered regulatory challenges to adoption in the United States.” The ASA specifically highlights an opportunity to align with CE mark regulatory processes in Europe to help accelerate market access for novel products.

Mayo Clinic

Provider Organization

· Supports the proposal to remove 510(k) requirements for digital pathology devices, including: Whole Slide Imaging Systems (PSY); Digital Pathology Display (PZZ); and Digital Pathology Image Viewing and Management Software (QKQ).

· States that organizations such as the College of American Pathologists (CAP, comments below) and Digital Pathology Associations (DAP, comments above), amongst others, could establish minimum specifications to help ensure continued quality and standardization.

College of American Pathologists

Provider Association

· Cautions against the proposal to remove 510(k) requirements for digital pathology devices, including: Whole Slide Imaging Systems (PSY); Digital Pathology Image Viewing and Management Software (QKQ); and Automated Digital Image Manual Interpretation Microscopes (OEO). CAP cites concerns about device standardization and quality as a key reason to oppose the proposal.

· Supports the proposal to remove 510(k) pre-market notification requirements for Digital Pathology Display (PZZ) devices.

What’s Next

The original proposal was issued by HHS on January 8, only a few weeks before the Biden administration took office. However, the incoming leadership of HHS has not indicated if it will seek to move this particular proposal forward. In general, it seems unlikely at this point that these exemptions will be finalized as proposed by the previous HHS Secretary.

Regardless of what HHS decides to do, the life sciences industry’s responses to the proposal do highlight some key issues and concerns.

First, several stakeholders make the case that certain digital pathology devices should not be subject to FDA’s 510(k) process. These commenters largely point to regulatory requirements out of CMS, known as the Clinical Laboratory Improvement Amendments (CLIA) regulations. While the FDA has the authority over the products themselves, CMS sets standards for the facilities in which these products are used – called CLIA labs – that include requirements for laboratory and pathology professionals to validate their tools before use. Several stakeholders argued these regulations can be duplicative and that the CMS CLIA expectations for end-users can safely and adequately ensure the quality of certain digital pathology tools. These comments may put these

products on FDA's radar for a case-by-case exemption, in accordance with the agency's "least burdensome" mandate.

Second, several digital health product developers raised concerns with the proposals to exempt their products from regulatory review requirements, citing a lack of established understanding of these technologies. This also brings up an interesting point, with which the agency has recently grappled: how should the relative risks of digital health and software-based products be considered? While a fully digital behavioral health tool, such as the EndeavorRx video game-based device for ADHD, may not present the types of risks that the FDA has traditionally considered for medical devices (e.g., biocompatibility, fracture or migration), the product itself is likely to present other risks to patients. The question, then, is how the FDA will consider these risks relative to its methods of regulation.

Finally, the comments largely highlight the need for better guidance from the FDA about regulatory pathways for digital products, especially software-based products.

While the FDA is working to develop frameworks for digital health tools, the agency's new Digital Health Center of Excellence (DHCoE) is not expected to release its first official guidance documents until Q4 2021. FDA has indicated that certain best practices can be used within regulatory submissions now, even without established guidance from the agency (e.g., pre-specified change control plans for software products and cybersecurity considerations). However, without formal guideposts from FDA, industry still faces regulatory uncertainty in bringing digital tools to market.

Key Documents and Dates

- Docket No. FDA-2021-N-0009· AgencyIQ: HHS wants to exempt dozens of device types from pre-market requirements