ORIGINAL ARTICLE

An FDA Guide on Indications for Use and Device Reporting of Artificial Intelligence-Enabled Devices: Significance for Pediatric Use

Brandon J. Nelson, PhD[a], Rongping Zeng, PhD[a], Marla B. K. Sammer, MD, MHA[b], Donald P. Frush, MD[c], Jana G. Delfino, PhD[d]

Abstract

Radiology has been a pioneer in adopting artificial intelligence (AI)-enabled devices into the clinic. However, initial clinical experience has identified concerns of inconsistent device performance across different patient populations. Medical devices, including those using AI, are cleared by the FDA for their specific indications for use (IFUs). IFU describes the disease or condition the device will diagnose or treat, including a description of the intended patient population. Performance data evaluated during the premarket submission support the IFU and include the intended patient population. Understanding the IFUs of a given device is thus critical to ensuring that the device is used properly and performs as expected. When devices do not perform as expected or malfunction, medical device reporting is an important way to provide feedback about the device to the manufacturer, the FDA, and other users. This article describes the ways to retrieve the IFU and performance data information as well as the FDA medical device reporting systems for unexpected performance discrepancy. It is crucial that imaging professionals, including radiologists, know how to access and use these tools to improve the informed use of medical devices for patients of all ages.

Key Words: Artificial intelligence, evaluations, indications for use, patient population, pediatrics

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[a]Division of Imaging, Diagnostics and Software Reliability, Office of Science and Engineering Labs, Center for Devices and Radiological Health, US Food and Drug Administration, Silver Spring, Maryland.
[b]Vice Chair for Clinical Affairs, Department of Radiology, Texas Children's Hospital, Houston, Texas; Chair of the Pediatric AI Workgroup in the ACR.
[c]John Strohbehn Professor of Radiology, Associate Faculty, Duke Medical Physics Graduate Program, Department of Radiology, Duke University Medical Center, Durham, North Carolina.
[d]Deputy Division Director, Division of Imaging, Diagnostics, and Software Reliability, Office of Science and Engineering Labs, Center for Devices and Radiological Health, US Food and Drug Administration, Silver Spring, Maryland.
Corresponding author and reprints: Brandon J. Nelson, PhD, US Food and Drug Administration, Center for Devices and Radiological Health, Office of Science and Engineering Labs, Division of Imaging, Diagnostics and Software Reliability, 10903 New Hampshire Ave, Silver Spring, MD 20993.

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INTRODUCTION: ARTIFICIAL INTELLIGENCE AS A DEVICE IN RADIOLOGY

Devices incorporating artificial intelligence (AI) and machine learning can be found in many areas of medicine, and radiology has been a pioneer in adopting AI-enabled devices into the clinic. The FDA list of cleared devices that include AI and machine learning technology is dominated by radiology [1]. However, the ACR reported in its first annual survey of clinical AI usage that 94% of AI users experienced inconsistent device performance. Most of these inconsistencies were reported as being due to variability across patient groups seen by the device [2].

The majority of these devices were reviewed and cleared by FDA for specific indications for use (IFUs). Thus, one possible explanation for this inconsistent performance is that the devices were unknowingly used in a patient group or manner outside of the cleared indications. Understanding IFUs may help bridge this gap in understanding and better support consistent device usage and performance. Pediatric patients are of particular concern because most medical devices designed for adults are eventually used on children.

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As data-driven AI devices become more prevalent, if these devices are not specifically designed for pediatric patients, then their safety and efficacy in these patients remain unclear. We provide a brief guide for practicing radiologists and device users on the FDA clearance and premarket evaluation process. Further emphasis is given on understanding pediatric indications and what to do if they are not explicitly given and the important role device users have in postmarket device monitoring to report issues regarding device safety and efficacy.

510(K) PREMARKET NOTIFICATION AND IFUs

The FDA regulates firms that manufacture, repackage, relabel, or import medical devices sold for clinical use in the United States. (It should be noted that there are situations in which AI can be developed and deployed clinically without FDA authorization, such as is done locally in some institutions.) Thus, the scope of this discussion is limited to FDA-cleared devices. The FDA takes a risk-based approach to medical device regulation. Medical devices are placed in one of three device classes (class I, class II, and class III) based on the level of regulatory control necessary to provide a reasonable assurance of safety and effectiveness. Class I devices are considered lowest risk, and class III devices are considered highest risk.

Most radiological imaging and therapeutic devices marketed in the United States are FDA class II medical devices subject to the 510(k) Premarket Notification process [3], which determines if a new device is substantially equivalent to a legally marketed predicate device [4].

Devices are cleared by FDA for a specific IFUs, which describes the general purpose of the device and the disease or condition the device will diagnose or treat, including a description of the intended patient population [3]. The performance data needed to support a premarket submission depends on both the IFU of the device and the device technology. Performance data are used to ensure that the safety and effectiveness are equivalent to the existing technology.

Many imaging and image-processing devices have a very general IFU that broadly cover large patient populations. This makes the device accessible to the largest number of patients. However, determining whether a particular device has been specifically evaluated for use in pediatric patients can be challenging in these situations. Figure 1 provides three examples of previously cleared IFUs that include varying degrees of detail on the pediatric population for which the device is intended to be used. Figure 1a illustrates how to find the IFU from the public summary in the FDA 510(k) database (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm). The IFU in Figure 1a describes a device specifically intended for neonates and infants ages 0 to 12 months. Figure 1b is more general, stating that adult and pediatric images can be processed by the device, whereas Figure 1c makes no mention of the indicated patient population. In these instances, users can refer to the summary of how the device was evaluated in the 510(k) summary or the device user manual to determine what patient subgroups were included in evaluations.

If pediatric performance data are not clear in either of these documents, users are encouraged to contact the device vendor to clarify whether information on the performance of the device in pediatric patients is available. Recently, the FDA has focused on ensuring transparency about the validation of AI-enabled devices, especially regarding inclusion of pediatric data. As transparency improves in public summaries, users are encouraged to follow the steps described here, which are summarized in Figure 2.

OFF-LABEL USE

Off-label use describes the situation in which a device is used outside of its IFU. Off-label use is considered a practice of medicine decision that is not regulated by FDA. A medical professional may use a device off-label based on their best medical judgment and at their own risk [4]. Off-label use of medical devices in the context of pediatric patients has been previously discussed [5], as the majority of cleared or approved devices do not include specific pediatric indications. To the best of these authors' knowledge, a discussion focusing on the off-label use of AI-enabled devices in pediatric patients has not previously occurred. Becuase it is generally accepted that AI solutions behave unpredictably when applied to data characteristically different than their training populations, additional analysis by multiple stakeholders would be helpful to understand the implications of off-label use of AI-enabled device technology in pediatric patients.

ADVERSE EVENTS AND FDA MEDICAL DEVICE REPORTING

After devices are cleared for clinical use, they will be exposed to larger populations of patients over longer time periods than originally tested. Imaging professionals, including radiologists, play an important role in promoting the safety of medical devices by reporting to the FDA and device manufacturers when devices malfunction. Medical Device Reporting is used by the FDA for postmarket monitoring and encompasses several mechanisms for reporting events depending on their severity [6]. Reports to the FDA inform the potential recall of marketed devices, aid in premarket device review, and inform other users of potential device problems.

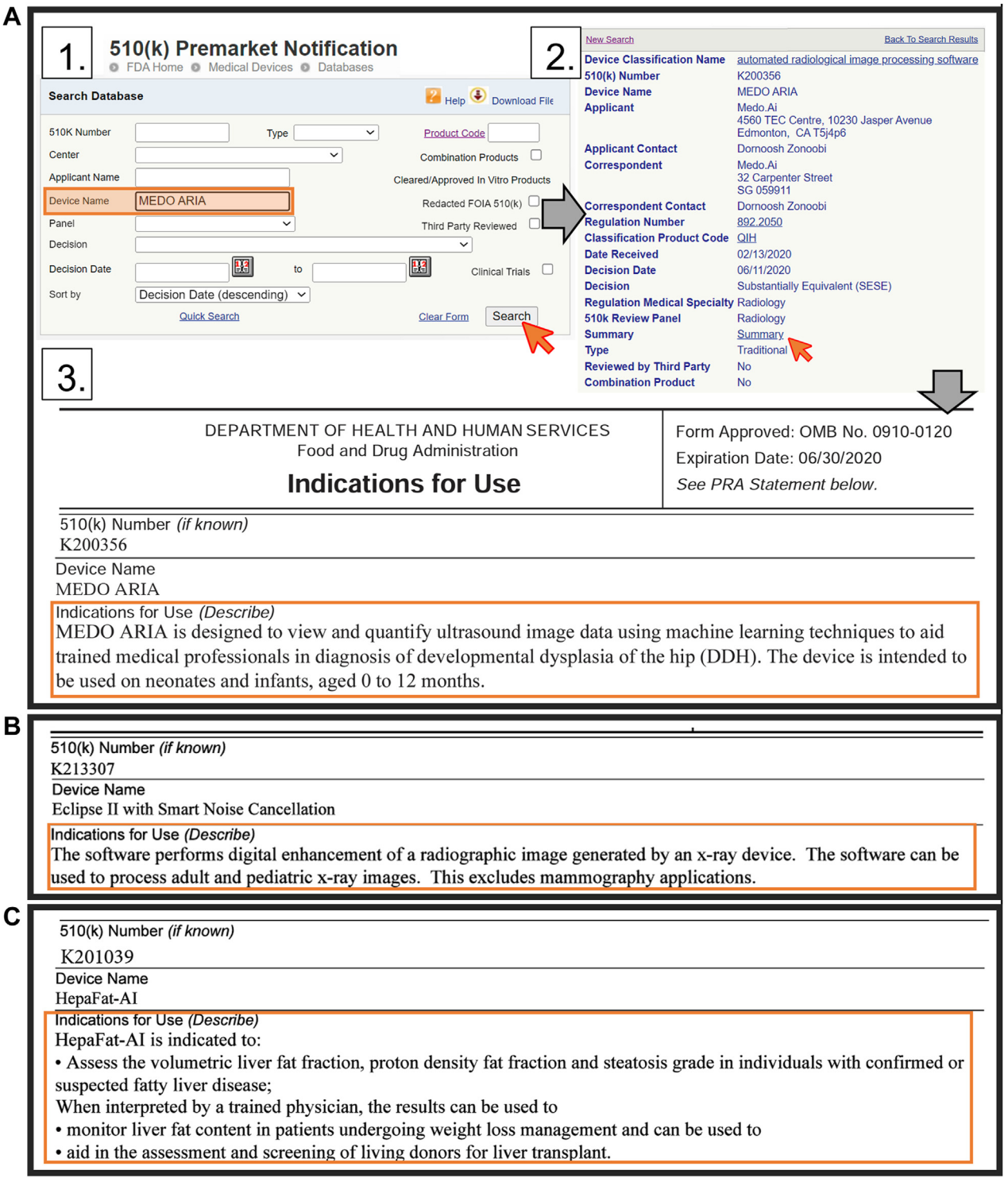

Fig. 1. Finding the indications for use (IFU) using the FDA 510(k) database: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm with three example IFUs. (a) Find a 510(k) summary using the 510(k) database starting with (1) searching for the product, then (2) selecting the "Summary" hyperlink in the database entry. (3) The IFU is found in the summary document. This IFU is an example in which pediatric patients with a specific age range are indicated. (b) An example IFU with broader patient indications. (c) Another IFU example in which pediatric patients are not mentioned at all in the indications.

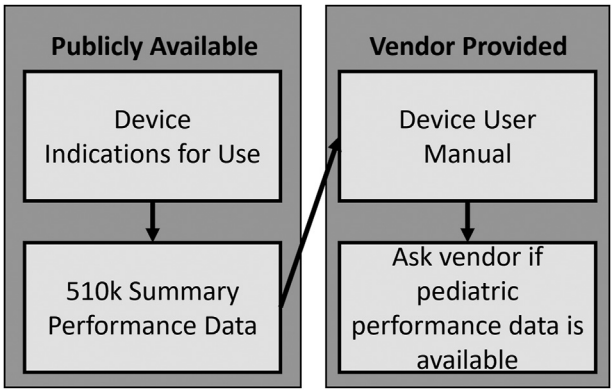

Fig. 2. Locating pediatric performance data. Starting with the indications for use, users can also check for performance data in the device 510(k) summary or user manual, or they can ask the vendor.

Device manufacturers must report events that may have caused or contributed to the death or serious injury of a patient as well as device malfunctions that, if they were to occur again, would be likely to cause or contribute to death or serious injury within 30 calendar days of becoming aware of the event.

User facilities must report device adverse events that contributed to the death or serious injury of a patient within 10 working days via the FDA Form 3500. FDA also accepts voluntary reports from patients and consumers who wish to alert the FDA to a medical device problem. (It is not uncommon for FDA to receive multiple adverse event reports for the same incident.) These reporting forms ask for patient information, as well as information about the incident, the suspected device, and the reporter. Reports providing feedback on device performance can be reported from individual incidents or summarized retrospectively. Providing more information about potential safety or efficacy concerns regarding FDA-regulated products can better inform a timely response and aid other device users in pre-empting similar issues. Redacted reports are freely available via FDA's Manufacturer and User Facility Device Experience database. Reporting forms and related information, including how to subscribe to notifications of device safety alerts, can be found at: https://www.fda.gov/safety/medwatch.

CONCLUSIONS

Medical devices are cleared for specific IFUs, and the performance data evaluated during the premarket submission support the IFUs. Understanding the IFUs of a given device—including the patient population in which the device is intended to be used—is critical to ensuring that the device performs as expected. Problems with devices are monitored primarily through a passive reporting system of failures and patient injuries. Thus, it is crucial that radiologists and users know how to access and utilize tools for determining IFUs and reporting systems to provide a stronger foundation for informed use of medical devices for patients of all ages.

KEY POINTS

- Medical devices, including software as a medical device incorporating AI, are cleared for sale and marketing by the FDA.
- The FDA clears devices based upon a specific indication for use (IFU).
- Performance of the device in the premarket submission must support the indication(s) for use.
- If information on the pediatric applicability of a device is not clear from either the IFUs or the summary of performance data, users are encouraged to contact the device vendor to clarify whether information on the performance of the device in pediatric patients is available.
- Reporting of known or suspected device failures is an important way to provide feedback about a device to both the manufacturer and the FDA.

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