FDA U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR DEVICES & RADIOLOGICAL HEALTH

Summary of the Patient Engagement Advisory Committee
October 22, 2020

Introduction:

The Patient Engagement Advisory Committee to the Food and Drug Administration (FDA) met October 22, 2020, to discuss and make recommendations on the topic ""Artificial Intelligence (AI) and Machine Learning (ML) in Medical Devices." Specifically, the Committee discussed the composition of the datasets on which the software "learns", components of the device information shared with patients, and factors that impact patient trust in the technology. Large clinical datasets are used to train and improve AI/ML algorithms, allowing transformational improvements in the diagnosis, clinical decision making, and treatment of patients. Devices using AI/ML technology will transform healthcare delivery by increasing efficiency of key processes in the treatment of patients. Health products powered by AI/ML are streaming into our lives, from virtual doctor apps to wearable sensors and drugstore chatbots to algorithms for detecting cancer in mammography and interpretations of chest X rays. Despite the rapid advancement and integration, AI/ML systems may have algorithmic biases, limited generalizability, and lack transparency in their assumptions based on potential limitations of training datasets. The recommendations provided by the Committee addressed the importance of including various demographic groups in AI/ML algorithm development. The recommendations also address the impact of the user interface and transparency including what information and how the information about the devices could be communicated to foster patient trust in the AI/ML devices.

Presentations:

Jeffrey, Shuren, M.D., J.D., Center for Devices & Radiological Health (CDRH), FDA, welcomed the Committee and public and provided opening remarks.

Bakul Patel, M.S.S.E., M.B.A., Director, Digital Health Center for Excellence, CDRH, FDA, presented on Artificial Intelligence-Machine Learning Communication.

Pat Baird, Head of Global Software Standards, Philips, CDRH, FDA, presented on Artificial Intelligence-Machine Learning Communication.

CAPT Terri Cornelison, M.D., Ph.D., F.A.C.O.G., Director, Health of Women, CDRH, FDA, presented on Representation of Diverse Groups in Tests Sets.

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10903 New Hampshire Avenue
Silver Spring, MD 20993
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Kimberly Kontson, Ph.D., Biomedical Engineer, Division of Biomedical Physics, CDRH, FDA, presented on Cognitive Human Factors.

Open Public Hearing:

Six open public hearing speakers presented and provided comments. Speakers included research organizations, industry, patients and patient advocacy groups.

Virtual Breakout Session:

During the Virtual Breakout Session, the audience was asked to discuss amongst their table a theoretical scenario about AI/ML software as a medical device.

Virtual Breakout Summations:

Concluding the Virtual Breakout Session, FDA representatives presented comments to the Committee and public generated by the Virtual Breakout participants. The comments from the Breakout Rooms revolved around the importance of including diverse patients from different demographic groups as well as with different diseases; the importance of the human connection when learning difficult diagnoses; the need to relay the diagnostic accuracy of the technology; and the need to have adequate resources to place diagnoses in context with clearly conveyed actions the user should take.

FDA Questions and Committee Discussion:

The Committee discussed approaches FDA and industry should consider as it pertains to Artificial Intelligence (AI) and Machine Learning (ML) in medical devices.

AI/ML are often developed using training and validation data sets that represent or capture patient outcomes. If the data used to train these devices are not representative across various demographic subgroups or across the disease spectrum (for a specific intended use), it would be unclear how well the devices will perform across the entire population of patients living with the condition. Research shows that multiple medical conditions show differences in outcomes by sex, gender, age, race, and ethnicity. In addition to demographic factors, there are multiple aspects of the dataset (e.g., types of diseases, severity of disease, comorbidities, duration of disease) that may impact the accuracy and applicability of the AI/ML device. The Committee generally believes that the best approach for a developer to clearly convey the demographic composition of the training and validation datasets is to increase the overall diversity in datasets and in order to successfully do that a wider net must be cast. The Committee believes the approaches FDA and industry should

consider to assure diverse groups of patients are reflected in training and validation data sets for the proposed intended use must not only seek to engage research communities and academia but must also include the community organizations and local providers for the populations they intend to reach. Manufacturers must address biases in data collection and work to have those biases removed. Having a fully represented community of developers throughout the process may help remove potential biases. The Committee recommended manufacturers establish advisory Committees that include patients as well as providers and practitioners that work with and care for under-represented populations. Federal agencies, particularly FDA, must also be involved to demand this is done. Participation will be greater, and trust improved if patients feel FDA is involved and requiring it. Furthermore, the Committee believes that the description of the data used to inform the algorithms should be transparently shared. They also emphasized that during the validation step it is critical to ensure the algorithms perform in the entire intended use population. Informed consent was also discussed. They agreed that the consent should involve how their data is going to be used. The informed consent language must be language patients can understand and that language should be tested in patient groups before implementing the informed consent document. Patients also need to be made aware which databases will contain their data and if the data will be shared across other medical device companies. The Committee also feels that manufacturers should not require that the potential user of a device share their data in order to receive the device. The assurances that FDA and industry could provide that would encourage patients to share their data to be used in these algorithms includes putting incentives in place to encourage patient participation. Assurances in datasets that could be used for any algorithms are transparency and candor throughout the process and diversity of validation to unsure unconscious biases. While acknowledging that FDA does not regulate the practice of medicine, the Committee mentioned how important it is to know which devices are using which AI/ML software because it may impact patient care and where and how patients seek care.

AI/ML device manufacturers update their programming for a variety of reasons. Some of these changes are submitted to FDA prior to implementation for marketing authorization while other updates can be implemented and documented for later review by the FDA. The different types of modifications include 1) *Modifications related to device performance, with no change to the intended use or type of input signals*. This type of modification includes re-training with new data sets of the same input signals and a change in the AI/ML architecture 2) *Modifications related to inputs, with no change to the intended use*. This type of modification includes changes to the algorithm for use with new types of input signals but does not change the intended use of the device and 3) *Modifications related to the device's intended use*. These types of modifications include those that change how the device is used. For example, a device that was previously used to aid in the diagnosis of a condition would instead provide a diagnosis to the patient. The determination of what information should be submitted and when that information is submitted to FDA is based on risk. Risk is defined as a combination of the probability of harm occurring and the severity of that harm. As such, every medical device including AI/ML devices has some associated

risks that are considered by the FDA. The Committee generally believes the types of software modifications to AI/ML medical devices that would be most concerning to them that warrant notifying FDA prior to implementation are changes that affect the intended use. The Committee believes the types of modifications that should trigger a communication update to the patients and the public are all the modifications that were listed. The Committee believes that greater transparency is warranted. They believed that the communication should also reveal what prompted the modifications. One example mentioned was the importance of knowing about improved device performance if the patient was tested on an earlier version of the device, given that AI/ML technological cycles are rapid. Equally troubling to the Committee is the patient not knowing how the manufacturers are adding to the data and utilizing it. The Committee also believes that the communication should confirm if the updates to the device are being done to meet the original promise of the device or is the update for better performance. Their decision on communicating about modifications was that it should be the same for patients and providers and should not be impacted _by where the device is used (e.g., in the home, in the clinic) or by who is using it (e.g., doctor, patient). The Committee believes the approaches FDA and industry should use to share with patients any added benefits (such as improvement in accuracy), changes in performance (such as decreased performance) or risks (such as limited applicability in certain populations) associated with using the AI/ML medical devices should consist of news flashes and media to announce changes made to a device as well as pushes through patient advocacy and provider communities. The media message must be specific to health communities and providers so that they are made aware of the modifications. FDA should also send out notices. Manufacturers should also be held accountable for notifying the individual user of changes in device performance, risks and failures and FDA should monitor that manufacturers fulfil their responsibility of notifying users. For some devices, at the time of the marketing authorization, there are periodic planned modifications (types of anticipated modifications and method to implement the modifications) to the AI/ML device. The information including level of detail about the planned changes the Committee believe should be made available to patients to increase their trust in the device are input/output relationships. Manufacturers should be transparent about the operating principle and not about the ongoing algorithm changes.

With all AI/ML including those that are continuously learning, there is the potential for the performance of the software algorithm to exceed the original reference gold standard (such as the current standard of care). This increased performance may raise the bar for other devices that may be seeking entry into the market. The Committee generally believes you balance the benefits of infusing this improved performance standard (i.e., “better than standard of care” bar) for subsequent devices with the potential risk of inhibiting innovative technologies from having a chance to enter the marketplace. Specifically, they discussed that adding new innovative technologies to the marketplace should not impact or lead to the removal of other devices that are

successfully working and providing care to patients at an acceptable level. Others on the Committee favored "raising the bar" and letting it be dynamic so that it may help promote innovation, creating an "arms race" for new devices. The Committee noted that updates to software evolve faster than updates to hardware, noting that the raised bar may impact more than just the software if the device is used as a unit. Postmarket considerations currently assume that the device is static. AI/ML devices may need a new framework for postmarket surveillance. The Committee emphasized that the pressure of competing technologies should not choke out acceptable and affordable technologies on the market or from entering the market.

Some AI/ML algorithms are shifting decision making from the current settings of a specialist to that of generalist or to the patient at their home. In addition, AI/ML devices are becoming capable of taking autonomous actions such as to call 911 or alerts their health care provider. The Committee believes mitigations that should be put in place to protect patients (e.g., informed consent, qualifying language in the diagnosis provided, warning/caution statements) if the decision-making setting is shifted as described above. The Committee expressed some concern around autonomous decision-making, specifically that the device may be indicated to make one diagnosis, but patients are complex with multiple diseases. There was concern that the AI/ML may not be "intelligent" enough to account for that complexity. FDA needs to ensure that manufacturers are including accountability with their instructions and take account of how the news communicated by the device can impact an individual, family and household. They also mentioned the manufacturer should be accountable for the "decisions" or "diagnoses" made by the device. The device instructions need to come with contact information so patients are clear about who they should contact if they have questions about the results and how to manage the results. Instructions stating that the patient should call his/her doctor may not be sufficient. There should be an "algorithm" for patients to follow if they get a positive or negative result that allows the person to take ownership of the information received and make deliberate decisions. The Committee also believe that when a device does not work properly there should be checks and balances incorporated in the device that signals to a patient when their device is not working properly. The Committee mentioned alarms but expressed concerns with that approach and also mentioned a colorimetric system could be useful. The Committee believes all of these recommendations are approaches that will help patients understand the probability of the harm and the severity of that harm (i.e., risk) associated with devices that take autonomous actions.

For AI/ML devices intended to be used by patients, the "information" that patients may see includes GUI (Graphical User Interface), menus, dialog boxes, and error and status messages. In addition, there may be information associated with the device placed directly on the device, on the company's website, and in tutorials informing how to use the device. These communication materials often include the software version number, the instructions for use, the user's guide, the "About" menu button and other information typically found in the software's splash-screen. In

contrast, other devices may be intuitive to use, where patients do not need an instruction manual or how-to guide to begin using them. Some devices may have functions that are locked to patients and only visible/available to their providers, while others may display readings to the patients to share with their healthcare provider. The Committee believes manufacturers of AI/ML medical devices should consider human factors in its device designs. The manufacturer needs to factor in age and generational differences in the design of the devices to ensure it is designed for the intended user in order to integrate intuitive features in their devices. The Committee emphasized that intuitive features cannot be assumed and should be tested with the specific patients that will be using the device. Personalization of the interface would also be important—that it is adaptable to different patients. They also mentioned the importance of access to a technology assistant would be critical to address any use challenges. For understanding the effectiveness of mitigations such as warnings/caution statements and information for use, the Committee does consider human factors/usability testing to be an important step. The Committee also discussed the importance of patient preference in the design features and that it could be used early on to address these concerns. The Committee believes the data usage, how much of the data will be shared, and the implications of sharing the data is the type of information that should be included in the communication materials made available to patients using AI/ML medical devices. The Committee strongly believes patients should have the ability to see functions or data that are visible to their healthcare provider. The Committee further explained their response as patients should have the same information provided to doctors and that the information should be provided in a way that is understandable to the patient. The Committee suggested the type of mitigations that should be put in place to ensure patients understand and appropriately respond to the information presented includes ensuring patients have access to technology which is directly impacted by the connectivity. The overall issues of disparities in national infrastructure for connectivity must be addressed to ensure that AI/ML is not associated with greater health disparities by demographic groups. The technology needs to work for all people and populations, and it goes beyond a specific device. The Committee also suggested that it might be helpful if online patient communities using a particular device could be fostered by manufacturers. These communities could be where patients go to connect with each other and share the data from their connected devices.

Contact:
Letise Williams, Designated Federal Officer
301-796-8398, Letise.Williams@fda.hhs.gov

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Free State Reporting, Inc.
1378 Cape St. Claire Road
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5600 Fishers Lane, HFI-35
Rockville, MD 20851
(301) 827-6500 (voice), (301) 443-1726