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June 3, 2019 Submitted electronically at www.regulations.gov

Norman E. Sharpless, MD
Acting FDA Commissioner
c/o Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: Docket No. FDA-2019-N-1185 "Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) - Discussion Paper"

Dear Acting Commissioner Sharpless:

Public Responsibility in Medicine and Research (PRIM&R) appreciates the opportunity to comment on the Food and Drug Administration (FDA)'s "Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) - Discussion Paper," published April 2, 2019.

PRIM&R is a nonprofit organization dedicated to advancing the highest ethical standards in the conduct of research. Since 1974, PRIM&R has served as a professional home and trusted thought leader for the research protections community, including members and staff of human research protection programs and institutional review boards (IRBs), investigators, and their institutions. Through educational programming, professional development opportunities, and public policy initiatives, PRIM&R seeks to ensure that all stakeholders in the research enterprise understand the central importance of ethics to the advancement of science.

PRIM&R appreciates the FDA's efforts to rethink its regulatory framework for devices as the use of adaptive AI/ML-based technologies become increasingly prevalent in the health and wellness space. Although these emerging technologies have the potential to improve health and health care for both healthy individuals and patients, they also have implications for the protection of human subjects of research. The FDA discussion paper focuses primarily on how continuous learning by AI/ML may affect devices' performance, safety, and risk profile, and how to ensure effective safeguards as an

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algorithms' "output" or use changes. These are no doubt important issues.

As the FDA determines appropriate oversight of adaptive AI/ML-based technologies, **we urge it to also consider the ethical impact of generating training data and optimizing algorithmic models through data that comes from and interacts with human beings in real time.** Any new proposed regulatory framework should address the protection of individuals whose personal information and data are being used in the creation and ongoing testing of these technologies via AI/ML.

More specifically, in what follows, we urge the FDA to use this opportunity to:

1. Evaluate whether the scope of the FDA's definition of software as a medical device (SaMD) is broad enough to cover the range of health and disease-related AI/ML-based applications currently being developed. This should include applications that aim to prompt behavioral and psychological responses, whether or not they are identified as "medical" or "health" programs, and whether or not they are developed by entities operating within the traditional medical/pharmaceutical realm.

2. Seek to clarify when and how the process of developing and validating the continuously learning algorithms that underlie AI/ML-based SaMD of the sort covered by this proposed framework ought to qualify, for reasons specified below, as human subjects research, and therefore be subject to requirements for the protection of the rights and welfare of the individuals involved.

To illustrate our concerns, we turn to the recent revelations that Facebook has developed and is using algorithms, based on AI, to identify users who may be at risk for suicide, and then, in some cases, notifying local authorities who may call on such individuals at their homes.[1] Facebook does not consider its algorithms a medical device, but it could be argued, and some have, that this application fits the definition of a device given that the algorithms serve to "diagnose" those at risk for suicide.[2] If so, then an important question is how the AI algorithms were developed. In a press release, Facebook indicated that their algorithms were developed and tested using research that involved connecting identifiable information about individuals from their Facebook profiles (we presume this includes telemetric and self-reported data on gender, age, location, and ethnicity) with specific outcomes (e.g., whether or not people attempted suicide), as well as from interactions with friends, relatives, and acquaintances.[3] And if that is the case, then development of the algorithms was likely supported by human subjects research without oversight by a research ethics review committee independent of the research team.

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[1] 'We Don't Have Any Data': Experts Raise Questions About Facebook's Suicide Prevention Tools. Thielking, M. (2019). *STAT*.
[2] Suicide Prediction Technology is Revolutionary. It Badly Needs Oversight. Marks, M. (2019). *The Washington Post*.
[3] How Facebook AI Helps Suicide Prevention. Card, C. (2018). Facebook.
Ethics, Transparency, and Public Health At the Intersection of Innovation and Facebook's Suicide Prevention Efforts. Barnett, I. & Torous, J. (2019). *Annals of Internal Medicine.*

Facebook is of course not the only company exploring how AI and machine learning can be used to develop products and applications that could fall under the Federal Food, Drug, and Cosmetic Act.[4] However, given that these activities are largely not funded by federal entities, they would currently be subject to research ethics oversight only to the extent that the research results are used in a device that is subject to FDA licensure and hence subject to the agency's rules. Since, as we detail below, oversight seems critical for these cases, we urge the FDA, as it revises its regulatory framework for such products, to consider how the private sector is using AI/ML in the development of health and wellness products. This is especially important given the lack of federal oversight of private sector software and social media companies that depend on not just observing, but also manipulating, human beings' engagement with software to develop their products and services.[5]

Companies seeking to develop products no longer rely solely on archives of existing data or secondary data sets to improve their health and wellness products. They increasingly use real-world data and experience, frequently interacting with human beings and collecting data and information from those interactions. AI testing, for example, often involves perturbing aspects of people's real-world and online engagements and private lives. Companies must constantly collect data to identify patterns of decision-making that provide training data for developing algorithmic models.[6]

Typically, individuals are unaware that such interactions are designed to produce data about them and their behavior for research purposes.[7] Such activities go far beyond "market research," in which companies study the response of consumers to new or proposed products in order to make improvements to those products or how they are marketed. Rather, in these cases, the "products" consist of programs that are built with the results of the interactions; when cumulated, such data become part of the algorithms that are the product. That product is, then, intended to influence the behavior and the environment of future users. **Our concern is that federal oversight has not kept pace with how companies are treating users of their platforms and systems as unwitting human subjects in the creation of new health and wellness technologies.**

A number of human research protection issues are raised by the development of the AI/ML-based software used in healthcare, including:

- *Honoring people's wishes regarding the use of, and access to, their information*: Ideally, people would always be asked about how they want their data (especially

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[4] Google Searches for Ways to Put Artificial Intelligence to Use in Health Care. Harris, R. (2019). *NPR*. As Tech Companies Move Into Health Care, Here's What to Watch in 2019. Our Bodies, Our Tech Companies. Chen, A. (2019). *The Verge*.
[55] Journal That Published Facebook Study Responds to Backlash. Lupkin, S. (2014). *ABC News*.
[6] Amazon Reportedly Employs Thousands of People to Listen to Your Alexa Conversations. Valinsky, J. (2019). *CNN Business.* Detecting Parkinson's Disease From Interactions With a Search Engine: Is Expert Knowledge Sufficient? Allerhand, L., Youngmann, B., Yom-Tov, E., & Arkadir, D. (2018). CIKM '18 Proceedings of the 27th ACM International Conference on Information and Knowledge Management.
[7] It's Time to Panic About Privacy. Manjoo, F. (2019). *New York Times*.

their health data) used at the time it is collected, and then those expectations would be honored. We recognize, however, that this is not always the current practice in health care. At the very least, companies that conduct the sort of testing of technologies via AI/ML discussed here should be required to fully disclose to users the potential ways they expect participant's data to be used in the future, including (when this is the case) a statement that all future uses of the data are not now known.

- *Privacy risks, including risks of re-identification of anonymized data*: As technology advances, it is no longer possible to ensure that data that are "non-identifiable" when collected will remain de-identified.[8] Companies should be required to fully disclose whenever a person's data may be shared or linked with another data set, since this exponentially increases the chance of re-identification given the possibility of cross-referencing data from one set with another to reconstruct identity. This is especially important when special risks are involved as, for example, when data about sensitive matters (such as suicidality) are being collected.

- *Transparency*: Although the discussion paper mentions promoting the principle of transparency in several places (p.9, 10, 14), we suggest that any new regulatory framework specifically mandate the information that companies are required to share[9] with their customers/users and the public about how they collect and use data and how their AI/ML-based software is developed.[10] Companies should also be required to disclose when they cannot explain why a model has evolved in a particular direction. Transparency is important with regard to the source entities of data as well, e.g., the healthcare systems that provide the data that companies use to develop their AI/ML software.

- *Understandability*: Too often, disclosures originally meant to respect the rights and autonomy of individuals are written and presented in ways that defeat this purpose (e.g., typical end-user license agreements). Any disclosures or explanations of choices meant for individual customers and users, including those described above, should be provided in language and format that is understandable and, where appropriate, actionable.

In conclusion, as the FDA moves forward with crafting a regulatory framework to address AI/ML-based technologies, we urge it to think broadly in terms of the applications and technologies that should in today's environment qualify as medical devices. Any new proposed regulatory framework would benefit from fully addressing the experimental nature of AI/ML and the implications of adding AI/ML into SaMD regulatory frameworks.

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[8] The 18 Biggest Data Breaches of the 21st Century. Armerding, T. (2018). *CSO*.
[9] Assessment of the Data Sharing and Privacy Practices of Smartphone Apps for Depression and Smoking Cessation. Huckvale, K., Torous, J., Larsen, M. (2019). *JAMA Netw Open*.
[10] Suicide Prediction Technology is Revolutionary. It Badly Needs Oversight. Marks, M. (2019). *The Washington Post*.

If the FDA does not believe applications such as Facebook's suicide-risk program fall under its current regulatory purview, the agency should clearly articulate that the agency cannot adequately oversee these applications under its existing statutory authority. It is important to recognize that many "products" of this type that aim to affect the health and wellness of individuals are being developed by firms that do not identify themselves, as pharmaceutical and device manufacturers do, as healthcare companies.

This broader view of the technologies that should be subject to FDA oversight is essential not only to ensure the safety and efficacy of these AI/ML-based products, but also because these products are typically algorithms developed through the interaction with, and collection of data from, human beings. As AI/ML requires collecting data on many individuals to generalize to the population, the line between basic research and product development is increasingly blurry. AI/ML-driven adaptive systems require constant experimentation with people's environments to create the datasets to determine what happens when one set of variables is changed and not others. **The regulatory framework the FDA develops should therefore include provisions that protect the rights, welfare, and interests of the individuals involved in this process just as it now does for other human research subjects. It should also include provisions to protect the rights, welfare and interests of the friends, relatives, and acquaintances of the individuals being studied.**

Thank you again for the opportunity to comment. We believe the FDA's efforts to develop regulatory approaches to fit the rapidly evolving digital and AI landscape is a step in the right direction, and we hope our comments are helpful as you continue the process. My PRIM&R colleagues and I are available to discuss our comments further, should that be of interest. Please feel free to contact me at 617.303.1872 or ehurley@primr.org.

Respectfully submitted,

Elisa A. Hurley, PhD
Executive Director

cc: PRIM&R Public Policy Committee, PRIM&R Board of Directors