February 15, 2021

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

RE: Docket No. FDA-2021-N-0009: *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*

Dear Sir/Madam:

Roche Diagnostics ("Roche") respectfully submits these comments in response to the recently published federal register notice, *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* ("Federal Register Notice"). Roche's comments are focused on the digital pathology-related devices described within the Federal Register Notice, specifically product codes PSY, PZZ, QKQ, and OEO. Roche appreciates the Department of Health and Human Services (HHS) and the U.S. Food and Drug Administration (FDA) consideration of these comments as they contemplate the path forward.

Comment 1: Roche applauds the Department of Health and Human Services (HHS) for employing a risk-based approach to device regulation leading to the recommendation that 510(k) premarket notification is not required for product codes PSY, PZZ, QKQ, and OEO.

As healthcare advances and the risk profiles associated with existing, established technologies are well understood, it is important that health authorities revisit approaches to the regulation of devices to ensure that safety and effectiveness is balanced with speed of innovation. In its Federal Register Notice, HHS has endeavored to accomplish this

goal, identifying that, for devices with digital pathology-related product codes PSY, PZZ, QKQ, and OEO, 510(k) premarket notification is no longer required to assure safety and effectiveness. Roche appreciates the risk-based approach HHS has employed in its evaluation, and information from the MAUDE database, FDA's approach to premarket review of digital pathology devices during the COVID-19 Public Health Emergency, and the manner in which digital pathology devices are used in clinical practice supports the proposed recommendation to remove premarket notification requirements for product codes PSY, PZZ, QKQ, and OEO.

Digital pathology devices have a relatively lengthy marketing history – a search of the FDA's 510(k) database indicates that the first product clearance under the product code OEO took place in 2007. While the PSY, PZZ, and QKQ product codes have been established more recently, minimal adverse events related to these products have been reported in the MAUDE database since 2010, as described within the Federal Register notice:

Product Code	MAUDE Events from November 1, 2010 to November 30, 2020
PSY	3
PZZ	0
QKQ	0
OEO	1

These minimal values reflect the low-risk attributes of digital pathology devices and suggest that manufacturers are able to routinely commercialize safe and effective digital pathology devices that healthcare professionals can operate in a safe and effective manner.

During the COVID-19 Public Health Emergency ("PHE"), FDA has also recognized that removing premarket review requirements from devices having product codes PSY, PZZ, QKQ, and OEO does not result in undue risk. As described in its guidance *Enforcement Policy for Remote Digital Pathology Devices During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency: Guidance for Industry, Clinical Laboratories, Healthcare Facilities, Pathologists, and Food and Drug Administration Staff*, FDA has not objected to the marketing of new digital pathology devices having product codes PSY, PZZ, QKQ, or OEO during the PHE when a 510(k) premarket clearance has not been obtained. Presumably, FDA would not have applied this enforcement policy if the Agency determined that removing 510(k) premarket notification submission requirements for these product types would result in undue risk to patients. Further, no safety signals have been generated during the COVID-19 PHE to suggest that this decision was inappropriate.

Finally, it is important to keep in mind that the claims associated with PSY, PZZ, QKQ, and OEO product codes are adjunctive, meaning that these devices are intended to assist, and not replace, the decision-making of qualified pathologists. Ultimately, it is the

pathologist, and not the device, who has oversight over the imaging review and interpretation process. From a risk perspective, this is an important consideration that should be taken into account when considering if premarket notification should be required for devices using these product codes.

Considering the above factors, Roche appreciates the thoughtful, risk-based approach that HHS applied in its evaluation of product codes PSY, PZZ, QKQ, and OEO and is supportive of its recommendation.

Comment 2: Device safety and effectiveness will continue to be assured through general and special controls and manufacturers' adherence to design control and quality system requirements.

While HHS has proposed to remove 510(k) premarket notification requirements for devices having product codes PSY, PZZ, QKQ, and OEO, it is important to keep in mind that all other medical device regulatory requirements will continue to apply. In particular, digital pathology device manufacturers will still need to comply with general and special controls for their devices and ensure that they are developed, commercialized, and lifecycle managed in a safe and effective manner. Manufacturers will be required to develop products according to design control practices and conduct requirements planning, risk management actions, and verification and validation efforts, among other activities, and the FDA has the authority to conduct quality system inspections to ensure that these requirements are met. Additionally, manufacturers will need to continue to collect complaints and report adverse events, conduct any needed corrections and removals, register and list their products, and follow all other quality system requirements described within 21 CFR Part 820.

In short, FDA has many mechanisms and requirements at its disposal, beyond premarket notification, to ensure device safety and effectiveness. In the absence of premarket notification, these mechanisms and requirements are more than adequate in ensuring the safety and effectiveness of digital pathology devices marketed under product codes PSY, PZZ, QKQ, and OEO.

Comment 3: Removal of premarket notification requirements from these devices will free up FDA resources to focus on device technologies that are less well established and characterized, such as artificial intelligence-based algorithms that are used to support pathologist decision-making.

As discussed above, the digital pathology-related product codes that HHS has included within its Federal Register Notice are well-established technologies with well-defined risk profiles. These devices have been well characterized through a number of repeated development lifecycles, and risks related to their development and operation have been mitigated. Thus, these products pose little risk to patients (as demonstrated through the

previously referenced MAUDE analysis) and premarket notification is unnecessary to ensure their safety and effectiveness.

Other digital pathology devices, however, do not have a similar marketing history or risk profile. In particular, an increasing number of algorithms, many leveraging artificial intelligence, are being developed to support pathologist image interpretations. These algorithms have unique development challenges, emerging risks, and promising opportunities as compared to legacy digital pathology devices. As such, they could benefit from a more dedicated regulatory focus.

Removing premarket notification requirements for digital pathology devices having product codes PSY, PZZ, QKQ, and OEO would free up much needed FDA resources to focus on truly innovative device premarket reviews and regulatory submission approaches in the area of digital pathology. Specifically, these freed resources could be leveraged to support premarket reviews for innovative digital pathology algorithms and/or the development of innovative regulatory pathways tailored to the unique needs of digital pathology software products (such as evolving the FDA's *Predetermined Change Control Plan* concept described in its recent *Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) Action Plan*). Such an approach would enable FDA to focus on innovative solutions that could bring significant value to patients and healthcare professionals while alleviating unnecessary premarket notification requirements for well-established devices with well-defined risk profiles.

We appreciate HHS and FDA's consideration of the above comments, and please feel free to contact me for any questions or further discussion.

Respectfully,

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