Pre-Submission Feedback

Date:	June 21, 2019
To:	Brandon Gallas, Ph.D.
From:	Shyam Kalavar, MPH, CT(ASCP)
Through:	Soma Ghosh, Ph.D, Branch Chief, Molecular Pathology and Cytology Branch, Division of Molecular Genetics and Pathology
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Submission:	Q190346
Subject:	MDDT Incubator Phase
Device Name:	eeDAP System
Sponsor:	Brandon Gallas, Food and Drug Administration

I. Proposed Context of Use

eeDAP allows a WSI scanner manufacturer (sponsor) to design a "feature" study (analytical performance study) in which pathologists can evaluate prespecified fields of view (FOVs) containing the specified feature(s) on WSIs. These FOVs are selected in advance based on the review of glass slides. These FOVs are then localized or identified with an x,y position which the eeDAP tool will verify corresponding to the FOVs containing the feature(s) in a WSI. The eeDAP tool ensures that the FOV selection between glass slide on a microscope and a corresponding WSI is the same.

II. Sponsor Questions and FDA Responses

1. **Sponsor Question**
   Does the FDA believe that the updated COU (with revisions) can lead to a successful MDDT qualification? What kind of revisions does the FDA believe the COU needs?

   FDA Response
   The updated COU that you agreed to via email on June 5, 2019 is as follows: "eeDAP allows a WSI scanner manufacturer (sponsor) to design a "feature" study (analytical performance study) in which pathologists can evaluate prespecified fields of view (FOVs) containing the specified feature(s) on WSIs. These FOVs are selected in advance based on the review of glass slides. These FOVs are then localized or identified with an x,y position which the eeDAP tool will verify corresponds to the FOVs containing the feature(s) in a WSI. The eeDAP tool ensures that the FOV selection between glass slide on a microscope and a corresponding WSI is the same." We believe that the updated COU has the potential to advance this MDDT proposal to the qualification stage. MDDT qualification can only be determined after the review of the data supporting the eeDAP as an MDDT. Also, please note that the COU will be finalized after the review of the performance data that supports this as a MDDT.

2. **Sponsor Question**
Would the FDA recommend adding language to limit the COU so that users understand that eeDAP is not meant to be the interface for viewing WSIs or would the FDA like this to be addressed elsewhere in the future submission?

FDA Response
Please see FDA response to question 1.

3. **Sponsor Question**
Do the registration accuracy studies provide the kind of evidence that can support this MDDT?

FDA Response
You have provided a brief overview of two studies you performed to assess the registration accuracy of the eeDAP tool as follows:

a. The purpose of the first study was to evaluate registration accuracy of evaluation environment of eeDAP. You state that the eeDAP was developed to help conduct studies in which pathologists view and evaluate the same fields of view (FOVs), cells, or features in a glass slide on a microscope and in a whole slide image (WSI) on a digital display by registering the two domains. Two readers independently registered 60 FOVs from 6 glass slides, which covered different tissue types, stains, and magnifications. The results show that when the camera image is in focus, the registration was within 5 micrometers in more than 95% of the FOVs.

b. The second registration accuracy study was designed and performed by collaborating pathologists with no experience using eeDAP. The goal was to determine if users that are not eeDAP experts can design and execute a registration accuracy study and get similar results. The collaborators were provided a tutorial and could troubleshoot issues with FDA scientists, but the work was done by the collaborating pathologists in their lab. Rather than exploring different tissue types and stains, two pathologists designed and conducted their study with 20 H&E stained glass slides (10 mouse brain + 10 human GIST tumor slides). While we intend to summarize the study in detail for the qualification submission the registration accuracy was within 5 micrometers in more than 95% of the FOVs.

We consider these as preliminary studies but we agree in principle that these types of studies may support the COU for this tool. We recommend you perform an additional study to assess the registrational accuracy of the eeDAP tool to support the stated COU and to support the use of the eeDAP as an MDDT tool. Please provide a detailed study protocol for FDA review and feedback.

4. **Sponsor Question**
What additional information about the studies would the FDA like to know?

FDA Response
Please see FDA response to question 3.

5. **Sponsor Question**
We plan to recommend that every task-based eeDAP study be preceded by a registration accuracy study using the task-based eeDAP study slides and FOVs. Would the FDA prefer to require such a

registration accuracy study for any task-based study submitted to the agency as a condition under which the MDDT is qualified?

FDA Response
Please clarify if this question refers to requirements to be placed on future users of this tool, i.e. device manufacturers to obtain performance data for a marketing submission. If it is, then it is premature to address this issue currently. Please also see response to question 3.

6. **Sponsor Question**
Are the changes to the COU and the evidence summarized here adequate to advance us to the pre-qualification phase or the qualification phase?

FDA Response
After Review of the information provided, the Agency has concluded that the changes to the COU and the preliminary evidence submitted is sufficient to advance the proposed MDDT tool to the pre-qualification phase.

Shyam Kalavar -S
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