



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2014-N-0505]

Proteomics in the Clinic; Public Workshop; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public workshop; request for comments.

The Food and Drug Administration (FDA) is announcing the following public workshop entitled "Proteomics in the Clinic." FDA seeks input from interested stakeholders on how best to develop a regulatory framework targeted toward the complex issues involved in transforming research-level assays into validated in vitro diagnostics (IVDs) that can be used with patients. The topic to be discussed is the state of the art and challenges surrounding validation of proteomic methodologies for IVD tests.

Date and Time: The public workshop will be held on June 13, 2014, from 8:30 a.m. to 5 p.m.

Location: The public workshop will be held at the FDA White Oak Campus, 10903 New Hampshire Ave., Building 31 Conference Center, the Great Room (rm. 1503), Silver Spring, MD 20993-0002. Entrance for the public workshop participants (non-FDA employees) is through Building 1 where routine security check procedures will be performed. For parking and security information, please refer to

<http://www.fda.gov/AboutFDA/WorkingatFDA/BuildingsandFacilities/WhiteOakCampusInformation/ucm241740.htm>.

Contact Person: Julia Tait Lathrop, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. 5564, Silver Spring, MD, 20993-0002, 240-402-5034, email: julia.lathrop@fda.hhs.gov.

Registration: Registration is free and available on a first-come, first-served basis. Persons interested in attending this public workshop must register online by 4 p.m. on June 4, 2014. Early registration is recommended because facilities are limited and, therefore, FDA may limit the number of participants from each organization. If time and space permits, onsite registration on the day of the public workshop will be provided beginning at 7:30 a.m.

If you need special accommodations due to a disability, please contact Susan Monahan, Center for Devices for Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. 4321, Silver Spring, MD 20993-0002, 301-796-5661, email: susan.monahan@fda.hhs.gov no later than 4 p.m. on May 30, 2014.

To register for the public workshop, please visit FDA's Medical Devices News & Events-Workshops & Conferences calendar at <http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/default.htm>. (Select this public workshop from the posted events list.) Please provide complete contact information for each attendee, including name, title, affiliation, email, and telephone number. Those without Internet access should contact Julia Tait Lathrop to register (see Contact Person). Registrants will receive confirmation after they have been accepted. You will be notified if you are on a waiting list.

Streaming Webcast of the Public Workshop: This public workshop will also be Webcast. Persons interested in viewing the Webcast must register online by 4 p.m. on June 4, 2014. Early registration is recommended because Webcast connections are limited. Organizations are

requested to register all participants, but to view using one connection per location. Webcast participants will be sent technical system requirements after registration and will be sent connection access information after June 9, 2014. If you have never attended a Connect Pro event before, test your connection at

https://collaboration.fda.gov/common/help/en/support/meeting_test.htm. To get a quick overview of the Connect Pro program, visit http://www.adobe.com/go/connectpro_overview.

(FDA has verified the Web site addresses in this document, but FDA is not responsible for any subsequent changes to the Web sites after this document publishes in the Federal Register.)

Comments: FDA is holding this public workshop to discuss with interested stakeholders the issues surrounding validation of proteomic methodologies for IVD tests. In order to permit the widest possible opportunity to obtain public comment, FDA is soliciting either electronic or written comments on all aspects of the workshop topics. The deadline for submitting comments related to this public workshop is July 11, 2014.

Regardless of attendance at the public workshop, interested persons may submit either electronic comments regarding this document to <http://www.regulations.gov> or written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. In addition, when responding to specific questions as outlined in section II of this document, please identify the question you are addressing. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at <http://www.regulations.gov>.

Transcripts: Please be advised that as soon as a transcript is available, it will be accessible at <http://www.regulations.gov>. It may be viewed at the Division of Dockets Management (see Comments). A transcript will also be available in either hardcopy or on CD-ROM, after submission of a Freedom of Information request. Written requests are to be sent to the Division of Freedom of Information (ELEM-1029), Food and Drug Administration, 12420 Parklawn Dr., Element Bldg., Rockville, MD 20857. A link to the transcripts will also be available approximately 45 days after the public workshop on the Internet at <http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/default.htm>. (Select this public workshop from the posted events list).

SUPPLEMENTARY INFORMATION:

I. Background

Basic research in proteomics, the study of all of the proteins and their interactions in an individual, has led to new understanding of proteins' contributions to health and disease. It has also driven the advancement of powerful analytical technologies used to explore these contributions. Translating these discoveries and technologies into IVD tests presents expanded opportunities to improve patient care; however, the complexity of these technologies raises challenging questions on how to evaluate the safety and effectiveness of these tests. FDA is holding this public workshop to invite discussion with industry, academia, government, and the public on how best to adapt current regulatory strategies to the challenges presented by proteomic approaches to IVDs, while still accelerating and supporting the introduction of innovative diagnostic tests into the clinic.

Over the past 20 years, basic proteomic research has spurred intense innovation in biochemical analytic technologies (e.g., mass spectrometry, multiplex arrays, bioinformatics).

This research has led to new insights into how proteins interact to maintain health and to cause disease; however, it is only recently that these technologies have matured to the point that their introduction into the clinic appears practical and useful. Fundamental to using IVDs in the clinic is the need to demonstrate that the tests are safe and effective--that the results claimed are accurate and precise and that the interpretation of the results are supported by science. FDA's regulatory process is designed to ensure that intended use claims are supported with appropriate data. However, the range of variables that can be included in proteomic IVDs such as technological approaches, variety of sample types and preparation methods, data capture, and analysis algorithms, poses unique regulatory challenges, as more complex the information gathered, more challenging is the validation of results. At this point, what we need is a regulatory framework, tuned to proteomic technologies, which will facilitate the introduction of validated IVDs into the clinic.

The intent of this workshop is not to discuss the limitations and strengths of the proteomic discovery process. The theoretical analytical performance of proteomic technologies have been well demonstrated, and in the past few years a number of initiatives have been launched to bring standardization and quality control to the discovery and pre-clinical development of proteomic-based assays. However, this level of quality control does not ensure that these assays have been validated for their intended use as IVDs tests that are used for diagnosis of disease and clinical management of patients; e.g., assessment of risk, monitoring of disease, prediction of response to therapy, and selection of treatment.

Strategies are needed that will guide the successful transfer of research and discovery-level assays into the clinic. This includes their use in clinical trials, so that the analytical and clinical validity of the test procedure and outcome are assured. As a general rule, the

requirements for analytical and clinical validation of IVDs are much greater than the studies that are commonly performed in a research and development setting. To support the least burdensome approach to assay development, FDA is willing to discuss unconventional approaches to IVD validation driven by, for example, the theoretical precision of multiple reaction monitoring assays. However, theoretical performance must be balanced by the recognition that there are few, if any, recognized reference standards for the analytes or the assays with which to assess the performance of proteomic IVDs. The impact of the lack of standards may be substantial: Assays that combine the measurements of several, if not dozens, of individual analytes into a single, actionable "score" may require validation of each individual analyte separately and in combination. Thus, the objective of this public workshop is to obtain feedback from academia, government, industry, clinical laboratories, and other stakeholders on the development of a regulatory approach that may reduce the burden of assay validation while assuring that the assays are safe and effective.

II. Topics for Discussion at the Public Workshop

We plan to include the following topics at the public workshop.

- State of the art: Current state of proteomic IVD landscape and FDA's perspectives;
- Community initiatives: Overview of community (governmental and non-governmental) initiatives to help standardize proteomic technologies and provide quality control to discovery;
- Success stories: Description of FDA experience in the clearance of IVDs that use proteomic technologies, with lessons learned and challenges discovered in bringing proteomic-based assays to the clinic; and

- Case study open discussion: In an open discussion, FDA will present a hypothetical case study that includes assay design and validation issues with which FDA has experience. The goal is to stimulate discussion with attendees regarding what expectations from FDA are reasonable, what validation by manufacturers is possible and other challenges inherent in bringing these tests to the clinic and the Agency. Possible points of discussion will be solicited from the attendees, and may include:
 - How can or should the FDA use community-developed reference standards/assays to assess IVD validity?
 - How can manufacturers assess accuracy in a multiplex/multipeak assay without a reference standard for the analytes?
 - Are there general rules for assay validation that cannot or should not be applied to different platforms?
 - How can or should late-stage validation considerations be incorporated into early-stage assay development?

Dated: May 7, 2014.

Leslie Kux,

Assistant Commissioner for Policy.