4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2013-N-0046]

Clinical Flow Cytometry in Hematologic Malignancies; 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 "Clinical Flow Cytometry in Hematologic Malignancies." The purpose of this public workshop is to seek public input from academia, Government, laboratorians, industry, clinicians, patients and other stakeholders on the role of clinical flow cytometry in hematologic malignancies, in order to develop a specific regulatory policy for this class of in vitro diagnostic devices.

Date and Time: The workshop will be held on February 25 and 26, 2013 from 8 am to 5 pm.

Location: The public workshop will be held at FDA's White Oak Campus, 10903 New Hampshire Ave., rm. 1503 (Section A of the Great Room) in Bldg. 31, Silver Spring, MD 20993-0002. All visiting public workshop participants (non- FDA employees) must enter through Building 1 for routine security check procedures. For parking and security information, please visit the following Web site: http://www.fda.gov/AboutFDA/WorkingatFDA/BuildingsandFacilities/WhiteOakCampusInformation/ucm241740.htm.

Contact Person: Carol Krueger, Center for Devices and Radiological Health (CDRH), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. 5437, Silver Spring, MD 20993-0002, 301-796-3241, Carol.Krueger@fda.hhs.gov.

Registration: Registration is free and on a first-come, first-served basis. Persons interested in attending this public workshop must register online by 5 p.m. on February 11, 2013. Early registration is recommended because facilities are limited and, therefore, FDA may limit the number of participants from each organization. If time and space permit, onsite registration on the day of the public workshop will be provided beginning at 7 a.m.

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, mailing address, email address, and telephone number. Those without Internet access should contact Carol Krueger 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.

If you need special accommodations due to a disability, please contact Susan Monahan (email: Susan.Monahan@fda.hhs.gov or phone: 301-796-5661) no later than February 11, 2013.

Streaming Webcast of the Public Workshop: This workshop will also be available via Webcast. Persons interested in viewing the Webcast must register online by 5:00 p.m. on February 11, 2013. 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 February 20, 2013. 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.)

Requests for Oral Presentations: This workshop includes public comment sessions. If you wish to present during a public comment session, you must indicate this at the time of registration. At the time of registration identify which discussion topic you wish to address. The topics under consideration for this workshop are identified in section II of this document. FDA will do its best to accommodate requests to present. Individuals and organizations with common interests are urged to consolidate or coordinate their comments, and request time to present a joint comment. Following the close of registration, the Agency will determine the amount of time allotted to each presenter, the approximate time each comment is to begin, and will select and notify speakers by February 20, 2013. All requests to make oral presentations must be received by the close of registration on February 11, 2013. No commercial or promotional material will be permitted to be presented or distributed at the workshop.

Comments: FDA is holding this public workshop to obtain information on the topics identified in section II of this document.

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 public workshop topics. The deadline for submitting comments related to this public workshop is March 29, 2013.

Regardless of attendance at the public workshop, interested persons may submit either electronic or written comments. Submit electronic comments to http://www.regulations.gov. Submit 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. Please 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 9:00 a.m. and 4:00 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

The earliest determination of B and T cell subsets was based on microscopic counting of cells expressing surface immunoglobulins for B cell enumeration, and sheep red blood cells

rosette formation was used to enumerate T cells. The subsequent development of leukocyte-specific monoclonal antibodies and flow cytometry contributed to the automation of lymphocyte subset analysis. Flow cytometric lymphocyte subset analysis was initially used to immunophenotype hematological malignancies; however, the HIV epidemic led to a large number of 510(k) submissions addressing use for HIV immune monitoring in AIDS.

In response to these submissions, Draft Guidance for 510(k) Submission of Lymphocyte Immunophenotyping Monoclonal Antibodies was issued September 26, 1991. Prior to this draft document, reagents for CD2 and CD20 were 510(k) cleared based on methodological correlation with accepted reference methods. Following the issuance of the 1991 draft guidance, several test systems identifying CD3 T cells, CD4 and CD8 T cell subsets, NK cells and B cells were cleared under 510(k), with either single reagents or combination of reagents based on the previous clearance of CD2 and CD20 reagents. These clearances for flow cytometry system devices included flow cytometers, reagents, controls, and associated software for data acquisition and data analysis.

In 1997, the FDA issued the Analyte Specific Reagent (ASR) Rule (21 CFR 864.4020) to provide some assurance that 1) critical reagents manufacturers provided to laboratories for use in tests developed by the laboratories were made under current Good Manufacturing Practices (cGMP), 2) manufacturers registered with the FDA and listed such reagents, and 3) manufacturers reported malfunctions, injuries and deaths related to the use of such reagents to the FDA (62 FR 62260, November 21, 1997). Subsequent to publication of the ASR rule in 1997, some manufacturers began to bundle individual ASRs together in the form of reagent panels ("cocktails") creating devices that went beyond the single reagent ASRs that the rule had anticipated. In 2007, the Agency reiterated and clarified the intentions of the ASR rule in the

Guidance for Industry and FDA Staff on Commercially Distributed Analyte Specific Reagents (ASRs): Frequently Asked Questions http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm078423.htm. The 2007 guidance clarifies that the bundling of ASRs into a panel of multi-analytes is inconsistent with the definition of an ASR per 21 CFR 864.4020. Subsequent to issuance of the guidance, many uncleared, multi-analyte panels were withdrawn from distribution in order to comply with the interpretation of the "ASR rule."

Clinical flow cytometry plays a major role world-wide in the diagnosis of leukemia and lymphoma and more recently in the detection of minimal residual disease (MRD). Because there are currently no FDA cleared or approved in vitro diagnostics (IVD) panels for the diagnostic evaluation of hematological malignancies, FDA recognizes that there is an unmet need for such products to assist clinical laboratories in performing this testing. FDA has been working to define the regulatory guidelines for the review of this family of devices and has been actively working with industry and academia to help bring additional products for clinical flow cytometry to market that are safe and effective.

In partnership with the National Institutes of Health (NIH) and National Institute of Standards and Technology (NIST), CDRH intends to utilize the findings of this workshop in the development of an appropriate, risk-based regulatory framework for Clinical Flow Cytometry, which promotes innovation and protects patient safety.

II. Topics

Topics for discussion during this workshop include: (1) Overview of Quality control and standardization issues associated with Clinical Flow Cytometry (FCM), including discussion of a NIST traceable standard; (2) Biological controls in Clinical FCM: the use of stabilized whole

blood samples and cryopreserved cells for normals and chronic lymphocytic leukemia (CLL); (3) Third-party flow cytometry data analysis software; and (4) Overview of FDA regulation of Clinical FCM using the 510(k) clearance process.

The FDA is seeking representation from both North American and European clinical investigators at this workshop. This Clinical FCM Workshop is being planned to occur just prior to a CDER Workshop on the role of MRD in CLL which will be held February 27, 2013 (77 FR 76051, December 26, 2012). An FDA workshop for acute lymphocytic leukemia (ALL) MRD was held April 18, 2012, and a separate workshop on acute myelogenous leukemia (AML) MRD will be held March 4, 2013 (77 FR 76050, December 26, 2012).

Dated: January 17, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

[FR Doc. 2013-01419 Filed 01/23/2013 at 8:45 am; Publication Date: 01/24/2013]