FDA/Industry IVD Roundtable Meeting

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Center for Biologics Evaluation and Research
Food and Drug Administration

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Agenda

- CBER Management
- Inter Center Agreement
- Medical Devices Review Responsibilities within CBER
- MDUFA Device Review Performance
- Sponsor/Applicant Meetings with CBER
- Significant Device Approvals in CBER
- CBER Initiatives to meet MDUFA goals
- Significant Intercenter Activities
- Current Device Challenges

CBER Management

- **Karen Midthun, M.D.,** Acting Director, CBER
- **Robert Yetter, Ph.D.,** Associate Director for Review Management
- **Diane Maloney, J.D.,** Associate Director for Policy
- **Sheryl Lard-Whiteford, Ph.D.,** CBER Ombudsman (jurisdictions)

- **Jay S. Epstein, M.D.,** Director, Office of Blood Research and Review
- **Celia M. Witten, M.D., Ph.D**., Director, Office of Cellular, Tissue, and Gene Therapies
- **Robert Ball, M.D**., Director, Office of Biostatistics and Epidemiology
- **Mary Anne Malarkey**, Director, Office of Compliance and Biologics Quality
- **Norman W. Baylor, Ph.D.,** Director, Office of Vaccines Research and Review

Inter Center Agreement

Intercenter Agreement CBER and CDRH

- Intercenter agreement outlines the responsibilities of each center for medical device activities. Effective date is October 31, 1991.
- www.fda.gov/CombinationProducts/JurisdictionalInformation/ucm121175.htm

Intercenter Agreement
CBER and CDRH

Programs that CDRH will administer (lead center):

- Major policy development
- Promulgation and interpretation of procedural regulations.
- Regulates all medical devices not assigned to CBER.
- Small business assistance programs.
- Registration and listing – CBER to receive printouts
- GMP Advisory Committee – invite CBER to participate.
- Medical Device Reporting – provide monthly reports to CBER.

Intercenter Agreement
CBER and CDRH

Programs that both CBER and CDRH will administer:

- Surveillance and compliance actions.
- Educational programs directed at users.
- Promulgation of performance standards and application of special controls.
- Review activities – PMA, IDE, 510(k), Product Development Protocols advisory committees

Intercenter Agreement
CBER and CDRH

Medical Devices for which CBER is the lead:

- Medical devices used or indicated for the collection, processing storage, or administration of blood products, blood components, or analogous products, as well as screening or confirmatory laboratory tests associated with blood banking practices.

- In vitro tests which are ***required*** for blood donor screening or reentry are licensed under the PHS Act.

Medical Device Review Responsibilities within CBER

Medical Devices Review Responsibilities in CBER

- **Office of Blood Research and Review**
  - Blood related devices
- **Office of Cellular, Tissue, and Gene Therapies**
  - Cell/tissue/gene therapy related devices
- **Office of Vaccines Research and Review**
  - Limulus Amebocyte Lysate tests
- **Office of Compliance and Biologics Quality**
  - Inspections and Lot release
- **Office of Biostatistics and Epidemiology**
  - Statistical Review

MDUFA Device Review Performance

MDUFA Performance FY09

Submissions Received from October 1, 2008 to Sep 30, 2009; Actions through Oct 31, 2009.

Application Type	Rec'd/ filed	Within Goal		Goal Date Reached-% Completed Within Goal
		Completed	Pending	
BLAs (Priority)	**0**			
BLAs (Standard)	**8** (6 in 1 Bundle)	**0**	**8** (Within goal so far)	
Efficacy Supplements Priority	**0**			
Efficacy Supplements Standard	**1**	**0**	**1** (Within goal so far)	
BLA Suppl. Prior Approval, Manufacturing.	**95**	**89**	**6** (Within goal so far)	**100%**

MDUFA Performance FY09 (cont.)

Application Type	Received		Within Goal		Goal Date Reached-% Comp.W/G
			Completed	Pending	
BLA/Efficacy Supplement Resubmissions	**29**	**Class* 1**	**29**	**0**	**100%**
		Class* 2	**0**	**0**	

Class 1: Review and act on within 2 months

Class 2: Review and act on within 6 months

510(k)s Received in FY09

(Oct 1, 08 – Sep 30, 09)

510(k) Type	OBRR	OCTGT	Total Number
Traditional	33	8	41
Special	8	1	9
Abbreviated	0	0	0
Total	**41**	**9**	**50**

CBER 510(k) Cycles

(SE/NSE only - From Receipt to Final Action

Submissions Received from October 1, 2008 to Sep 30, 2009 Actions through Oct 31, 2009)

510(k) Type	SE/NSEs*	Avg.	Under Review **	1st Cycle Completed***
Traditional	17	1.76	5	19
Special	9	1.11	0	0
Abbreviated	0	0	0	0
Total	26	1.54	5	19

*Completed Final Action. **Pending with no action yet.
***Pending with one cycle completed.

CBER 510(k) Times (All Decisions) FY09 Receipt Cohort (cont.)

(OCT 1, 08 – SEP 30, 09)

Time to Final Decision (SE/NSE/WTH/EXEMPTs/RTA)			
510(k) Type	Number	FDA Time (Days, Avg)	Total Time (Days, Avg)
Traditional	17	80.9	121.7
Special	9	27.2	29.7
Abbreviated	0	0	0
Total	**26**	**62.3**	**89.8**

MDUFA Performance FY09

Submissions Received from October 1, 2008 to Sep 30, 2009; Actions through Oct 31, 2009.

Application Type	Rec'd -Filed	Goal	Within Goal		Goal Date Reached - % Completed Within Goal
			Completed	Pending	
PMAs, Panel Track Suppls, PDPs, PMRs	**2**	**180 Days**	**1**	**1** (Within goal so far)	**100%**
180-Day Suppl.	**7**	**180 Days**	**3**	**4** (Within goal so far)	**100%**
Real Time Suppl.	**4**	**60 Days**	**4**		**100%**
510(k)s (Traditional, Special, Abbreviated)	**50**	**90 Days**	**26**	**24** (Within goal so far)	**100%**

Sponsor / Applicant Meetings with CBER

Meeting with CBER

- **CBER SOPP 8101.1: Scheduling and Conduct of Regulatory Review Meetings with Sponsors and Applicants (May 18, 2007)**

  www.fda.gov/cber/regsopp/81011.htm

FORMAL VS. INFORMAL MEETING

Formal Meeting (SOPP 8101.1):

- Either FDA or “firm” initiated
- Official request
- By Day 14(21) confirmation
- Meeting package
- Official Minutes by Day 30

FORMAL VS. INFORMAL MEETING

Informal Meeting (SOPP 8104)

- Either FDA or “firm” initiated
- “I need to clarify an issue”
- Whenever convenient
- Pre-meeting information encouraged
- Documented
- No minutes sent to “firm”
- Interactive Review (Devices)
- No MDUFA Milestones

MEETING TYPES

Type A

- A meeting which is necessary for an otherwise stalled drug development program to proceed (e.g., to address an issue that has resulted in a clinical hold or refuse to file, dispute resolution meetings, special protocol assessment meetings requested by the sponsor/applicant after FDA's evaluation of protocols in assessment letters).

MEETING TYPES

Type B

Type B meetings include the following: Pre-IND, End of Phase 1, End of Phase 2/Pre-Phase 3, or a Pre-BLA/NDA meeting. Each sponsor/applicant should usually request only one of each of these Type B meetings for each potential application.

Type C

Any other type of meeting (e.g., cost recovery, facility design, and general product issues meeting).

MEETING TYPES Timelines

Meeting Type	Confirmation (days)	Scheduled to Occur Within (days)	Receipt of Meeting Materials
A	14	30	T -2 weeks
B	21	60	T-4 weeks
C	21	75	T-4 weeks

Sponsor/Applicant RESPONSIBILITY

- Before requesting a meeting
  - Consult other sources of input
- Submit the request
  - Fax, email, electronic, hardcopy (not all options appropriate)

  Prepare a complete meeting request
- Prepare a comprehensive meeting packet
- Submit meeting packet on time

Pre-submission Meeting Statistics
Meetings Held in FY09

Type	Goal	Mtg Requests Rec'd	Actions Within Goal			Actions Overdue			Goal Date Reached % Completed Within Goal
			Completed	Pending	Total	Completed	Pending	Total	
A	Response	1	1	0	1	0	0	0	100%
	Held	1	0	1	1	0	0	0	0%
	Minutes	0	0	0	0	0	0	0	0%
B	Response	15	14	0	14	1	0	1	93%
	Held	13	8	4	12	0	1	1	89%
	Minutes	7	5	1	6	0	1	1	83%
C	Response	16	16	0	16	0	0	0	100%
	Held	16	13	2	15	1	0	1	93%
	Minutes	9	4	2	6	2	1	3	57%
Total	Response	32	31	0	31	1	0	1	97%
	Held	30	21	7	28	1	1	2	92%
	Minutes	16	9	3	12	2	2	4	71%

Significant Device Approvals in CBER

OBRR BLA and Major Supplement Approvals – FY09

Trade name/ **Proper Name**	**Indication for Use**	**MFTR**	**Approval Date**
BLAs			
Cobas TaqScreen MPX Test	In vitro test for the detection of HIV-1 Group M RNA, HIV-1 Group O RNA, HIV-2 RNA and HBV DNA in human plasma	Roche Molecular Systems, Inc.	12/30/08
ABBOTT PRISM HIV O Plus	To detect antibodies to HIV-1 (anti-HIV-1) Groups M and O and/or antibodies to HIV-2 (anti-HIV-2) in human serum and plasma specimens	Abbott Lab	9/18/09
BLA Supplements			
ORTHO T. cruzi ELISA Test System – Trypanosoma cruzi (T. cruzi) Whole Cell Lysate Antigen	Revise the package insert to include adding cadaveric specimens under the Intended Use section and changes to Specimen Collection and Preparation section by adding Serum Separator Tube (SST).	Ortho-Clinical Diag., Inc.	2/18/09

OBRR 510(k) Clearances – FY2009

Trade name **/ Proper Name**	**Indication for Use**	**MFTR**	**Approval Date**
TRUGENE HIV-1 Genotyping Kit and OpenGene DNA Sequencing System	Intend for use in detecting HIV genomic mutations that confer resistance to specific types of antiretroviral drugs, as an aid in monitoring and treating HIV infection. Operating System Upgrade to OS X v4.1	Siemens Medical Solutions Diagnostics	Traditional 10/20/08
TRUGENE HIV-1 Genotyping Kit and OpenGene DNA Sequencing System	Intended for use in detecting HIV genomic mutations that confer resistance to specific types of antiretroviral drugs, as an aid in monitoring and treating HIV infection. The modification to revise the GuideLines Rules within the software of the device from GuideLine Rules 12.0 to GuideLine Rules 14.0	Siemens Medical Solutions Diagnostics	Special 01/15/09
Ortho VERSEIA Pipetter as part of the Ortho Summit System	Pipetting of enzyme linked immunosorbent assays (ELISA), including licensed blood screening tests distributed by OCD.	Ortho-Clinical Diagnostics, Inc.	Traditional 05/27/09

OBRR PMA Approvals – FY2009

***Trade name*/ Proper Name**	**Indication for Use**	MFTR	**Approval Date**
Avioq HIV-1 Microelisa System	Is an enzyme linked immunosorbent assay (ELISA) for the qualitative detection of antibodies to HIV-1, in human specimens collected as serum, plasma, dried blood spots, or oral fluid specimens obtained with OraSure HIV-1 Oral Specimen Collection Device. The Avioq HIV-1 Microelisa System is intended for use as an aid in diagnosis of infection with HIV-1. It is not intended for use in screening blood donors.	Avioq, Inc.	Traditional 09/21/09

CBER Initiatives to meet MDUFA goals

Initiatives in CBER to Assure MDUFA II Goals are Met.

- Formalized training of all personnel in Managed Review Process, MDUFA and PDUFA Goals
- Daily briefings with management to discuss “coming due” submissions.
- Monthly application status review meetings with OBRR management to discuss show stoppers and review progress.
- Address “show stoppers” during the first half of the review cycle

Initiatives in CBER to Assure MDUFA II Goals are Met

Interactive Reviews

- Communication among review staff and with CDRH to assure consistency in reviews
- Encourage interactions between industry and CBER reviewers during the review cycle
  - Reduces number of requests for information near end of review cycle
  - E-mail, telephone, FAX

Initiatives in CBER to Assure MDUFA II Goals are Met

Interactive Review: Email Interactions with Sponsors/Applicants

- Secure email is preferred at CBER
- E-mail only from business email to business email
- E-mail should be exchanged with only those persons indicated by the sponsor/applicant
- Emails are accepted by CBER as regulatory documents only if agreed to (same as the FAX policy)
- Emails are not acceptable for original submissions

Initiatives in CBER to Assure MDUFA II Goals are Met

Guidance/Rules issued in FY08-09

- Issued nine guidance documents and
- Published three Rules.

Documents available on CBER's website at

- **www.fda.gov/cber/blood/bldpubs.htm**
- **www.fda.gov/cber/dap/devpubs.htm**

Selected Guidance Documents – OBRR

- Draft Guidance for Industry: Use of Serological Tests to Reduce the Risk of Transmission of Trypanosoma cruzi Infection in Whole Blood and Blood Components for Transfusion and Human Cells, Tissues, and Cellular and Tissue-Based Products

- Assay Migration Studies for In Vitro Diagnostic Devices

- Draft Guidance for Industry: Requalification Method for Reentry of Blood Donors Deferred Because of Reactive Test Results for Antibody to Hepatitis B Core Antigen (Anti-HBc)

- Draft Guidance for Industry: Use of Nucleic Acid Tests to Reduce the Risk of Transmission of West Nile Virus from Donors of Whole Blood and Blood Components Intended for Transfusion and Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)

Joint CBER/CDRH Guidance Documents FY08-09

- Interactive Review for Medical Device Submissions: 510(k)s, Original PMAs, PMA Supplements, Original BLAs, and BLA Supplements (Draft) (2/28/08)
- In Vitro Diagnostic (IVD) Device Studies – Frequently Asked Questions (Draft) (10/25/07)
- Expedited Review of Premarket Submissions for Devices (2/29/08)

OBRR Scientific Workshops - FY09

- Approaches to Reduce the Risk of Transfusion Transmitted Babesiosis in the United States

- Blood Establishment Computer Software: Understanding What to Include in a 510(k) Submission; Public Workshop,

Current Device Challenges

Current Device Challenges

- **Emerging threats to blood safety**
  - Guidance documents and donor deferral
- **Counterterrorism**
  - Guidance documents and detection technologies for BT agents
- Development of criteria for approval of molecular testing for RBC genotyping
- Development of Criteria for Approval of an Over-the-Counter Home Use HIV Test Kit

How to Obtain Additional Information on MDUFA - General

- **Visit the MDUFA website for general guidance, reference materials, and new information:**

  www.fda.gov/cdrh/mdufa

- **Send an e-mail to:**

  MDUFA@cdrh.fda.gov

How to Obtain Additional Information on MDUFMA - CBER

- **Check CBER Website:**

  www.fda.gov/cber/devices/mdufa

- **E-mail CBER:**
  - **Manufacturers:**

    matt@cber.fda.gov
  - **Consumers, health care professionals:**

    octma@cber.fda.gov