Overview of the Office of Blood Research and Review
Device Regulation

Anne Eder, M.D., Ph.D.
Office of Blood Research and Review
CBER
Overview:

- Office of Blood Research and Review (OBRR)
- Regulation of devices in OBRR
- Guidance, Advisory Committees, Standards
- What’s new? Resources for developers
- Today’s meeting – Outline
Overview:

- **Office of Blood Research and Review (OBRR)**
- Regulation of devices in OBRR
- Guidance, Advisory Committees, Standards
- What’s new? Resources for developers
- Today’s meeting – Outline
OBRR Organizational Chart

Nicole Verdun, MD
Director

Anne Eder, MD, PhD
Deputy Director (Acting)

Office of the Director,
policy, research oversight,
program management and
administrative staff

Hira Nakhasi, PhD
Director
Division of Emerging and
Transfusion Transmitted
Diseases (DETTD)

Orieji Illoh, MD
Director
Division of Blood Components
and Devices (DBCD)

J. Peyton Hobson, PhD
Deputy Director, DETTD

Wendy Paul, MD
Deputy Director, DBCD

Review (1) and Research (3)
Branches

Review (3) and Research (2)
Branches
Devices Reviewed by OBRR

**DETTD**
- Blood donor screening and supplemental tests
  - Babesia, Chagas, CMV, HBsAg, HBc, anti-HBV, HCV, HIV, Syphilis, WNV, Zika
- Source Plasma donor screening tests
- Retroviral diagnostic tests (HIV/HTLV)
  - Diagnosis
  - Monitoring
  - Supplemental

**DBCD**
- Blood grouping reagents
- Reagent Red Blood Cells
- Anti-Human Globulin
- Automated immunohematology analyzers
- Molecular erythrocyte typing tests
- HLA, HNA, HPA - antigen and antibody test kits
- Bacterial detection tests
Offices that Review or Contribute to OBRR Submissions

- Office of Biostatistics and Epidemiology (OBE)
- Office of Compliance and Biologics Quality (OCBQ)
  Manufacturing, CMC, Quality Systems
  Lot release
  Compliance, adverse event reporting, labeling
  Inspections
- Office of Tissues and Advanced Therapy (OTAT)
  Cadaveric claims (heart beating or non-heart beating)
- Office of Product Evaluation and Quality (OPEQ), OHT7 (formerly OIR), Center for Devices and Radiological Health (CDRH): CLIA categorization
Overview:

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- **Regulation of devices in OBRR**
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In Vitro Diagnostics (IVDs) are:

- Reagents, instruments, and systems used in diagnosis of disease or other conditions...in order to cure, mitigate, treat, or prevent disease.
- Intended for use in the collection, preparation, and examination of specimens taken from the human body.
- Medical devices per 201(h) of Food, Drug, & Cosmetic (FD&C) Act
- May also be biologic products subject to section 351 of Public Health Services Act

[21 CFR 809.3]
Governing Acts and Regulations

Most OBRR devices are regulated under two acts and two sets of regulations

• Public Health Service Act (42 U.S.C. sec. 351):
  – Blood and blood products are therapeutic biological products
  – Tests used to ensure that blood is pure, potent, safe, effective
  – Regulated under 21 CFR 600s

• Food, Drug and Cosmetics Act (21 U.S.C. sec. 301):
  – In vitro diagnostic devices
  – Regulated under 21 CFR 800s
Device Review is Based on the Intended Use

Intended Use (IU) includes:

• What indication?
• What population?
• What samples?
• What mode of operation?
• What other clinical information?
ACME® WNV test for use on Acme® 103i Systems, is a qualitative in vitro nucleic acid screening test for the direct detection of West Nile virus (WNV) RNA in human plasma.

This test is intended for use to screen donor samples for WNV RNA in plasma samples from individual human donors, including donors of whole blood and blood components, as well as other living donors.

This test is not intended for use as an aid in diagnosis of WNV infection.
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Basis of Pre-market Device Review: Safety and Effectiveness

Safety

...the probable benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh any probable risks. [21 CFR 860.7(d)(1)]

Effectiveness

...the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results. [21 CFR 860.7(e)(1)]
Safety/Risks to Health

• A false negative test result:
  – Wrong result in compatibility testing: Transfusion of incompatible blood to a patient causing hemolytic transfusion reaction
  – Negative result in infectious disease testing: Transfusion of blood from infected donor causing disease in recipient

• A false positive result:
  – RhD+ result in RhD-negative pregnant woman resulting in missing RhD immunoglobulin shot and possible hemolytic disease of fetus and newborn
  – Positive for infectious disease: unnecessary follow-up testing, additional diagnostic studies, and psychological stress to the donor
## IVD Submission Types

<table>
<thead>
<tr>
<th></th>
<th>Class I</th>
<th>Class II</th>
<th>Class III</th>
<th>BLA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Decision</strong></td>
<td>Marketed</td>
<td>510(k) cleared (SE/NSE)</td>
<td>De Novo Granted</td>
<td>PMA approved</td>
</tr>
<tr>
<td><strong>Marketing</strong></td>
<td>Registered and listed,</td>
<td>Predicate Device</td>
<td>Safety and effectiveness</td>
<td>Safety and</td>
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<tr>
<td><strong>Authorization</strong></td>
<td>cGMP</td>
<td>Substantial equivalence</td>
<td>effectiveness</td>
<td>effectiveness</td>
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<tr>
<td><strong>Standard</strong></td>
<td></td>
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<td>Post-market</td>
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<tr>
<td><strong>Interactions</strong></td>
<td>NA</td>
<td>Interactive Review (IR),</td>
<td>IR, AI</td>
<td>IR, Complete</td>
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<td>Additional information (AI)</td>
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<td>response (CR)</td>
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<td>request</td>
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<tr>
<td><strong>Time to decision</strong></td>
<td>NA</td>
<td>90 days</td>
<td>150 days</td>
<td>180 days</td>
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<td><strong>(FDA days)</strong></td>
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<td>6 months (priority)</td>
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BIMO: Bioresearch Monitoring
# IVD Submission Types

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## Change Management for Marketed Devices

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<tr>
<th></th>
<th>510(k)a</th>
<th>PMAb</th>
<th>BLAc</th>
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<tbody>
<tr>
<td><strong>Major changes</strong></td>
<td>New 510(k)</td>
<td>180-day, Panel track, Manufacturing site change</td>
<td>Comparability, efficacy, Labeling, Manufacturing (PAS)</td>
</tr>
<tr>
<td>May effect safety and effectiveness (S&amp;E)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Require pre-approval</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Moderate changes</strong></td>
<td>Special 510(k), abbreviated 510(k)</td>
<td>30-day notice, Real time, Labeling, CBE</td>
<td>CBE, CBE-30</td>
</tr>
<tr>
<td>Little effect on S&amp;E</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Notification</td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Minor changes</strong></td>
<td>CLIA categorization (CR)</td>
<td>Annual report</td>
<td>Annual report</td>
</tr>
<tr>
<td>No effect on S&amp;E</td>
<td></td>
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### References

a[https://www.fda.gov/media/99812/download](https://www.fda.gov/media/99812/download)
## Representative Changes

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<thead>
<tr>
<th></th>
<th>510(k)</th>
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<th>BLA</th>
</tr>
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<tbody>
<tr>
<td><strong>Major</strong></td>
<td>• New antibody</td>
<td>• New antibody</td>
<td>• New key reagents</td>
</tr>
<tr>
<td></td>
<td>• Remove limitation</td>
<td>• Mfg site change</td>
<td>• Mfg site change</td>
</tr>
<tr>
<td>New 510(k),  180-day, panel track</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Moderate</strong></td>
<td>• Add clinical data</td>
<td>• Add QC step</td>
<td>• Automate process</td>
</tr>
<tr>
<td>30DN, CBE, CBE-30, special 510(k)</td>
<td>• Update reference range</td>
<td>• New cleaning process</td>
<td>• Labeling changes</td>
</tr>
<tr>
<td><strong>Minor</strong></td>
<td>• Add a limitation</td>
<td>• Extend stability per approved protocol</td>
<td>• Add timepoints to stability protocol</td>
</tr>
<tr>
<td>CLIA categorization, Annual report</td>
<td>• Clarify instructions</td>
<td>• Tighten specifications</td>
<td></td>
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</tbody>
</table>

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Search for FDA Guidance Documents

The table below lists all official FDA Guidance Documents and other regulatory guidance. You can search for documents using key words, and you can narrow or filter your results by product, date issued, FDA organizational unit, type of document, subject, draft or final status, and comment period.

This feature is provided to give a convenient way to search for all FDA guidance documents from a single location.

If you cannot find the document you’re looking for here, you can browse separate collections of guidance documents by topic.

Browse Guidance Documents By Topic

- General and Cross-Cutting Topics
- Advisory Committees
- Animal and Veterinary
- Biologics
- Clinical Trials
- Import and Export Guidance Documents
- International Council for Harmonisation (ICH) Guidance Documents
- Combination Products Guidance Documents
- Advisory Committee Guidance Documents
- Clinical Trials Guidance Documents
- Search General and Cross-Cutting Topics Guidance Documents
- Search for FDA Guidance Documents

https://www.fda.gov/regulatory-information/search-fda-guidance-documents#guidancesearch
Least Burdensome Guidance

Finalized Feb. 2019

“Least burdensome”: the minimum amount of information necessary to adequately address a relevant regulatory question or issue through the most efficient manner at the right time.
The Q-submission Program

Finalized May 2019

Changes to timelines
Guidances Applicable to Devices

- Device guidances
  https://www.fda.gov/vaccines-blood-biologics/general-biologics-guidances/devices-guidances

- Application submission guidances
  https://www.fda.gov/vaccines-blood-biologics/general-biologics-guidances/application-submissions-guidances

- MDUFA IV performance goals
  https://www.fda.gov/media/102699/download
Blood Products Advisory Committee (BPAC)

- FDA’s Advisory Committees provide independent advice from outside experts on relevant issues.

- Composition
  - Voting: Authorities knowledgeable in blood banking, medicine, immunology, epidemiology other professionals.
  - Non-voting: Industry representative, consumer rep (device panels).

- Meet regularly to provide advice on issues of importance to FDA/CBER/OBRR
  - Specific device approvals as needed.
  - Classification, reclassification of devices.
  - Pathogen reduction of blood components.
Recognized Consensus Standards

• Standards produced by experts to present best practices for specific aspects of validation

• FDA recognizes certain standards

FDA Standards Website: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm
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What’s New? Product Codes for BLA Devices

- Random three-letter codes used for
  - Adverse event reporting
  - Searching databases
- Manufacturers will receive letters with new product codes (procodes)
Resources for Sponsors

• Reagents
  – Reference panels for development
  – Analyte reference standards for validation
  – DNA reference samples

• Workshops
  – Disease-specific: Babesia spp.
  – Technology-specific: Next-Gen Sequencing
  – Education and Outreach: IVD roundtable
CBER Office of Communications, Outreach & Development

Manufacturer’s Assistance and Technical Training Branch (MATTB)

– How to submit-eCopy, etc.
– Registration and listing
– Email
– User fees

Email: Industry.biologics@fda.hhs.gov
Phone: 240-402-8020 or 1800-835-4709
Website: https://www.fda.gov/vaccines-blood-biologics/industry-biologics/manufacturers-assistance-and-technical-training-branch-mattb
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Elements Covered in the Workshop

Pre-Market: Common Elements

PreSubmission
Iwona Fijalkowska

IND/IDE
Caren Chancey

CMC
Rana Nagarkatti
Lori Peters

Software
Lisa Simone

Lot Release
Kori Francis

BIMO
Bhanu Kannan

Pre-Licensure Inspection
Nicole Li

Not every element applies to every device
Elements Covered in the Workshop

Pre-Market: Indication-Specific Considerations

- **Infectious Disease Screening**
  - Analytical
    - Krishna Ketha
  - Clinical
    - Babita Mahajan
  - Cadaveric Claims
    - Brychan Clark

- **Donor-Recipient Compatibility**
  - Immunohematology
    - Kimberly Bigler
    - Annette Ragosta
  - Molecular Tests
    - Zhugong (Jason) Liu

Not every element applies to every device
Elements Covered in the Workshop

Post Market

CLIA Categorization
Peter Tobin

Biological Product Deviation Reporting
Sharon O’Callaghan

Medical Device Reporting
Bima Patel

Not every element applies to every device
Thank you!
Anne Eder
Anne.Eder@fda.hhs.gov